MONASH University

Innovation and Evolution in Hospital Pharmacy Practice

A Collection of Published Works

1973 to 2018

Ian Larmour

Bachelor of Pharmacy, Monash University, 1969

Fellow (by examination), Society of Hospital Pharmacists of Australia, 1975

Master of Science Degree (Pharmacology),

Monash University, 1986

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Dedication

The Thesis is dedicated to my wonderful wife, Laurise Zelle, and my two fantastic sons, Luke Ian and Paul John.
Your support and encouragement over my career have provided me with the inspiration and dedication needed to write this Thesis. I love all of you so very much.

Table of Contents

Summary of the Development of the Work

The Thesis examines Innovation and Evolution in Victorian Hospital Pharmacy Practice, as illustrated by the 28 publications and related information produced from 1973 to 2018 that comprise the Thesis. The overall underlying theme of the Thesis is patient medication safety, including promoting the efficient use of medications to enable resources to be allocated to the development of medication safety services. A variety of research methodologies, both quantitative and qualitative, have been applied in these publications, with the method chosen reflecting the nature of the subject under consideration.

This work is presented in Five Chapters with the papers being listed chronologically under each Chapter`s title.

Declaration for Higher Doctorate submitted work

Declaration

This thesis is an original work of my research and contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

Signature: ……

Print Name: **IAN LARMOUR**

Date: …….

Thesis including published works declaration

I hereby declare that this thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

This thesis includes 28 original papers published in peer reviewed journals. The core theme of the thesis is Innovation and Evolution in Hospital Pharmacy Practice. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the student, working within the Medical and Health Sciences faculty under the supervision of Peter Ebeling.

The inclusion of co-authors reflects the fact that the work came from active collaboration between researchers and acknowledges input into team-based research.

In the case of chapters 1 – 5 my contribution to the work involved the following:

Thesis Chapter	Publication Title	Status	Nature and % of student contribution	Co-author name(s) Nature and % of Co-author's contribution	Co-author(s), Monash student Y/N
1	Clinical Activities of Ward Pharmacists - A Five Year Perspective - Part 1 - Guidelines of Practice	Published	100%	-	-
1	Clinical Activities of Ward Pharmacists - A Five Year Perspective - Part 2 - The Importance of the Pharmacists Role	Published	100%	-	-
1	Clinical Ward Pharmacy Quality Assurance	Published	90% Refer to Declaration Summary – Category 1	1) Allinson Y (4%) 2) Manser A (3%) 3) Spalding G (1%) 4) Brett K (1%) 5) Swan S (1%)	N N N N N
1	Clinical Ward Pharmacy Survey - Victorian Hospitals 1982	Published	90% Refer to Declaration Summary – Category 1	1) Allinson Y (4%) 2) Manser A (3%) 3) Spalding G (1%) 4) Brett K (1%) 5) Swan S (1%)	N N N N N
1	The Application of Peer Review to Clinical Pharmacy	Published	90% Refer to Declaration Summary – Category 2	1) Allinson Y (6%) 2) Dolphin R (2%) 3) Spalding G (2%)	N N N
1	My Medication, Your Information	Published	100%	-	-
1	Policy Guidelines for Quality Assurance in Hospital Pharmacy Practice	Published	90% Refer to Declaration Summary – Category 1	1) Allinson Y (6%) 2) Andrews J (1%) 3) Brice R (1%) 4) Jackson J (1%) 5) Reed B (1%)	N N N N N
1	Report of the Quality Assurance Committee of Speciality Practice	Published	100%	-	-
1	Survive and Thrive with Quality Assurance, Quality Assurance COSP Workshop Report	Published	100%	-	-
1	Performance Indicators in Hospital Pharmacy Practice	Published	100%	-	-
1	Spend more on pharmacists and less on drugs - Letter to the Editor	Published	80% Refer to Declaration Summary – Category 1	Thomson W (20%) – collected and provided data	N
1	Hospital Pharmacists and the Challenge of Quality	Published	90% Refer to Declaration Summary – Category 1	1) Creber E (5%) 2) Manser A (3%) 3) Wong E (1%) 4) Wood M (1%)	N N N N
1	Impact of a surgical preadmission clinic pharmacist on the quality of medication management from preadmission to discharge: A randomised controlled trial	Published	33% Refer to Declaration Summary – Category 3	1) George L (32%) 2) Senturk-Raif R (32%) 3) Hodgkinson M (2%) 4) Emmerton M (1%)	N N N N
2	A prospective Study of Hospital Admission due to Drug Reactions	Published	85% Refer to Declaration Summary – Category 1	1) Dolphin R (1%) 2) Baxter H (2%) 3) Morrison S (1%) 4) Hooke D (1%) 5) McGrath B (10%)	N N N N N

Thesis Chapter	Publication Title	Status	Nature and % of student contribution	Co-author name(s) Nature and % of Co-author's contribution	Co-author(s), Monash student Y/N
2	Identification of Adverse Drug Reactions Using the ICD-IO Australian Modification Clinical Coding Surveillance	Published	50% Refer to Declaration Summary – Category 3	1) Hodgkinson M (40%) 2) Dirnbauer N (10%)	N N
3	The impact of an integrated electronic medication prescribing and dispensing system on prescribing and dispensing errors: a before and after study	Published	50% Refer to Declaration Summary – Category 3	1) Hodgkinson M (45%) 2) Lin S (1%) 3) Stormont A (4%)	N N N
3	Cultural Change and Drug Expenditure	Published	95% Refer to Declaration Summary – Category 1	Creber E (5%)	N
3	Introduction of Pharmaceutical Benefits Scheme Reforms at Three Victorian Public Health Services	Published	50% Refer to Declaration Summary – Category 1	1) Thomson W (30%) 2) Tsui M (10%) 3) Weeks G (10%)	N N N
3	A therapeutic equivalence program: evidence-based promotion of more efficient use of medicines	Published	80% Refer to Declaration Summary – Category 1	1) Pignataro S (5%) 2) Barned K (5%) 3) Mantas S (5%) 4) Korman M (5%)	N N N N
3	Therapeutic Equivalence Program: continued economic Benefits in the context of rising costs and increased demand	Published	55% Refer to Declaration Summary – Category 2	Chynoweth T (45%)	N
3	Mathematical Representation of Pharmacy Outpatient Workloads	Published	100%	-	-
4	Education Outreach to the Community: Does Hospital Pharmacy Have a Role	Published	85% Refer to Declaration Summary – Category 2	1) Alvarez S (6%) 2) Tapley N (5%) 3) Buick M (1%) 4) Greene L (1%) 5) Hines L (1%) 6) Davies J (1%)	N N N N N N
4	Patient and General Practitioner Perspectives of the Hospital Outreach Medication Review Service at Monash Health	Published	48% Refer to Declaration Summary – Category 3	1) Hanna M (48%) 2) Wilson S (3%) 3) O'Leary K (1%)	N N N
4	The Impact of a Hospital Outreach Medication Review Service on Hospital Readmission and Emergency Department Attendances	Published	48% Refer to Declaration Summary – Category 3	1) Hanna M (48%) 2) Wilson S (3%) 3) O'Leary K (1%)	N N N
5	Intermittent Subcutaneous Apomorphine Injection Treatment for Parkinsonian Motor Oscillations	Published	20% Refer to Declaration Summary – Category 4	1) Kempster P (60%) 2) Iansek R (20%)	N N
5	Chemotherapy delays progression of motor neuron disease in the SOD1G93A transgenic mouse	Published	5% Refer to Declaration Summary – Category 4	1) Bruce K M (45%) 2) Narayan K (25%) 3) Kong H C (5%) 4) Lopes EC (5%) 5) Turner BJ (5%) 6) Bertram JF (5%) 7) Cheema SSv (5%)	N N N N N N N

Thesis Chapter	Publication Title	Status	Nature and % of student contribution	Co-author name(s) Nature and % of Co-author's contribution	Co-author(s), Monash student Y/N
5	Assessment of aminoglycoside dosing and estimated glomerular filtrate rate in determining gentamicin and tobramycin area under the curve and clearance	Published	20% Refer to Declaration Summary – Category 5	1) Lim A (65%) 2) Mathanas-enarajah G (15%)	N N
5	Deferasirox at Therapeutic Doses is Associated with Dose-Dependent Hypercalciuria	Published	5% Refer to Declaration Summary – Category 5	1) Wong P (60%) 2) Polkinghorne K (5%) 3) Kerr P (5%) 4) Doery J (5%) 5) Gillespie M (5%) 6) Fuller P (5%) 7) Bowden D (5%) 8) Milat F (5%)	N N N N N N N N

I have not renumbered sections of submitted or published papers in order to generate a consistent presentation within the thesis.

Student name: IAN LARMOUR

Student signature: **Date:**

I hereby certify that the above declaration correctly reflects the nature and extent of the student's and co-authors' contributions to this work. In instances where I am not the responsible author, I have consulted with the responsible author to agree on the respective contributions of the authors.

Main Supervisor name: PETER EBELING

Main Supervisor signature: **Date:**

Acknowledgements

I wish to thank the following people for their assistance in the submission of this Thesis.

Dr Karen McConalogue, Faculty of Pharmacy and Pharmaceutical Sciences, Monash University, for her outstanding guidance, support, advice and encouragement. In particular for investigating the availability of this type of Thesis at Monash University.

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Kangi Donaldson, Emma Bryme and Cassandra Meagher, Research Office, Faculty of Medicine, Nursing and Health Sciences, for their outstanding assistance in navigating the various administrative requirements for this Thesis.

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I would also like to sincerely thank all my co-authors for their assistance, guidance and advice. I particular, I thank them for agreeing to work with me on the important and valuable projects covered in the papers included in this Thesis.

Declaration Summary

There are 28 original papers published in peer reviewed journals. Of these, there are 4 papers in which I am the sole author and a further 23 papers and one letter, in which there are co-authors. There is also one unpublished document that I produced on behalf of the Society of Hospital Pharmacists of Australia (SHPA) for the Conference of Heads of Australian Pharmacy Schools (CHAPS) in 1990. The Executive Summary of this document is listed as an Appendix at the end of the Thesis.

The core theme of this work is Innovation and Evolution in Victorian Hospital Pharmacy Practice, with an underlying focus on medication safety.

In order to efficiently and clearly explain my level of contribution in each of the co-authored papers, I have defined five levels or categories of involvement. I have done this because my involvement in the various papers are often very similar and to list this involvement for each of the papers will involve considerable detail and tedious duplication and this detail may also make it difficult to follow.

On examination of the various papers I have determined that my involvement falls into five categories and I have listed the appropriate Category Level against each of the acknowledged papers on the list below.

The details on each of the five Categories of Involvement are as follows.

Category One

Explanation

These are papers in which I am listed as the first author with a number of co-authors.

Level of Involvement

- I wrote the paper with comments and review provide by the other authors.

- I played a leading role in providing in providing ideas and input into the development of the research concept and in generating and synthesis of scientific questions, including the design and structure of the research and associated processes.

- Analysis and collection of data or the supervision of data collection.

- Organising and facilitating the research project through the provision of funding and support.

- Supervision and guidance of the research project.

Category Two

Explanation

These are papers in which I am not listed as first author, but nevertheless, I was the lead author. In these cases, at the time of publication, I decided to list my staff member, who was involved in the project, as first author in order to encourage their ongoing interest in research. In one case I decided to allocate authors in alphabetical order. In technical terms of contribution and standard University practice, I believe I should be considered as either the last or first author of these papers.

Level of Involvement

- I wrote the paper with comments and review provided by the other authors.

- I played a leading role in providing ideas and input into the development of the research concept and in generating and synthesis of the scientific questions, including the design and structure of the research and associated processes.

- Analysis and collection of data or the supervision of data collection.

- Organising and facilitating the research project through the provision of funding and support.

- Supervision and guidance of the research project.

Category Three

Explanation

These are papers in which I have been extremely closely involved and by standard University practice I should have been listed as last or supervising author. Unfortunately, I was not aware of this University practice when the papers were written and published.

Level of Involvement

- I significantly assisted in the writing and review of these papers, in close co-operation with the first author.

- I played a leading role in providing ideas and input into the development of the research concept and in the generation and synthesis of scientific questions, including the design and structure of the research and associated processes.

- I played a leading role in the analysis of the data and the supervision of the data collection.

- Organising and facilitating the research project through the provision of funding and support.

- Supervision and guidance of the research projects.

Category Four

Explanation

These are papers in which I contributed to as a collaborative member of the research tea**m.**

Level of Involvement

- Review and input into the writing of the paper in collaborative with the team of authors.

- Review and input into the data analysis in collaboration with the team of authors.

- Provided data and advice on pharmacological matters, dosage advice, pharmacokinetics, medication side effects, formulation aspects and other relevant advice, depending on the project.

- Providing general input into the design, ideas and concept of the research project.

- Facilitated and organised the manufacture and/or preparation of the research product used in the research project.
  e.g. Apomorphine injection.

Category Five

Explanation

These are papers in which I contributed as a collaborative member as part of a research team.

Level of Contribution

- Review and input into the writing of the paper in collaboration with the team of authors.

- Review and input into the data analysis in collaboration with the team of authors.

- Providing data and advice on pharmacological matters, dosage advice, pharmacokinetics, formulation aspects, medication side effects and other relevant advice, depending on the project.

- Provided general input into the design, ideas and concept of the research project.

Contribution to Co-Authored Papers

In the case of Chapters One to Five, my contribution to the work involved the following:

Chapter	Publication title	Nature and extent of candidate's contribution
One	3. Ward Pharmacy Quality Assurance Larmour et al (1984)	Category One
One	4. Clinical Ward Pharmacy Survey – Victorian Hospitals 1982 Larmour et al (1984)	Category One
One	5. Application of Peer Review to Clinical Pharmacy Allinson et al (1985)	Category Two
One	7. Policy Guidelines for Quality Assurance in Hospital Pharmacy Practice Larmour et al (1988)	Category One
One	8. Report of the Quality Assurance Committee of Speciality Practice Larmour et al (1992)	Category One
One	9. Survive and Thrive with Quality Assurance Larmour et al (1993)	Category One
One	10.Performance Indicators in Hospital Pharmacy Practice Larmour et al (1996)	Category One

One	11. Spend more on pharmacists and less on drugs Larmour et al (1997)	Category One
One	12.Hospital Pharmacists and the Challenge of Quality Larmour et al (1998)	Category One
One	13. Impact of a surgical preadmission clinic pharmacist on the quality of medication management from preadmission to discharge: A randomised controlled trial George et al (2011)	Category Three
Two	14. A prospective Study of Hospital Admissions due to Drug Reactions Larmour et al (1991)	Category One
Two	15. Identification of Adverse Drug Reactions Using the ICD-10 Australian Modification Clinical Coding Surveillance Hodgkinson et al (2009)	Category Three
Three	16.The impact of an integrated electronic medication prescribing and dispensing system on prescribing and dispensing errors: a before and after study Hodgkinson et al (2017)	Category Three

Three	17. Cultural Change and Drug Expenditure Larmour et al (1995)	Category One
Three	18. Introduction of Pharmaceutical Benefits Scheme Reforms at Three Victorian Public Health Services Larmour et al (2016)	Category One
Three	19. A therapeutic equivalence program: evidence-based promotion of more efficient use of medicines Larmour et al (2011)	Category One
Three	20. Therapeutic Equivalence Program: continued economic benefits in the context of rising costs and increased demands Chynoweth and Larmour	Category Two
Four	22. Education Outreach to the Community: Does Hospital Pharmacy Have a Role Alvarez et al (2001)	Category Two
Four	23. Patient and General Practitioner Perspectives of the Hospital Outreach Medication Review Service at Monash Health Hanna et al (2015)	Category Three

Four	24. The impact of a Hospital Outreach Medication Review Service on Hospital Readmission and Emergency Department Attendances Hanna et al (2016)	Category Three
Five	25. Intermittent Subcutaneous Apomorphine Injection Treatment for Parkinsonian Oscillations Kempster et al (1991)	Category Four
Five	26. Chemotherapy delays progression of motor neuron disease in the SOD1G93A transgenic mouse Bruce et al (2004)	Category Four
Five	27. Assessment of aminoglycoside dosing and estimated glomerular filtrate rate in determining gentamicin tobramycin area under the curve and clearance Lim et al (2015)	Category Five
Five	28. Deferasirox at Therapeutic Doses is Associated with Dose-Dependent Hypercalciuria Wong et al (2016)	Category Five

Chapter One

(Papers 1 – 13)

Examination the Emergence of Clinical Pharmacy Practice in Victorian Public Hospitals.

In this Chapter, the Thesis examines the emergence and development of Clinical Pharmacy Practice in Victorian Public Hospitals and considers the influence of this work in the wider arena, in particular Australian public hospitals. The concept of Clinical Pharmacy services emerged in Victorian Public Hospitals in the mid 1970s. The initial focus was on Clinical Pharmacy in the hospital wards, but this role has since evolved into a variety of settings, especially various types of outpatient clinics, emergency departments and, more recently, a number of other roles such as, Public Hospital Pharmacy Department outreach services, where Clinical Pharmacy services are provided to patients in their own homes.

The basis for this interest in Clinical Pharmacy services was founded on two factors:

1. A feeling that the skills of pharmacists were generally very much underutilised, as evidenced by the limited scope of the pharmacist`s practice role at that time.

2. The increased complexity of medication therapy due to the rapid growth in the number and types of new medications available, which in turn, created greater pressure on prescribers and increased the associated risk of medication errors. This then led to the opportunity for pharmacists to provide assistance in medication management and safety.

While there was considerable excitement at the development of Clinical Pharmacy services in Victorian Public Hospitals, there was a distinct lack of clarity on what the service involved. The management at Prince Henry`s Hospital (PHH) in Melbourne were very supportive of the development of these services and in my role, at that time, as Deputy Director of Pharmacy, I was encouraged to foster the clarification of

this clinical role. Part of my duties included working on one ward, initially the Neurology Ward and, over time, a variety of general medical wards. I also worked in the PHH Epilepsy Clinic for several years. This direct clinical practice provided an excellent background learning opportunity on which I was able to develop a model of clinical practice that could be followed or considered by others. I was also able to build on my experience on ward rounds in my time as a pharmacist at the 2 Military Hospital in Sydney in 1970-71.

The review of the patient`s medication administration chart was the starting point in specifying ward clinical pharmacy services, but it very quickly became clear that there were many other aspects that needed to be considered. It also became very clear that the academic training of pharmacists, while excellent in terms of pharmacology and pharmaceutics, needed to change if pharmacists were going to be able to make a meaningful contribution to patient medication safety. It became clear that significant details needed to be included in the specifications of the clinical role to enable pharmacy academia, as well as the ward clinical pharmacists, to understand the changes in training that would be needed in the future.

Subsequently, using the clinical experience and skills that I developed over five years and through an extensive review of the literature relating to various aspects of the clinical role, I produced two papers to clarify and specify the roles that a ward clinical pharmacist could undertake (Larmour 1980).

In the first paper, five types of tasks are specified, with a sixth being listed in the second paper. Considerable detail is included, since at that time many of these details may not have been readily known by many pharmacists. The paper also introduced the concept of using high-risk diseases and high-risk medication as an alert to the clinical pharmacist that patients with these high-risk factors needed special attention.

An algorithm to provide guidelines on how the various roles and decision-making steps fitted together, was developed and included. Both papers aimed to encourage and empower clinical pharmacists to document and report Adverse Drug Reactions.

In paper two, greater detail was provided on the day to day roles of clinical pharmacists. This paper also includes details on the clinical workload and activity of a ward pharmacist in a 22 bed medical ward that I collected over a 30 day survey period. Details on various surveys, like the monitoring of gentamicin, are discussed and the concept of drug utilisation review was introduced.

Clearly defining the scope of practice of a new and evolving professional practice is always a primary task. However, equally important are the systems and concepts that need to be developed to meaningfully evaluate the skills and performance of clinical pharmacists in this new role. Due to my obvious interest in Clinical Pharmacy Practice, I was asked by the Victorian Branch of the Society of Hospital Pharmacist (SHPA) to form a small team to develop systems and methods to promote and ensure the Quality Assurance of Clinical Pharmacy Practice in public hospital wards (Larmour 1984).

Checking procedures to ensure careful and accurate medication dispensing are well established in the practice of the Pharmacy profession. However, clinical pharmacy practices presented a new challenge, because:

1. It is a service rather than an end point product and has few assessable end points and

2. Ward clinical pharmacists work in an autonomous manner outside of the Pharmacy Department.

Therefore, new and modified approaches were needed. In the deliberations on this aspect, it was considered that there were two fundamental principles that needed to be addressed in any Quality Assurance Program for Clinical Pharmacists:

1. Pharmacists needed to be adequately educated and trained to carry out the tasks that they were expected to perform.

2. Pharmacist needed to be fully appraised on the duties required and the standard of performance expected.

A key focus of the paper was to discuss the various forms of education that could be provided. In particular, considerable attention is given to the undergraduate education of pharmacists. The aim was also to provide guidelines on the skills and knowledge that clinical pharmacists needed to possess, in the hope that this would also be of benefit to academic pharmacy when developing their teaching curriculum. A key point in this paper was to encourage the joint clinical training of undergraduate pharmacists in a clinical setting, in particular, working in hospital wards.

But realising that changes in academia move slowly, considerable attention was given to training options that could be used by Hospital Pharmacy Departments and the SHPA to help overcome many of the deficiencies in the training of pharmacists to perform the role of a clinical pharmacist.

The most important concept introduced was that of “Peer Review”, in a model suitable for clinical pharmacists.

Extensive guidelines were provided on the need for communication, transparency and support practices to effectively engage clinical pharmacists in a meaningful manner. The underlying focus was that Peer Review was not to be an arbitrary administrative process, but rather a helpful supportive process to encourage pharmacists to achieve their full potential through continuous improvement. A key element of Peer Review was the concept of ward visits, were the clinical pharmacist being reviewed attended the ward with a Peer Review Committee (PRC) member, to jointly review aspects of practice, according to a pre-set check list. Importantly, the report and comments needed to be agreed and understood by both pharmacists. Not surprisingly, this concept, at this time, created a degree of resistance to change, therefore considerable effort was made to present the concept as a friendly supportive practice.

Concurrently, it was felt that a survey of the extent of Clinical Pharmacy Practice in Victorian Public Hospitals, at that time, was required to gain knowledge on the “State of the Art” (Larmour et al 1984).

A questionnaire was subsequently sent to 52 Victoria Hospitals who were thought to have a Pharmacy Department.

This achieved a 75% response rate, with 35 hospitals claiming they provided a Clinical Pharmacy Service. Pleasingly there was a response from all (24) of the larger hospitals. Of the 11,679 beds covered by the 35 hospitals, 66% (7756) of beds were covered by a clinical pharmacy service. However, only 33% (13) of hospitals indicated that their clinical pharmacy service was provided to all their beds. The hours spent working in the wards varied significantly, which perhaps reflected the scope of the service provided and, in particular the complexity of the patient`s condition and their medication requirements. At the time of the survey it was reported that there were 102 clinical pharmacist positions (covered by 172 personnel) in Victoria and 87% of these pharmacists believed they required additional training.

The most popular place to gain this training was thought to be Pharmacy Department in-service training and an upgrading of their hospital`s Pharmacy Intern (Traineeship) program. Various academic training options were also thought to be important, especially that the clinical training and experience required could only be realistically learnt in the ward environment and 74% of respondents felt this should be a joint training program run by the University (Victorian College of Pharmacy) in conjunction with the hospital Pharmacy Department providing the clinical ward pharmacy service.

Disappointingly, there were only 9 hospitals providing regular ward pharmacist meetings for their clinical pharmacists. The review of duties conducted confirmed that the “Drug Chart Review” was the key focus for clinical pharmacists. However, the monitoring of patient clinical parameters was disappointingly low, indicating the need for more in-depth clinical training.

Even in the early days of development of clinical pharmacy services in Victorian public hospitals, it had become clear that a high frequency of medication errors occurred at the time of the patient`s hospital admission and at the time of discharge from hospital. Therefore, it was disappointing to see the relatively low attention being

given by many to collecting medication histories at hospital admission and in providing medication counselling when patients were discharged from hospital.

Nevertheless, the survey did provide a very useful Benchmark study on the state of clinical pharmacy ward practice in Victorian Public Hospitals in 1982.
Having provided a model for Clinical Pharmacy Quality Assurance (QA), the next step was to put the concept into practice.

I was appointed the Director of Pharmacy Services at PHH in 1980 and consequently I had the responsibility to develop these QA concepts for my Department. I established and led a small team of clinical pharmacists at PHH in this task. The most critical task being to develop and apply the concept of the model of "Peer Review" that was previously developed for Clinical Pharmacy (Allinson et al1985). The Clinical Pharmacy Peer Review Program was fully established at PHH and continued on at Monash Health after the closure of PHH. This paper lists very detailed information in order to provide guidelines to others on how to apply these QA concepts in practice.

In order to minimise backlash and resistance to change, a deliberate "soft" approach was taken. A critical component of this task was to fully involve all staff at the PHH Pharmacy Department in the decision-making process and in the sharing of experiences and knowledge. A type of "Quality Circle" which I developed and adapted for this application. A concept that I later more broadly applied to all individual service components of the Pharmacy Department, for example, dispensing, manufacturing, clinical drug trials, education and so on.

The paper focuses on three components, namely Clinical Pharmacy Meetings (including in-service education), Peer Review Ward Visits and the clinical training component of the Pharmacy Intern (Traineeship) year. In particular, the paper describes Peer Review Ward Pharmacists visits in great detail, with a clear emphasis being made on the need for total transparency. It is hard to estimate how many other Australian hospitals took up this new concept in the following years. However, the general concept was adopted by United Kingdom pharmacists in a slightly different format. In recent years the general concept was adopted by the

SHPA in their ClinCat clinical pharmacy training module on a National basis. The initial papers described in this Thesis (Larmour et al 1984 and Allinson et al 1985) are listed as key references in this SHPA ClinCat training module.

An important component in Clinical Pharmacy Services, in any setting, is patient medication counselling, although this unfortunately is often not fully recognised.

In 1985 there was much discussion within the pharmacy profession on what patients needed to be told about their medication in order to minimise patient medication non-compliance (non-adherence) and to reduce the risk of medication misadventure. However, little information on what the patients actually wanted to know about their medication was available. I therefore decided to conduct at survey of patients at PHH to gain an insight and understanding of what patients actually wanted to know about their medication (Larmour 1985).

The survey involved 84 patients who attended the PHH outpatient clinics and who obtained their medication from the PHH Pharmacy Department. The survey interviews were conducted separately from the normal patient medication counselling provided by the Outpatient Section pharmacists.

The survey provided many useful insights, not the least being that the perceived needs of patients in regard to their medication information varied very widely from patient to patient. A distinct preference for verbal discussions on these matters was found. The paper enabled a number of different approaches to patient medication counselling to be explored and considered to provide further guidelines on this aspect of clinical pharmacy practice. The most obvious and notable findings being that clinical pharmacists need to seek the patient`s advice on what and how much medication information they desired.

Because of my work in the development of Quality Assurance (QA) Programs for ward clinical pharmacists, the Federal Council of SHPA asked me to establish a Committee of Specialty Practice (COSP) for QA. The objective being to consider and develop various options to establish QA Programs across all sections and services of a hospital Pharmacy Department.

This work led to the publication of a series of papers on this topic. Three of the papers (Larmour et al 1988, Larmour et al 1992, Larmour et al 1994, Larmour et al 1998) provided very detailed guidelines on all aspects of QA within a hospital Pharmacy Department, the aim being to encourage pharmacists to develop QA systems within their Departments.

These papers, published over several years, demonstrate a gradual refinement and evolution of the concepts of QA with respect to a hospital Pharmacy Department. This includes the incorporation of relevant QA concepts from other industries, especially the manufacturing industries.

There are four main themes underlying these papers, namely;

1. Planning for Quality

The design of systems and practices in an attempt to ensure errors are avoided as much as possible. This incorporates the theme of "Getting it Right the First Time" with the aim of "Zero Defects".

2. Monitoring for Quality

The selection of Key Performance Indicators (KPI) and to then routinely monitor these KPIs to detect unexpected deviations or problems.

3. Continuous Improvement

When problems or errors are detected, conduct a full and detailed review of the incident to establish the possible causes of the problem. The next step is to then make changes to the system and practices to prevent the recurrence of this problem. It also involves ongoing monitoring of this issue to ensure the changes made have been effective. If not, the review process should continue.

4. Staff Training and Involvement

Ensuring staff are fully involved in the decision- making process. Importantly, it is essential to avoid the "Blame Game", but to instead focus on preventing recurrences of the problem. Concentrating on staff qualifications, staff experience, on-site training programs, staff fatigue, rosters, documentation and checking processes are all

critical components to review. This involvement of staff should include the use of a modified application of the “Quality Circles” concept. This type of staff involvement in management was a concept that was not always understood at that time.

The concept of the cost of “Quality Failure” was also introduced in the paper to explain the stark reality of Quality Failure and the urgent need for QA systems to be in place. The development of a set of National KPIs for hospital pharmacist departments was thought to be another possible stimulus to encourage hospital pharmacy departments to develop their own QA Programs.

The practicality of collecting the data and the importance of the area of practice to the profession, were the key factors considered in the selection process for these KPIs. Four KPIs were chosen, they covered medication counselling of patients on their discharge from hospital, stock shortages due the failure of the hospital pharmacy department systems, the number of attempted “Interventions” made by clinical pharmacist working in the wards and the acceptance rate of these Interventions by the ward medical and nursing staff.

It was decided that the opinions of the broader hospital profession on these KPIs should be requested to gain an understanding of the practicality of collecting the data and the usefulness of the KPIs chosen. The survey also invited respondents to put forward other options for KPIs, but unfortunately none were received. A further aim of the survey was to obtain benchmark information on the KPIs selected.

The survey was sent to 300 hospitals across Australia in November 1994. The response rate was 37%, but unfortunately, usable data was only able to be obtained from 24% of hospitals (Larmour et al 1996).

While useful results were obtained, the wide variation in the results suggested that a wide range of different methodologies may have been used when the data was collected.

In some ways, the concept of hospital pharmacy department KPIs, in this setting, may have been slightly ahead of its time. However, the baseline data obtained was

valuable and there has been growing interest in this concept in recent years, as evidenced by the very high number of readers, from all parts of the world, of this paper on the Research Gate electronic data base. Indicating that the paper has proved a useful reference for many others.

Importantly, this paper did introduce the concept of KPIs to Australian hospital pharmacists and provided benchmark information on National KPIs, although further refinement and education on the subject was obviously a long-term goal.

There is a tendency for clinical pharmacists of today to assume the services they provide have always existed. Very few have an understanding of the battles that had to be fought in order to justify each and every position.

Generally, the documentation of the clinical Interventions made by clinical pharmacists to improve patient medication safety and the avoidance of adverse drug reactions (ADR) provided the strongest evidence to support the need for these clinical pharmacy services. The excellent support from hospital medical and nursing staff for these services was also extremely important in gaining the support of the hospital`s management group. However, the cost of providing clinical pharmacy services continued to be an issue for some management sections and the multitude of business consultants, employed over the years, were always keen to point out these costs. The greatest challenge on these costs came in the late 1990s when the Victorian Government adopted a policy of “Competitive Neutrality” which challenged whether all or some hospital services should be contracted out or outsourced.

This policy was naturally of great concern to Victorian Directors of Pharmacy, especially since it had been noted that the cost of pharmacy services in Victorian Public Hospitals (due to the clinical pharmacy services) was higher than in other States.

It was therefore decided that a Benchmark Survey of the major public hospitals across Australia should be conducted. Bill Thomson, the Director of Pharmacy at Austin Health, and I agreed to undertake this study.

Subsequently, a survey form requesting data on the annual drug expenditure, annual Pharmacy Department salary costs and the number of bed days per year was sent to the large major general teaching hospitals in Melbourne, Sydney, Hobart, Brisbane, Adelaide and Perth. The confidentiality of the hospital`s identity was guaranteed. Responses were received from 10 hospitals, including three major Melbourne teaching hospitals.

Bill Thomson collected the data and sent it to me for analysis. The first task was to determine if the data could be standardised. Unfortunately, at the time, Victorian was the only State using the CASEMIX funding system. Therefore, the less precise parameter of occupied bed days had to be used.

When examining the drug cost data, I decided the Section 100 drug costs (provided under the Highly Specialised Drug Program) should be excluded. Firstly, because these drugs were only for outpatient use and secondly, because these costs were refunded by the Government and were therefore not a cost to the hospital.

I commenced the analysis by reducing pharmacy salary costs and drug expenditure (excluding S100 drugs) to a cost per bed day. I then examined the relationship between these two variables. This graph showed a direct relationship between these drug costs and pharmacy salary costs. I therefore asked a very experienced epidemiologist and biostatistician to examine this data. The linear regression analysis conducted, based on 1997 costs, found that drug costs (excluding S100 drugs) decreased by an average of $5.20 (95% confidence interval $2.38 to $8.01) per bed day for every dollar of pharmacy department salary cost per bed day.

This data in support of the financial benefits of pharmacy department services, especially clinical pharmacy services, was provided to Hospital Management and the Consultants and this successfully concluded the matter. This general financial benefit was later confirmed by a separate study sponsored by the SHPA in conjunction with a Consulting Company and a number of hospitals involved in the study.

Given the shortage of useful data on the financial benefits provided by Public Hospital Pharmacy Departments, it was decided that the information found in the benchmark study should be distributed to others as soon as possible. It was resolved that this could best be achieved by presenting the data as a Letter to the Editor in the AJHP, rather than as a paper. This publication was strongly supported by the Editor of the Journal. I would not normally include a “Letter to the Editor” as a publication in this Thesis. However, because of the significance and importance of this information at the time of publication, the shortage of such Australian studies on this subject and the innovative nature of the analysis, I decided to include this data in this Thesis.

In order to provide greater substantiation to the publication, I have included the data used in the study, along with a copy of the report provided by the epidemiologist/biostatistician.

In Victoria, Clinical Pharmacy Services commenced and was developed in the hospital ward setting, as outlined earlier in this Chapter. However, since this time Clinical Pharmacy Services have expanded into hospital emergency departments and a wide range of hospital outpatient clinic types. These clinical pharmacy services have always been very well regarded and appreciated by the medical and nursing staff working in these areas. The benefits of these services have also always been well supported by a range of statistics, especially the Interventions and accurate medication record documentation made by the clinical pharmacists. Nevertheless, very little formal research on the benefits of clinical pharmacists in these hospital emergency departments and outpatient clinics was available.

One such hospital outpatient clinic, at Monash Health, was the Medical Preadmission Clinic for elective admission of Medical patients. The objective of this clinic was to streamline the elective patient hospital admission process, including the reduction of problems associated with medication errors at the time of hospital admission. The clinical pharmacist`s involvement in this Clinic was very successful and it was therefore thought that the same concept could be applied to a Surgical Preadmission Clinic (PAC).

It was decided that the development of the Clinical Pharmacy Services in this Clinic would present a good opportunity to examine the impact and benefits of this new service and to gain the support of the hospital`s Administration Team for future service developments. I therefore established a small group of pharmacists to implement this project.

The study utilised a Prospective Randomised Control design where selected elective surgery patients, attending the Surgical PAC, were allocated to an Intervention Group or a Control Group. The elective surgical patient selection criteria applied basically to those patients requiring elective orthopaedic, vascular or colorectal surgery (George et al 2011). During a 13 month period, a total of 171 patients were allocated to the Intervention Group and 184 patients to the Control Group. The characteristics of the two groups were well matched and the average length of stay as an inpatient was similar for both Groups, as was the average time between the patient`s visit to the Surgical PAC and their admission to hospital.

In the Intervention Group, the patient received the standard care provided by the Surgical PAC, plus an interview with the Surgical PAC clinical pharmacist. This pharmacist also made a telephone call to these patients after their attendance at the clinic, but before their hospital admission. When the patient was admitted to the hospital ward, they received the normal ward based clinical pharmacy service.

The Control Group received standard Surgical PAC care when they attended the clinic but had no contact with the Clinic`s pharmacist. However, when they were admitted to the hospital ward, they did receive the normal ward based clinical pharmacy services. This study found that medication reconciliation at the time of hospital admission was provided to 81% of the Intervention Group of patients and to 75% of patients in the Control Group. Medication reconciliation was provided to 90% the patients in both groups, when they had their hospital discharge medication provided. It was found that the Intervention Group patients had a more complete medication history than the Control Group of patients. The number of Interventions made by a clinical pharmacist was 31% higher for the patients in the Intervention Group than it was in the Control Group of patients. This was mainly due to the additional Interventions made by the clinical pharmacist in the Surgical PAC.

However, the percentage of Interventions graded as Moderate or Severe, was almost identical in both Groups. The main conclusions of the study were that a Surgical PAC clinical pharmacist enabled an improvement in the detailed documentation of the patient`s medication history and led to an increased number of Interventions made by a clinical pharmacist. The results also supported the valuable medication safety role carried out by the clinical pharmacists based in the wards. In addition, the paper outlined several areas for future improvement and development of the role for clinical pharmacists working in the Surgical PAC.

These changes in pharmacy practice, in a variety of areas, led to the gradual understanding in academic circles of the need to teach a range of new skills to undergraduate pharmacists. This realisation led to the need to expand the pharmacy undergraduate from a three year to a four-year course.
Due to my interest in clinical pharmacy practice I was requested by the SHPA and the Joint Four-Year Course Committee to prepare a document titled The Changing Role of Hospital Pharmacists and the Need for a Four-Year Pharmacy Undergraduate Course. My experience in this field and the various papers that I had written on this subject were of great benefit when I was writing this submission. The document was tabled at the Pharmacy School Heads Conference in 1990. Unfortunately, this document was not published, however because of the amount of valuable information contained in the document and its relationship to the development of clinical pharmacy practice, I considered including this document as an Appendix for this Thesis. However, due to the length of the document I decided to only include the Executive Summary in the Appendix.

Chapter Two

(Papers 14 -15)

Examining the Impact and Detection of Adverse Drug Reactions.

One of the key driving forces of change for the introduction of Clinical Pharmacy Services was the rapid increase in the number of new medications and the subsequent increased complexity of medication therapy.

While the side effects of medication, minor or major, had long been recognised as a problem, in Australia, it was not until 1963 that formal Government sponsored pharmacovigilance was introduced. This change followed the discovery of thalidomide induced embryopathy.

During my role as a clinical pharmacist, I became very aware of the risks of side effects and Adverse Drug Reactions (ADR) and their dire effect on patients. While many ADRs are not predictable, there are many more that are potentially avoidable. Developing an understanding of the various factors involved in the occurrence of an ADR therefore became a key interest. Part of this process involves the clear and thorough documentation of such events.

Therefore, I promoted the role of clinical pharmacists in reporting and documentation of ADRs, even though many pharmacists at the time were not sure whether they were authorised to produce ADR reports. This meant there was a need for in-service training on this subject. However, clinical pharmacists did recognise the need for their Intervention to avoid a potential ADR. This enabled a greater understanding of this matter by the clinical pharmacists at our hospital.

It also became evident that there were many patients who were admitted to hospital due to an ADR. I therefore thought there would be benefit in having a closer look at this issue and to determine whether there were any common factors associated with these ADRs. This issue had been investigated by others, but the majority of this work was conducted overseas.

Therefore, in association with the Hospital`s Quality Assurance Committee, I organised a small group of Medical and Pharmacy staff to set up a study to examine drug related hospital admissions to the Prince Henry`s Campus of Monash Health. This involved a prospective study, over six months, of all patient admissions to hospital, apart from day patients. Clinical pharmacists reviewed all patients admitted to the wards or Emergency Department and those cases were an ADR was thought to be possibly involved were noted. These cases were then thoroughly further examined by a review group. There were 35 cases excluded in this review process because no clear association between the hospital admission and drug therapy could be established. A total of 5623 cases admitted over the six months were included in the study. Of these, 136 cases (2.4%) were thought to be drug related. This included 90 (1.6%) cases that were due to an ADR. A separate smaller study was also conducted to gain greater details on some aspects of a control group, specifically the number of medications patients in different age groups were taking. This part of the study was conducted over two weeks and involved 364 patients who had not had an ADR.

The 90 cases with an ADR involved 84 patients. There were four patients who had two hospital admissions and one had three hospital admissions.

Importantly, of the 90 cases involving an ADR, 27 cases (30%) were thought to involve a drug interaction. Of these there were 6 pharmacokinetic based drug interactions and 21 were pharmaco-dynamic or pharmacological in nature. Very few other studies have addressed the importance of drug interactions as a risk factor in the occurrence of an ADR.

Of the ADR cases, 88% were considered definite or probably related to the patient`s drug therapy and 97% were considered to be severe or moderately severe. A matter of concern was that only 19% of the cases were considered idiosyncratic. The rest had a potential iatrogenic involvement.

The most common ADRs involved the gastrointestinal tract, especially bleeding, and the cardiovascular system, especially cardiac arrhythmias. The most frequently

involved medications were non-steroidal anti-inflammatory drugs (NSAID), warfarin, digoxin, theophylline and methotrexate.

The drugs most commonly involved in an ADRs due to drug interactions were NSAIDs, digoxin and warfarin. There were 5 fatalities and two of these involved a warfarin drug interaction and two were due NSAID precipitated haematemesis and melaena. The study confirmed that patients received additional medication as they got older. It also found that the risk of an ADR increases with age, with 53% of patients who experienced an ADR being over 70 years of age compared 14% of patients in the control group. The risk of an ADR, not surprising, also increased with the number of medications being taken by the patient, with the mean number of medications being taken by the ADR group being 4.9 +/- 2.6 compared to 3 +/- 2.8 in the control group.

No other predisposing factors could be clearly linked to the risk of an ADR. Surprisingly, this included patients experiencing a previous ADR. The study found 24% of the patients admitted to hospital reported that they had experienced a previous ADR, but only 6% of patients who experienced an ADR had any link to their previous ADR.

The ADRS associated with hospital admissions, in this study, largely involved the actions of those outside of the hospital. Many of the reported ADRs could be considered unpredictable, however there were many more that could be considered to be iatrogenic in nature. In some of these cases it was then possible to observe the outcome consequences that could occur if a clinical pharmacist had not made an intervention to prevent this problem in another setting. This therefore indirectly provided evidence of the benefits of having competent clinical pharmacists working in the hospital.

The study also illustrated the need for education on ADRs and especially the very real potential risks that drug interactions present. Often there has been a tendency to consider many drug interactions as being theoretical and not important. This study provides evidence that these risks are real.

It was also noted that the future computerisation and integration of prescribing and pharmacy dispensing systems would offer significant benefits in reducing the risk of avoidable drug toxicity and ADRs. These benefits are now starting to be realised, as outlined in the first paper in Chapter Three (Hodgkinson et al 2017)

The few cases involving patients with multiple hospital admissions also provide an insight into the communication problems encountered between hospital and community practitioners, which can then often lead to an inappropriate hospital readmission.

This issue is addressed in more detail in the papers in Chapter 4.

During this study, I also became familiar with the International Classification of Disease 9th Revision (ICD 9), which included a number of E sub-codes which related to a range of adverse effects associated with medication therapy.
It therefore occurred to me that the use of these E sub-codes would be a potential approach to detecting ADRs. However, investigations of this option found that it was not practical, at that time, due to coding issues and limited computer systems.

But over time, as the sophistication of computer systems developed and the ICD 9 code was replaced by the more detailed International Classification of Disease, 10th Revision, Australian Modification (ICD-10-AM) coding. Another change that occurred was the introduction of Casemix Funding to Victoria Hospitals. To ensure these Hospitals gained their full funding entitlement, it was necessary for additional resources to be put into ensuring accurate and thorough coding for each patient. The E sub-codes of ICD 9 were replaced by the Y sub-codes in the ICD-10-AM coding.

Therefore, due to the improved computer system data base, the feasibility of using Y sub-codes to detect ADRs was now a reality. For many years the Pharmacy Department has, and still does, receives a computer printout listing all patients who had a Y sub-code entry recorded in their medical history. This has provided, and still does, an opportunity for routine education and research on ADRs and patient medication safety.

However, due to the sheer volume of reports, it became obvious that a more concentrated research study would be needed to evaluate this method of monitoring ADRs. I therefore organised a small team in my Department to conduct a study on this matter.

The study involved the retrospective review of the medical records of multiday patient separations who had a Y sub-code recorded in their medical record. This involved patients who were discharged from three Monash Health hospitals over a three-month study period. This involved Y sub-codes Y40 to Y59. Non-admitted Emergency Department patients, Hospital in the Home patients and single day admission patients were excluded from the study. A total of 552 separations were reviewed but 140 separations were not able to be included, mainly due to the unavailability patients medical record or, alternatively, when the study selection criteria was not able to be met for various reasons.

Details on all spontaneously reported ADRs that occurred during the study period, were also recorded.

There were 412 (3.3%) separations where an ADR was recorded. This included 15 separations where the ADR was captured from both the coding and spontaneous reports. Most patients had a single ADR, but there were 31 patients who experienced more than one ADR. There were 157 (1.3%) separations where an ADR was thought to cause a hospital admission. This figure was surprisingly similar to the ADR related admissions of 1.6% reported in the previously discussed paper (Larmour et al 1991)

There were also 29 (0.4%) ADRs only reported spontaneously. On investigation, it was found that these ADRs were not detected by the coding system because there were inadequate details recorded in the patient`s medical record. Of the ADRs reviewed, 57.6% of case were considered to be definite or probably drug related and 51% of cases were considered to be serious in nature. In summary, 86% of the medical records reviewed led to the identification of an ADR and it was found the ICD-10-AM Y sub-coding was correctly and appropriately assigned in 94% of cases.

The medium age of patients was 65 years and the median number of drugs per patient was 8 for those patients who experienced an ADR.

The most common drugs involved were digoxin, frusemide, glyceryl trinitrate, morphine and warfarin. Reflecting that the majority of ADRs were related to inpatient care. The most common medication groups involved were antibacterial drugs, opioids, diuretics, various cardiovascular drug groups, anticoagulants, antineoplastic drugs, corticosteroids, anaesthetic drugs and anti-inflammatory or anti-rheumatic drugs. The most common types of ADR were nausea and vomiting, generalised skin reactions, haemorrhage and various cardiovascular conditions. The Type of ADR obtained from the coding system were mainly Type A (dose related), whereas the spontaneous ADRs were more likely to be Type B (not dose related), which perhaps indicates the unexpected ADRs were most likely to attract the attention of medical and pharmacy staff.

The study strongly endorsed the belief that ADRs are substantially under reported. Spontaneous reporting alone would have led to 44 ADRs but would have missed the 397 additional ADRs detected by the coding system. On the other hand, the study established that the coding system is an efficient and effective method of identifying ADRs. Post Marketing Surveillance, especially for newer medications, remains an important challenge for patient medication safety. Given the extensive under reporting of ADRs, there would seem to be a need to establish more effective systems.

The intensive ADR monitoring produced by programs like the Boston Collaborative Drug Surveillance Program are obviously beneficial, but very labour intensive.
It would seem that the coding system, described in this paper, would therefore be an acceptable alternative. This approach has labour and time implications, but at a median of 18 minutes needed per case, it would be manageable if the program was limited to specific hospitals.

The coding system described in this study continues to be operated at the Monash Health Pharmacy Department, although limited resources prevent all reports from being reviewed. Nevertheless, it remains as a potential ongoing research project.

The direct comparisons of the findings of other ADR studies is difficult because of methodology variations, even to the extent of defining an ADR, and, in particular, the population group being studied. The World Health Organisation definition of an ADR has been used in both the studies in this Chapter.

Chapter Three

(Papers 16 -20)

Examining New Concepts in Hospital Pharmacy Management Strategies.

The introduction of clinical pharmacy services was of the most important actions to be taken to improve patient medication safety in hospitals. However, the development and introduction of new technologies has become increasingly important in these endeavours. This has occurred in many ways, but one of the most important systems of change for hospital Pharmacy Departments has been the introduction of pharmacy computer systems. Early changes included the introduction of full patient medication histories, improved labelling of medication, improved efficiency in the dispensing of prescriptions, prescription records, improved inventory control systems and bar code verification systems for patients and medication.

These changes and improvements were introduced over a number of years. However, the unavailability of a fully integrated dispensing and prescribing system remained a major shortcoming.

The main reason for this was that there were only very limited electronic prescribing systems readily available in Australia at that time. The Victorian Government recognised this problem and attempted to solve numerous computer system deficiencies with a program called Health Smart.

Each Victoria public hospital group was included in various sections of the program. Unfortunately, Monash Health was not allocated to the Clinical Systems Modules.

Therefore, if Monash Health was to obtain an electronic prescribing system within a reasonable time, it would have to be from outside of the Health Smart program.

Due to ongoing interest in patient medication safety, I began to examine alternative options. After extensive investigations, it became obvious that the most logical option would be for the software provider of the pharmacy dispensing system, Pharmhos Pty Ltd, to develop an electronic prescribing system on the front end of the

Pharmacy Department dispensing system. Using this approach enabled a number of common aspects to be utilised in both components of the system. The software company willingly agreed to this project, but unfortunately the same cannot be said for the Monash Health Computer Systems Committee.

Eventually, after much discussion and the presentation of a number of very extensive Business Case presentations, it was agreed that the Pharmacy Department could proceed with the proposal on two conditions.

Firstly, the cost was to be entirely met from the Pharmacy Department Budget and secondly, that the system had to demonstrate an actual improvement in patient medication safety.

Subsequently I organised a project group within the Pharmacy Department to develop, introduce and evaluate a fully integrated electronic prescribing and dispensing system. Other relevant expert personnel, especially medical staff, were also co-opted. The system was successfully introduced, initially covering Outpatient Clinic prescriptions and Emergency Department prescriptions and, later, this was extended to also cover prescriptions for patients being discharged from the hospital.

Other patient medication safety components of the system included the use of bar-codes in the entry and verification of the patient`s identity and the verification of the medication supplied on the prescription. The system also enabled the time spent on each component of the dispensing process to be automatically recorded.

Details on the Pharmaceutical Benefit Scheme (PBS) prescribing aspects were also included in the software.

In the design phase, it was also decided that the prescribing and dispensing computer system should logically be the “source of truth” for patient drug hyper-sensitives, allergies and previous ADRs. This meant this information needed to be integrated into the hospital`s Medical Record system.

In order to evaluate the medication safety benefits of the system, it was necessary to examine dispensing and prescribing errors before and after the integrated prescribing and dispensing system was introduced (Hodgkinson et al 2016).

The study involved the survey of 379 patient prescriptions (654 medications) over a two-week period, prior to the introduction of the new system, compared to a separate two-week survey conducted several months after the new system was introduced. The second survey involved 375 patient prescriptions (635 medications). Both groups were considered to be well matched.

The paper discusses the error analysis in detail and the major findings were as follows.

The number of prescribing errors per patient was reduced from 2.98 errors per patient to 0.2 errors per patient (93% reduction).

The number of prescribing errors per medication was reduced from 1.72 per medication to 0.12 per medication
(93% reduction).

The number of dispensing errors per patient was reduced from 1.27 per patient to 0.027 per patient (97.9 % reduction).

The number of dispensing errors per medication were reduced from 0.76 per medication to 0.17 per medication (97.8 % reduction).

The median out-patient prescription waiting time was reduced from 27 minutes to 13 minutes (52% reduction).

Using the error severity assessment scale, the mean severity score of clinical prescribing and dispensing errors in each group was graded as minor (Category 2). There were three moderately severe prescribing errors found in the before group.

The conclusion was that the fully integrated prescribing and dispensing system did in fact lead to a significant reduction in prescribing and dispensing errors. These results were well accepted by the Monash Health Executive Group.

The ability to develop and introduce clinical pharmacy services, innovative computer systems and other medication safety technology depends on the ability to obtain funding to cover these costs. The three most common mechanisms available for Pharmacy Department Directors are:

1. Developing a Business Case for the hospital`s senior executive group to explain the benefits and to outline the costs.

2. Managing the Pharmacy Department Budget to create efficiencies and reduce waste so that the funds saved can be allocated to medication safety projects. This includes negotiating improved medication prices.

3. Create new sources of revenue, for example the introduction the Pharmaceutical Benefits Scheme into Public Hospitals.

Another important factor is the need to recognise that one of the largest Budgets in Public Hospitals is the Drug Budget. Consequently, it is likely to draw the attention of the Hospital's senior executive group. In addition, given the complexity of the funding systems for pharmaceuticals and the wide variety of medication used, the funding structure and costs are generally poorly understood by the senior executives. Therefore, considerable effort needs to be made to provide them with appropriate education on this matter, especially in regard to where and why the medication expenditure occurs.

The next series of papers aim to explain these complexities and to outline various projects adopted to obtain funding and to improve the efficient use of medication.

The first of these papers, titled "Cultural Change and Drug Expenditure" (Larmour et al 1996) outlines the development of a framework for change and introduces the concept for the promotion of "Drug Utilisation Efficiency".

The first part of the paper focuses on various concepts which aimed to involve medical staff in the decision-making process in relation to the use of medication. Outlining a Complex Matrix of communication and negotiation.

There are a number of themes running through this paper on this matter.

The first of which relates to the Therapeutics Committee and Drug Formulary processes at Monash Health. The Therapeutics Committee, often called the Drug Committee in many hospitals, had been in place for many years. However, it was felt that a new approach to involve key medical staff in the decision-making process, in relation to the management of medication, would be beneficial. These changes included:

1. The selection criteria to be used when considering applications for the admission of a new drug onto the Hospital`s Drug Formulary was simplified and modified into two levels. Three clinical benefit criteria were specified in the Level One Criteria. At least one of these criteria had to be met. Once it was resolved that there was a clinical benefit and where there were al*so* significant costs involved, then the Level Two Criteria would be considered. This focused on all benefits, not just cost. This involved significant negotiations with the relevant Senior Medical staff.

2. All Drug Formulary applications had to be sponsored by the relevant Head of Unit, rather than by a pharmaceutical company.

3. A Finance and Drug Utilisation subcommittee was established to deal with the complex negotiations and to run special projects to improve medication safety. This included a program to encourage the early conversion of antibiotic therapy from intravenous to oral therapy when appropriate. The development of drug use protocols to promote medication safety, especially for warfarin and the strength standardisation of intravenous heparin infusion solutions. Many such projects are now standard practice. There was also a strong focus on the negotiations to establish the Patient “Selection Criteria”

that needed to be met for a specific patient before a specific high cost drug could be prescribed for that patient.

4. In some cases, ongoing reports on the effectiveness of some very high cost medications were required by the Therapeutics Committee to gain ongoing support for this patient. In other cases, a small local evaluation study was conducted.

5. The term “Prescribing Restriction” was replaced by the term “Prescriber Authorisation”. There was also considerable delegation of this prescribing authority to key Heads of Unit, Service Division Chairs and several specialist Teams, such as the Pain Team, the Antibiotic Advisory Team and the Parenteral Nutrition Team.

The paper`s second theme in relation to involving medical staff in decisions related to the management of drug expenditure involved a process called Duplex Budgeting. This involved the overall management of the drug budget by the Pharmacy Department together with key medical staff to jointly managing a number of Sub-Budgets. The joint managers of these Sub-Budgets had a degree of control of that drug expenditure but were not held totally accountable for budget over-runs.
Three types of Sub-Budgets were developed:

1. The Chair of the various Service Division Sub-Budgets,
2. The Head of Units with high cost drug expenditure.
3. The key Facilitator for a specific group of drugs, such as Anaesthetic Drugs, Antibiotics or specific teams.

Naturally there was a degree of overlap between these various Sub-Budgets and these factors had to be given consideration. If a change occurred in prescribing patterns that meant there was a significant gain or loss in expenditure, the various Sub-Budgets were adjusted. Normally this could only be done fairly at the time when the next Financial Year`s Budgets and Sub-Budgets were being negotiated.

The Third theme in the paper aimed to promote more “efficient drug utilisation”. This aims to encourage the use of the cheapest alternative drug from a group of drugs

used for the same Indication, where there was evidence of no difference in efficacy or safety.

This involved the Therapeutics Committee in negotiations with key stakeholders to identify potential target drug groups and to then negotiate their acceptance and promotion to prescribers. The experience gained in this project was the precursor to several later papers on the subject of Therapeutics Equivalence.

The second paper in this series relates to the introduction of the Pharmaceutical Benefits Scheme (PBS) into Victorian Public Hospitals in 2002, which enabled the inequality of access for many high cost drugs to be resolved and provided an independent source of funding to the hospital pharmacy departments involved.

In the early 1990s, Public Hospital Senior Executives and State Governments became aware of the opportunity to shift the cost of pharmaceuticals available under the “Pharmaceutical Benefits Scheme and Repatriation Benefits Scheme” (PBS) from the State Budgets to the Commonwealth Government. The extent to which States utilised this anomaly did vary. However, the Victorian Government provided general support to the public hospitals on this prospect, but without making it a definitive policy.

Consequently, Directors of Pharmacies in Victorian Public Hospitals were increasingly required by hospital management to not supply or to only provide a very limited supply of items available on the PBS for outpatients and patients being discharged from hospital. Patient were redirected to obtain these PBS items via a prescription written by their community Medical General Practitioner (GP) and dispensed by their Retail Pharmacy. A process that was of great inconvenience to patients and a wasteful duplication of health resources.

This situation was further exacerbated when a number of high cost oncology drugs were added to the PBS. This meant these high cost oncology drugs were readily available in a Private Hospital but were severely restricted in Public Hospitals. Thus, creating an unacceptable inequality of access situation. This led to the evolution of a number of dubious arrangements to obtain the high cost oncology drugs via the

PBS. Naturally there was strong opposition to these arrangements by many people. Leading the opposition to these arrangements was the multidisciplinary Melbourne Major Teaching Hospital Drug Usage Group (MTHDUG), now called the Victorian Therapeutic Advisory Group (VicTAG).

It was resolved by the MTHDUG that an approach needed to be made to State and Commonwealth politicians to correct these anomalies. Therefore, a document title "Position Statement Number One", of which I was the lead author, was produced and widely distributed to politicians across the country. This created a great deal of interest and led to the writing of a second discussion paper, which I was again the lead author, titled "Position Paper Number Two".

However, it took until the 1998 for the Australian Health Care Agreement on Pharmaceutical Reform to be agreed upon. The Victoria Government was the leader in commencing negotiations with the Commonwealth Government and formed the Pharmaceutical Reform Implementation Working Party (PRIWG). I represented Southern Health (now Monash Health) on this multidisciplinary working party. Similarly, at a later stage, the Pharmaceutical Reform Users Group (PRUG), which consisted mainly of senior hospital pharmacists, was formed.

Initially the PBS was designed for community practice and therefore adjusting the Scheme to work in a Public Hospital was a major change project and consequently it took several years to implement. Therefore, a small group of dedicated Victorian senior pharmacist resolve that a paper should be written to provide guidance to other Victorian and interstate Pharmacy Departments on the issues that needed to be addressed when introducing the PBS into their hospitals (Larmour 2003). The first three public hospitals to introduce the PBS, in January 2002, was Monash Health (previously called Southern Health), Barwon Health and Bayside Health.

At Monash Health, this change process involved three Phases of Change. The initial Alpha Phase, over the first 2 to 3 months, was the introduction of the major changes, with new areas starting on the PBS each week. This was followed by the Beta Phase over the next 6 months to consolidate, verify and refine systems and staff education.

This was then followed by the ongoing Gamma Phase process of ongoing continuous improvement and refinement over many years.

A critical factor required for the successful introduction of the PBS into a public hospital was to have a Pharmacy Computer Dispensing Software Program that could process PBS prescriptions. Monash Health covers a number of hospitals, including one private hospital and therefore had both the software and experience to assist with this process. This experience was useful to pass onto others, since many other Victorian Public Hospitals were also using the same Computer Dispensing System as Monash Health.

Similarly, Monash Health had a very extensive clinical pharmacy service in place, especially in the hospital`s wards, and therefore the compliance with the Australian Pharmaceutical Advisory Council (APAC) National Guidelines to achieve the continuum of quality use of medicines between Hospitals and Community was relatively straight forward. Some aspects of this work have been covered in the next Chapter of this Thesis.

The patient co-payment fees structure was matched to that of the standard PBS and therefore Public Hospitals had to restructure their methods for collecting these fees, including the interfacing of the Pharmacy Department Computer Software to the Hospital General Ledger. However, for public hospitals, all medication dispensed to patients, whether on the PBS or not, could be added the Patient`s Medication Safety Net. This was a very significant benefit to patients.

A major advantage for Victoria Public Hospitals was that generic dispensing and prescribing had been standard practice for many years. This meant they only had to stock one PBS brand product, which in turn meant that it was easier for Public Hospital to negotiate good prices. This then provided a revenue generating option for many medications.

Traditionally the Therapeutic Committee decides on which medications are held on the Hospital`s Drug Formulary. However, the introduction of the PBS required the Committee to revise this process and to accept medications added to the PBS but,

where applicable, not every brand. This saved a great deal of duplicated work for the Committee and enable greater standardisation of available medications in the community and hospital practice. The Committee however continued to oversee this process.

The introduction of the PBS into public hospitals also required changes to the format of prescriptions sheets. Due to the wide variations between hospitals and the community, it was necessary to redesign this new prescription form. The drafts for this document was done at the Monash Health Pharmacy Department. This, in turn, led to a standardised prescription sheet for all public hospitals for outpatient, hospital discharge patients and day oncology patients. This standardisation also aimed to promote medication safety by having a common format and set of requirements.

Another major requirement, especially for the bigger public hospitals, was to obtain additional Computer Hardware, especially printers and bar code scanners. This provided a welcome update of equipment for many public hospital pharmacy departments.

The paper also covers a number of other issues with the aim of providing a path for others to follow.

The next paper moves to the subject of a Therapeutic Equivalence Program (TEP), which further builds on the previously outlined strategy to improve and promote efficient and safe drug utilisation. The aim being to develop a method of creating competition where none previously existed. The objective being to provide a means to save on medication expenditure without compromising patient care. In doing so, providing an opportunity for additional funds to cover other expensive medication or for use by the Pharmacy Department in the development of clinical and related services.

Despite the very significant savings to Monash Health (previously called Southern Health) drug expenditure due to the introduction of the PBS and a number of other successful strategies to reduce medication costs and waste, the Chief Executive Officer felt other savings options should be undertaken. Not wanting to add a number

of new authoritarian restrictions and savings measure, I decided the concept of a voluntary Therapeutics Equivalence Program should be developed.

Importantly the savings achieved through TEP are quite different to the savings achieved by the availability of generic products that can occur once a medication`s Patent has expired.

In TEP, the objective is to examine medications that have the same pharmacological or therapeutic target receptors and are used for the same indication. Having chosen a particular therapeutic group of drugs, the task is to then to consider the evidence to determine if the members of this group are of equivalence in efficacy and safety. Once this is established and agreed upon by key stakeholders, the medication with the lowest therapeutic equivalent daily treatment cost is determined. This medication would then be designated as the “Preferred Medicine “of that group. Pharmaceutical Companies were given the opportunity to submit their best “effective price” in order to become the designated Preferred Medicine of a specified therapeutic group. The “effective price” being the cost price after all discounts and bonus stock effects had been taken into account.

This Preferred Medicine for a particular therapeutic group was then promoted as the drug of choice in that therapeutic group for new patients who needed that type of medication.
Patients already on another drug in this therapeutic group were not automatically changed to the Preferred Medicine of that type unless this was clinically indicated.

The key feature about the Monash Health TEP being that it was based on the voluntary collaboration of the Monash Health Medical staff. In doing so, prescribing the Preferred Medicine for new patients then became Unit or Department policy. The Monash Health TEP does not carry out mandatory substitution of medicine nor does it focus on patient co-payment fee strategies.

The TEP proposal was presented to and approved by both the Therapeutics Committee and the Medical Executive Committee. The TEP was over seen by a

High Cost Drug Working Party and a project pharmacist working with the Director of Pharmacy.

Gaining the agreement and support of the Monash Health medical staff was obviously critical, but advertising and promoting the TEP was also extremely important. Direct contact through routine medical staff meetings, academic counselling of key stakeholders, short and clear posters and leaflets and special pens, for promotion, were purchased. The presentations were always delivered at routinely held medical staff meetings, rather than trying to get medical staff to attend yet another meeting. This ensured there was always a good audience for the presentation. The concept was welcomed by junior medical staff because it simplified their prescribing for the TEP medication.

This paper covers the time frame of 2006/07 to 2009/10 Financial Years. During which there were 11 designated Preferred Medicines established.
Compliance with the TEP policy was monitored by examining the medication usage and prescribing data of each Preferred Medication each month. This showed a positive response in all cases.

A saving of $3.16 million was achieved in this time frame, which was equivalent to 1.7% of the total drug budget and 8.2% of the net drug budget at Monash Health. The net drug budget consists of the full drug budget less the expenditure reimbursement from the PBS and patient co-payment fees.

The throughput of patients is always a key factor in drug expenditure and over this time period, separations increased by 10.4%, however the savings achieved increased by 65.5%.

This TEP project achieved its objectives and importantly demonstrated that the collaboration of medical staff can be achieved in the correct circumstances. An aspect that many believed could not be achieved.

The TEP continued at Monash Health and an update on the results achieved were published in the Australian Health Review Journal in August 2018 (Chynoweth and

Larmour). These results cover the period from the 2006/07 to 2014/15 Financial Years.

In this second paper, there were 18 Preferred Medicines, which included 6 of the Preferred Medicines covered in the first paper. This illustrated the need to carefully monitor market dynamics and the life cycle of a medication. Especially in regard to the Patent expiry date of a medication. Of the Preferred Medicines withdrawn, in a few cases the saving were no longer available, but in most cases the medication was withdrawn because the medications Patent had expired, and this led to the emergence of generic competitors. For these medications, there were still significant savings, but these savings were not due to the TEP and therefore were not included in the TEP savings total amount.

The savings achieved over the 2010/11 and 2014/15 Financial Years were $7.18 million, which was equivalent to 2.1% of the drug budget or 9.3% of the net drug budget. Over this time separations increased by 23.2% and the savings increased by 81.4%.

The experiences gained from this ongoing study led to a greater understanding of the term stakeholders. Factors influencing the effectiveness of stakeholder leaders included leadership style, the size of the Unit or Department, ownership and the number of visiting medical staff.

In some cases, the complexity of stakeholder was influenced by previously unknown or unidentified stakeholders, multiple stakeholders or multidisciplinary stakeholders. This in turn, points to the need for careful and thorough investigation of who really are the stakeholders when negotiating an agreement. It was important to respond quickly and thoroughly when surprises are encountered.

The total savings achieved by the Monash Health TEP over the 2007/08 and 2014/15 Financial Years was $10.54 million. A significant saving and in line with the concept of Disinvestment to ensure limited resources are used in the most effective manner. Importantly, the TEP has demonstrated that medical staff can be collaboratively engaged, in the right circumstances, to achieve significant savings.

A key factor in medication safety is in having well trained staff and appropriate staffing levels in place to safely meet workload demands. Due to the variability of workload presentation, it is sometimes difficult to have appropriate staffing levels in place to deal with peaks in workload.

The next paper (Paper 20) in this Chapter examines a method of dealing with this issue. The objective was to develop a simple version of “Queueing Theory” to organise for additional pharmacists to be available at peak workload times in a Public Hospital Pharmacy Outpatient Section. This work was conducted at Prince Henry`s Hospital, which later became part of Monash Health.

This was the first paper that I published and was adapted from a conference presentation. Many aspects of this paper provide a reflection of the basic functions of a Public Hospital Pharmacy Departments on outpatient workload in 1975.

A significant concern was the outpatient section workload and resultant long waiting time for the patients presenting a prescription for dispensing. It was also recognised that there was a high-risk potential for medication errors to occur when staff workloads were too high.

The paper outlines a number of strategies to deal with this issue, including the early intervention to detect and correct prescriptions which contained an error or other problems.

However, there are many factors associated with the workload that were beyond the control of the Pharmacy Department. In particular the inflow of patients could not be controlled, so the only other option available was to increase the number of pharmacists available at peak times. The question being what the most efficient means of achieving this goal.

The first step being to study the daily workloads against time for each weekday of service. The standardisation of this data enabled a clear picture of peak and trough levels of activity.

To explain the factors involved in determining patient waiting time, a mathematical model was developed. This illustrated the impact of the queueing effect when the inflow of prescriptions exceeded the number of prescriptions dispensed.

From this, a proposal was developed that would enable the early prediction of peak workload and enable additional pharmacist to be in place before the peak waiting time was reached.

This work was conducted without the benefit of computer systems, although an electronic calculator was available. The mathematical model could be more easily applied with current pharmacy computer systems, but this has not yet been done. However, the mathematical model does provide a useful Queueing Theory model and it could be applied in a number of other settings where queueing occurs due to workload fluctuations.

Chapter Four
(Papers 21-23)

Examining the Potential Benefits of Hospital Pharmacy Outreach Services

Due to my interest in clinical pharmacy services and my research in relation to ADRs, I had become acutely aware of the communication difficulties encountered between hospital and community practitioners, especially in regard to medication errors. This in turn created an interest in examining opportunities to reduce or avoid these problems.

An opportunity to examine these problems occurred when Monash Health (then called Southern Health Care Network) was successful in gaining a grant from the Commonwealth Department of Health and Aged Care Program, in conjunction with the Victorian Department of Human Services, called the National Co-ordinated Care Trial (CCT).

The Monash Health Project involved 1500 clients in the intervention group and 657 control cases of consenting patients, 423 Medical General Practitioners (GPs) from the local GP Divisions and 5 Community Health Centres. The Monash Health Chief Executive Officer was well aware of the issues associated with medication safety and asked me to form a Pharmacy Strategy Group to conduct a sub-project on medication issues.

The aims of this Group were to:

1. Promote safe and effective drug use
2. Reduce unnecessary drug use
3. Promote relationships between clients and healthcare providers
4. Identify high risk clients
5. Identify high risk drug use.

The Group subsequently identified five Service Products to examine and develop.

1. Education Outreach Program

The aim of this Program was to use an experienced clinical pharmacist in the role of an “Academic Detailer” to provide education support to local GPs. All GPs in the Monash Health CCT were invited to participate in this Program. There were 40 GPs who immediately accepted the invitation and these GPs managed 224 CCT clients.

The Pharmacy Strategy Group, in consultation with Senior Medical Staff, selected two education topics;

1.The eradication of Helicobacter pylori in peptic ulcer disease
and
2. The rational use of non-steroidal anti-inflammatory drugs (NSAIDs)

The project pharmacist provided Academic Detailing to 27 GPs, on a one to one basis, and undertook four group sessions, with 13 GPs in each group and also a further 5 GPs not in the Monash Health CCT.

Each GP was provided with a copy of a peer reviewed documents on both topics. Each topic had a desktop handout and a more detailed concise background leaflet. All GPs who responded to the survey of these consultations advised that the presentation and support documents provided were either excellent or good. The survey also found the GPs felt the process was very useful or useful, with 75% indicated that they would take action on the advice provided and 96% requested a further visit

An attempt was made to examine the impact of the Education Outreach Program on the prescribing by these GPs. This was done through the use of a computer data base that was available for the CCT. Data was obtained from two three-month periods, before and after the intervention, were examined.

There were too many confounding factors involved in the Helicobacter pylori subject. However, when examining the prescribing of NSAIDs by GPs, the post intervention period showed a 54% reduction in prescriptions and a 28% reduction in patients who

were prescribed a NSAID. The control group showed no change in the prescribing pattern of NSAIDs. However, due to the small numbers of patients involved and the limitations of the computer data base, only limited interpretation of the results could be made, although the data did show a promising trend.

2.Drug Information Services

The Monash Health Pharmacy Department had been providing a Drug Information Centre for many years, a service to both hospital staff and the community, especially in regard to the safety of medication in pregnancy and breast feeding. Clients included medical specialists, GPs and the general public. It was therefore thought to be beneficial to offer this service to GPs in the CCT. A toll- Free number was therefore provided. The normal Service continuing to be busy with its standard clients, but there was very little uptake of this service by the CCT GPs. This was a disappointing result. Discussions with a focus group suggested that the benefits of such a service was not well understood by GPs. Many of the GPs in the focus group felt their own computer system had all the information they needed. It was also felt that the Drug Information Service availability and function was not given sufficient promotion by the CCT.

3. Special Medication Review and Counselling

This service was for patients who the GP thought were at high risk of medication misadventure. These patients could then be referred to the CCT Project Pharmacist, who would then organise a meeting with this patient to provide them with special medication counselling. The aim being to help them to more effectively manage their medication, described as empowering the patient to take greater control of their medication. The CCT Project Pharmacist would then advise the GP on all details of their discussions with the patient.

Unfortunately, this service was only utilised by one GP for one patient. This was a disappointing result and the lack of take up of this service was thought to be a due to the GP`s lack of understanding of what the service involved or what it aimed to achieve. However, the experience gained from this service concept did provide a

model for a modified form of this service for patients being discharged from hospital. The focus continued on patients who were thought to be at high risk of medication misadventure. This concept is further discussed in the next two papers of this Chapter. This service concept was also developed by the Pharmacy Guild of Australia for consultant pharmacists in the community setting.

4.Medication Check Up

The aim of this project was to provide local GPs in the CCT with the opportunity to utilise an experienced clinical pharmacist to conduct a detailed review of the full range of medication being taken by patients who met a predetermined high-risk category for medication problems and safety.

This was equivalent to the normal medication reviews conducted by Clinic and ward based clinical pharmacists. The GP provided details of the patient`s medication by fax. The clinical pharmacists then provided the GP with a written report on suggested interventions and undertook a follow up telephone conversation with the GP.

This service was provided to GPs for seven clients, including some multiple consultations, over a six-month period. Although there was a disappointingly low uptake of this service, those GPs who did use the service were very enthusiastic about the benefits they gained from this service product. The GPs surveyed indicated that they would act on suggested recommendations. This service product was also further developed and modified by the Pharmacy Guild of Australia as a service that could be provided by community pharmacists.

It also provided a model for the operation of a clinical pharmacy service in a GP Practice.

5. Data Analysis

The CCT was given access to an extensive patient computer data base. This contained details such as PBS drugs prescribed and the patient`s diagnosis. This date base offered the capacity to search for patients who may have been at risk of medication misadventure. Various search strategies were tried using contraindications, drug interactions or age as key search terms. This provided some useful information. However, this evaluation process quickly identified a number of deficiencies in this data base. In particular, data on non-PBS medication and PBS medication which cost less than the patient co-payment were not available. These deficiencies limited the value of this strategy.

At a later stage, adjustments were made to the PBS claiming process for Public Hospital to include all medication. Unfortunately, this data base may not be available for general research at this time.

The results achieved for some of the service concepts outlined were disappointing, however, the CCT did enable a number of new service concepts to be evaluated. Many of which have been further developed.

The next two papers expand on the learnings from the above study. The first of which (Hana 2015) examined the patient and GP's perspective of the Hospital Outreach Medication Review (HOMR) service at Monash Health.
The HOMR service was gradually developed from a range of projects, but I was finally able to get the service fully approved in 2006, as part of the Victorian Government`s Hospital Admission Risk Program (HARP) at Monash Health.

The aim of this service was to follow up patients who were discharged from Monash Health and who were considered to be at high risk of medication misadventure. This follow up visit by the HOMR team pharmacist was normally conducted in the patient`s home but, in some cases at an Outpatient Clinic. It involved detailed medication counselling and guidance being provided by an experienced clinical pharmacist. At the conclusion of their interview, patients were asked to complete an anonymous survey and to return it to the HOMR team.

In 2012 a total of 487 HOMR interviews were conducted and 217 patients (45%) returned this patient feedback form. There were 99% of patients who thought the HOMR visit was beneficial to them and 84% felt that it increased their knowledge and understanding of their medication. There were 88% of patients who felt the clinical pharmacist provided them with useful suggestions on how to manage their medication, of which 94% agreed with the suggestions and 92% felt that all their questions had been answered. Patients were comfortable with the HOMR team pharmacist visiting their home and were happy for their information to be passed onto their GP.

The patient`s designated GP was provided with a written report on the HOMR interview with the patient and they also were asked to complete a feedback survey. There were 115 GPs (21.6%) who returned this standardised survey form.
Of these, 96% agreed with the recommendations made in the HOMR report and 48% said they would adopt all recommendations and a further 46% indicated they would adopt some of the recommendations. In general, all responding GPs were positive about the benefits of this service to their patients.

The second paper examined the impact of a hospital outreach medication review service on unplanned hospital readmissions and emergency department attendances (Hanna et al 2016). The focus continued to be on those patients who were thought to be at high risk of medication misadventure, using the same HOMR patient selection criteria. Patients were required to provide verbal consent to actively participate in the study, although the statistical data analysis of the control group, which contained patients who had not agreed to participate in the study.

Due to the introduction of CASEMIX and the advancement of computer technology and the associated increased data base storage, the Monash Health computer system enables patient hospital admissions and discharges to be monitored. In this study, active and control patient admission were monitored for each patient for 12 months before and 12 months after the HOMR visit to the patient`s home. The aim being to determine if there was any impact on unplanned hospital readmissions, adverse drug related or not, after the HOMR intervention by an experienced clinical

pharmacist as compared to control patients, where no such intervention was conducted.

The HOMR visit involved information from three sources;

1. Details on the patient`s medication history.
2. Information obtained from the patient`s medical record and information obtained from the patient`s GP and community pharmacist.
3. Information obtained by the clinical pharmacist in their discussions with the patient.

The patient level of medication adherence was assessed by the clinical pharmacist using a standardised format.

The clinical pharmacist assessed the patient, including a review of their prescribed medication and recorded any Medication Related Problems (MRP). This has a broader concept than simply dealing with prescribing issues which are described as a clinical pharmacist Intervention.

These details, along with the patient`s medication goals were faxed to the patient`s GP and community pharmacist. This was done within 10 days for 62% of the patients being discharged from a Monash Health hospital ward or Emergency Department.

During 2012 there were 487 HOMR visits conducted and these visits had an even distribution between male and female patients.

A total of 398 patients were considered in the study, along with 118 controls. A great deal of effort was made to eliminate confounding factors. In particular, patients who required regular admissions as part of their planned and regular care were excluded from the analysis.

The analysis of patient unplanned hospital readmission divided patients into three age categories of 50 years or less, 51 years to 65 years and those patients more than 65 years of age.

No differences were found between the study and control groups, over all age groupings, in the number of patients readmitted to the Emergency Departments over the study period.

There was an increase in total admission for both the study and control groups after the designated HOMR intervention.

In regard to unplanned ward readmissions, the following was found;

1. For those patients with an age of 50 years or less, there was an increase in the number of unplanned hospital readmissions.

2. For those patients between the age of 51 years to 65 years, there was a 25% reduction in unplanned hospital readmissions compared to the control group. This was found to be statistically significant.

3. For those patients with an age of more than 65 years, there was also a reduction in unplanned hospital readmissions compared to the control group. However, these figures did not reach statistical significance

It is difficult to draw a definitive conclusion from this data and it is not clear why there are differences between the various age groups.

It may be that the younger patients, 50 years of age or less, are better able to manage their medication and that an external intervention by a clinical pharmacist does not have an additional impact.

In the 51 to 65 years of age group, the additional advice may have been of benefit in empowering patients to take greater control of their medication.

This possible benefit may have also partly continued into the more than 65 years of age group. However, the complexity of their disease or disease progress may have limited the potential benefit from a HOMR intervention.

Other factors such as language and cultural aspects, may also be confounding factors.

Despite the positive trend seen in this study, especially for older patients, which suggests that the HOMR intervention may be of benefit in reducing unplanned hospital ward readmissions, further studies are required to clarify this potential benefit.

However, this it is a difficult area of study in which to establish clear benefits of any intervention, due to the many potentially confounding factors, especially the variations in the characteristics of patients.

Chapter Five

(Papers 24 -27)

Examining the Benefits of Research Collaboration between Hospital Pharmacy and Medical Departments

This Chapter focuses on papers in which I have been involved with and where I have been a collaborator in the research in areas outside my normal practice. In my role as a Director of Pharmacy, it always seemed important to develop the research opportunities for both the Pharmacy Department and the Health Service in which I worked. To this end, I have had a close involvement in the Human Research and Ethics Committee for 40 years and I have constantly sought opportunities for collaborative research with other Monash Health Departments, especially in medical research. The following papers are examples of this involvement.

Publication one, “Intermittent subcutaneous apomorphine injection treatment for Parkinsonian motor oscillations”. (Kempster et al 1991), explores the use of apomorhine subcutaneous injections to assist with severe motor fluctuations in patients who have been on long term L-dopa treatment for Parkinson`s disease.

My involvement commenced when Peter Kempster approached me to determine if my Pharmacy Department could produce apomorphine subcutaneous injections for use in those Parkinson patients who had significant “off periods” in their treatment. While the Pharmacy Department was in a position to produce very small volumes of this injection, there was no capacity to regularly produce the large volumes of ampoules needed to provide regular and ongoing treatment for the number of possible patients who could benefit from this treatment. In addition, the use of apomorphine injection for this Indication was still in its early stage of development.

Details on the formulation were obtained and refined. Due to the expected volume of ampoules required, I decided to contact a local pharmaceutical manufacture, then called, David Bull Laboratories, to determine if they could make the product for our use. Prolonged discussions took place and the Company eventually agreed to manufacture the product under contract and in accordance with normal legal requirements.

This enabled the clinical trial to proceed. Initially 8 patients (5 male 3 female), mean age 59years of age with a mean duration of disease of 16.1 years, were recruited to the clinical trial. Clear selection criteria were specified, with the main feature being that the patient suffered from a significant loss of mobility during “off periods”, with more than three such episodes per day.

These patients also received domperidone (20mg three times a day) to counteract the nausea and vomiting associated with apomorphine.

Patients were admitted to hospital to be assessed and to determine their commenced treatment dose. Initially a 1mg subcutaneous dose was given to patients, at the beginning of treatment with a further dose being given 20 minutes later. If no response was achieved, further doses were administered until a response was achieved. The optimal dose ranged between 1.4mg and 3.6mg (mean 2.8mg) with the onset of action occurred between 2.5 to 13 minutes (mean 9 minutes) and the duration of action was between 55 and 75 minutes (mean 63 minutes).

Patients and carers were taught to administer the subcutaneous injections. This empowered these patients to take greater control of their treatment of their “off periods”. It also enabled patients to have greater confidence in leaving their home on excursions.

There were two patients who were withdrawn from the study, one because of angina and one because the patient`s carer became seriously ill and could no longer supervise his wife`s treatment. However, 6 patients continued on the treatment for a mean of 6.5 months. The mean number of daily injections being 3.8 and a mean total daily dose of 11.6mg. All patients had a satisfactory response to the apomorphine treatment with a sustained improvement in the control of motor fluctuations. Patients were empowered to determine the frequency of their apomorphine subcutaneous injection.

Following the success of this clinical drug trial, this treatment option was offered to other suitable patients. The contracted pharmaceutical manufacturer therefore decided to proceed to have the apomorphine injection Registered and marketed. I assisted the Company in this process and also in helping with their submission to have the product included in the Highly Specialised Drug Program, under Section 100 of the National Health Act 1953. This enabled the apomorphine injection to be readily available and affordable by other appropriate patients. The work I did on this project was done in a totally honorary capacity.

The second paper “Chemotherapy Delays Progression of Motor Neuron Disease in the SOD1 G93A Transgenic Mouse” (Bruce et al 2003) examines the potential benefits of vincristine in reducing the proliferation of glial cells in the spinal cord and brainstem of SOD1 G93A transgenic mice.

I was approached by the study investigators to prepare and supply the vincristine injection for the study. I agreed to this request. The preparation of the vincristine injection was carried out in the Pharmacy Department`s Cytogard Safety cabinet in accordance with the Department`s standard good pharmaceutical practice. I was closely involved in the planning and formulation of this product. Double blinding of the treatments was also required.

Amyotrophic Lateral Sclerosis (ALS) is the most common form of Motor Neuron Disease and mutant superoxide dismutase (SOD1) mice provide a suitable model for examining the familial form of ALS. Vincristine is a chemotherapy agent that halts mitosis at the metaphase of the cell cycle. It has demonstrated activity against glial cells (Glioma)and glial cells are present in many neurodegenerative diseases. The aim of the study was to examine whether the inhibition of gliosis may be an effective strategy for ALS therapy.

The double- blind treatment of these mice began prior to the onset of the disease at postnatal date of 68 days and continued until the specified study endpoint. The mice were sacrificed when the mice had one or more hind leg paralysed.

The mice were given as an intraperitoneal injected of vincristine, 0.1mg per kilogram of body weight (n=6) or sodium chloride 0.9% placebo injection (n=4). These injections were given once every two weeks. Disease progression onset was measured according to standardise criteria.

The mean survival of the vincristine treatment group was 132 +/- 4.1 days compared with 117.8 +/- 2.1 days for the placebo group. The authors state the death rate in the placebo group was 3.8 times that of the mice treated with vincristine. Some changes were also reported in glial cell growth.

While the numbers in this study are small, there were nevertheless some interesting findings. Obviously further studies would be needed to examine this concept in greater detail. However, it does illustrate the importance of the co-operation of a hospital pharmacy department in enabling this study to be conducted safely.

The third paper in this Chapter relates to the “Assessment of aminoglycoside dosing and estimated glomerular filtration rate in determining gentamicin and tobramycin area under the curve and clearance” (Lim et al 2015).

I was approached by Andy Lim in regard to considering a review of the data available on the use of aminoglycosides at Monash Health. The Pharmacy Department at Monash Health had participated in the monitoring of aminoglycoside infusions, using basic pharmacokinetic parameters, for a number of years. This data was available in the Aminoglycoside Levels and Daily Dose Indicator (ALADDIN) program based in the Pharmacy Department. I was involved in the discussions and review of the data and was responsible for the extracting of the required data from the ALADDIN data base.

The study involved the review of 496 aminoglycoside treatment episodes (319 patients) involving 1377 daily intravenous infusions. Of these, there were 216 treatment episodes involving tobramycin and 280 involving gentamicin. Data on amikacin infusions were excluded due to the small number of cases. Only patients who were 18 years of age or older were included. The data used was collected over the April 2010 to December 2012 time period.

The aminoglycoside clearance was determined from linear regression using a one compartment model. All analysis was performed on IBM SPSS version 20.

Since aminoglycosides are predominantly cleared by the kidneys, the consideration of glomerular filtration was thought to be an important factor when determining dosage.

To this end, the traditional Cockroft-Gault equation was compared to the Modification of Diet in Renal Disease Study (MDRD) and the Chronic Kidney Disease-Epidemiology Collaborative (CKD-EPI). Our study found that using the CKD-EPI equation, adjusted for body surface area, showed the highest correlation and best predictive model for aminoglycoside clearance.

The study found that the dosage guidelines in the Australian Therapeutic Guidelines for Antibiotics (version 14, 2010) dosage guidelines for aminoglycosides had limitations. It was observed that only 29.6% of patient on gentamicin and 33% of patients on tobramycin achieved their target Area Under the Curve (AUC) on the initial infusion for all treatment episodes. It was also noted that conformity with the Antibiotic Guidelines was achieved, if the prescribed and recommended dose was less than 15%.

In conclusion, it was considered that the Australian Therapeutic Guidelines for Antibiotics, of that time, for aminoglycoside dosage needed improvement. In particular, it was felt that renal function also needed to be considered, as occurs with the ALADDIN program were the drug plasma levels used reflect renal function and were serum creatinine levels and creatinine clearance are taken into consideration. However, this study did not take the patient`s disease severity into consideration, which may lead to some subtle variations.

The fourth paper in this Chapter relates to" Deferasirox at therapeutic dose is associated with dose-dependent hypercalciuria" (Wong et al 2016).

This project commenced due to concerns regarding the incidence of hypercalciuria in association with the use deferasirox in the treatment of iron overload in patients with a variety of haemoglobinopathies. There were also concerns in relation to osteoporosis and urolithiasis, although these aspects are not studied in this paper. I was approached to consider aspects of the data and was involved in the review of the manuscript. I was also involved in discussions with the Therapeutic Goods Administration in relation to reported medication safety issues associated with deferasirox, including bone loss.

Monash Health has a very large Thalassemia Unit and therefore has an extensive data base on the treatment of these and related patients.

The study involved a cross-sectional cohort of 152 adult patients in 2014, the vast majority of these patients suffered from beta thalassemia major (81.5%). These patients were matched with controls selected from patients enrolled the Australian Diabetes, Obesity and Lifestyle (AusDia) study.

The dose of the iron chelating agent used was standardised to mg/kg/day. A wide range of tests were conducted with the synchronous urine and biochemistry collection of samples. Bone mineral density was measured using dual energy X-ray absorptiometry (DXA). One-way ANOVA was used to determine differences between hypercalciuria severity with clinical and biochemistry variables.

The urine calcium to serum creatinine ratio was calculated for all patients and a ratio of greater than 0.4 mol/mol was defined as hypercalciuria. The severity of hypercalciuria was put into three groups according to these ratios. Normal was defined as less than 0.4 mol/mol, 0.5-1.5 mol/mol as moderate and greater than1.5 mol/mol was defined as severe. Increased urine protein excretion was defined as a urine protein to creatinine ratio of greater than 0.3.

The study cohort patients had a mean age of 34 years and 42% were males. There were 18 patients being treated with deferoxamine (also called desferrioxamine) with a mean dose of 44.1 mg/kg/day and 134 patients were treated with deferasirox with a mean dose of 23.2 mg/kg/day.

The study found hypercalciuria to be present in 91.9% of patients treated with deferasirox and in 83.4% of those patients being treated with deferoxamine, in the presence of normal serum creatinine. A significant positive association between the weigh-adjusted deferasirox dosage and the severity of hypercalciuria, after adjustment for confounding factors, was found. No such association was found between the weight-adjusted dose of deferoxamine and hypercalciuria severity, although there were only 18 patients in this group. Hypercalciuria was not found in the 124 control subjects.

There were 11% of male and 8% of females which had no hypercalciuria, 72% of male and 64% of females were considered to have moderate hypercalciuria and 17% of males and 28% of females were considered to have severe hypercalciuria.

From this novel identification, it was concluded that that therapeutic doses of deferasirox exacerbated hypercalciuria in a dose dependent association. This was therefore thought to be an important factor to consider in when patients taking this medication displayed urolithiasis and/or significant bone mineral density loss. This aspect is open for further research and has critical implications for the long-term safety of patients requiring deferasirox treatment.

Extent to Which the Work Contributes to the Advancement of Knowledge

The papers listed in this Thesis cover a wide range of issues
and the discussion will group the issues according to the Chapter of the Thesis.

Chapter 1 (papers 1 to 13)

Chapter one of the Thesis, covering papers 1 to 13, focuses on the emergence and development of clinical pharmacy practice. Papers 1 and 2 define the detailed tasks involved in clinical pharmacy practice, focusing on clinical services in the ward setting, but these principles can also be applied to other hospital pharmacy practice settings. These papers provide clear guidelines on the skills and knowledge that are required in clinical pharmacy practice. This information then provided assistance and guidance in the design and structure of academic and the in-service hospital training programs. Unfortunately, the latter was the only option initially available. This was further aided by the very detailed guidelines provided in papers 1 to 5 and 7 to 10.

The emergence of a new form of professional practice also requires the development of systems to promote, teach and monitor the associated standard of practice. This aspect is considered in papers 3 and 4. Due the absence of academic support at that time, considerable detail was developed on the types of in-service training that hospital pharmacists could provide to their staff. Due to the autonomous and independent nature of clinical pharmacy practice, direct supervision of performance was not practical in most settings. Therefore, the focus needed to be on education, training, experience and self-motivation. An important concept that was developed was Peer Review, especially the component of ward visits. To be successful, this review of a ward pharmacist`s skills and performance needed to be done in a positive and motivational manner. This concept has been further developed over many years and is now a key component of the SHPA Clinical Pharmacist Accreditation program.

A benchmark survey of Victorian clinical practice in paper 4, aimed to further promote the adoption of clinical pharmacy practice in public hospital pharmacy departments, especially in Victoria in 1984. This survey serves to illustrate how far the hospital pharmacy practice in Victoria has progressed since that time.

Paper 6 examines the views of patients on what medication information and counselling they would like to receive. This paper enabled further insights on this subject and provided guidelines for the development and preparation of future patient education information leaflets at the hospital. The emphasis of this work was to gain an understanding of the patient`s needs and wishes in relation to medication information. The study clarified that the needs of patient varies considerably from patient to patient.

Papers 7 to 10 focus on the development of Quality Assurance for all aspects of public hospital pharmacy practice, culminating in paper 10, Performance Indicators in Hospital Pharmacy Practice. These papers provide a template and guidelines to hospital pharmacists on the development and implementation of Quality Assurance systems and practices in their hospital pharmacy departments. Paper 10 concisely outlines how to establish an effective Quality Assurance Program, this structure can be applied in general or, in particular, to Hospital Pharmacy Departments. The paper has been especially popular and has been widely read on Research Gate. The paper was listed on Research Gate in late 1971 and as at 10 March 2020 there have been 1855 reads, currently there are between 15 to 42 reads per week by readers from all over the world. Indicating that the paper provides a valuable reference for others.

Paper 12 takes the principles in these other papers and explains and demonstrates how Quality Assurance Programs can be put into everyday hospital pharmacy practice.

Publication 11 provides a management model to examine the financial related benefit of hospital pharmacy salary expenditure and hospital medication costs. High pharmacy department salary costs are very closely related to the extent of the clinical pharmacy services being provided in that hospital. This is a very difficult area of study and hence there are very few publications on this subject and those that do,

involve very complex methodologies. The management evaluation model in publication 11, provides a simple innovative and useful high-level evaluation methodology to help in the support of budget submissions to extend clinical pharmacy services. This benchmark study, based on 1997 costs and using linear regression analysis, found that drug costs (excluding S100 drugs) decreased by an average of $5.20 (95% confidence interval of $2.38 to $8.01) per bed day for every dollar of pharmacy salary cost per bed day.

Paper 13 examines the concept of providing clinical pharmacy service in a surgical preadmission clinic. This prospective randomised controlled design study found that the Intervention Group of patients had a more complete medication history and 31% more clinical pharmacist interventions recorded than the Control Group. This study supports the importance of clinical pharmacy practice in a setting other a hospital ward, especially in various types of hospital outpatient clinics.

The information contained in the papers in Chapter One also provided the basis for the education sessions that I conducted for the Beijing Hospital Pharmacy Department in 2009 and 2011 to help and guide them in the development their clinical pharmacy services.

The experience and knowledge that I gained from writing the papers in this Chapter enabled me to produce and very detailed document titled The Changing Role of Hospital Pharmacist and the Need for a Four Year Pharmacy Undergraduate Course for the SHPA and the Joint Four Year Committee for presentation at the Pharmacy School Heads Conference in 1990. The Executive Summary of this document is included as an Appendix at the end of the Thesis. This document still provides an important historical record on the development of clinical pharmacy practice in Australia. The document is large so only the Executive Summary is included.

Chapter 2 (papers 14 and 15)

In Chapter 2, the subject of Adverse Drug Reactions (ADR) is considered. Paper 14 examined Drug Reactions as a cause of unplanned Hospital Admissions. This study examined 5623 cases admitted over a six months study period to the Prince Henry`s site of Monash Medical Centre. This found 2.4% of cases were drug related, of which 1.6% (90 cases) were due to an ADR. Of these 30% were thought to be related to a drug interaction and only 19% were considered to be idiosyncratic. Suggesting potential iatrogenic involvement in many cases. The study examined various risk factors and the drugs most frequently thought to be involved. The study also confirmed that increased age (53% over the age of 70 year compared to 14% in the control group) and increased numbers on concurrent medications (4.9 +/-2.6 verses 3+/-2.8 in the control group) were very specific risk factors. There were 5 fatalities, 2 of which involved a drug interaction with warfarin and 2 involved NSAIDs which precipitated haematemesis and melaena. The study also examined a number of multiple admission patients to obtain a greater understanding of the factors involved in these cases. This study provided valuable information on the extent and risk of drug related hospital admissions. In doing so it also illustrated the need for greater awareness of these risks of ADRs. It also emphasised the need for education and communication strategies on the impact and consequences of ADRs.

Paper 15 considers whether ADRs could be reliably identified in a Victorian public hospital through the use of the ICD-IO Australian Modification Clinical coding, especially the use of Y sub-codes, Y40 to Y59. The documentation of ADRs provides valuable information on the safety and risks associated with medication, especially after a medication`s Registration has been approved. However, the vast majority of this work has involved spontaneous reporting, rather than through a systematic evaluation process. The main drivers of this situation are the extensive workload demands and the associated labour costs needed for an effective systematic review process. This study illustrates how a thorough and extensive medical record coding service can be utilised to produce a systematic and effective process to detect ADRs that have occurred in a specific Victorian public hospital.

The study involved the retrospective review of multiday stay discharge patient separations (excluding Hospital in the Home patients) who had a Y40 to Y59 sub-code in their medical record. There were 412 separations (3.3%) over the study period were an ADR was recorded, including 157 (1.3%) separations where an ADR was thought to cause a hospital admission. Of the medical records reviewed, it was found that an ADR was identified in 86% of cases and that the coding allocated was correctly and appropriately assigned in 94% of cases. Of the ADRs reviewed, 51% were considered serious and 57.6% of cases were considered to be probably or definitely drug related. This study identified that coding led to the identification of an additional 397 ADRs that would otherwise have been missed if spontaneous reporting had been used on its own. Supporting the belief that ADRs are substantially under reported.

The study confirmed that the systematic review of ICD-10 Australian Modification Clinical Coding is an effective cost-efficient approach for the identification of ADRs and provides another option for Post Marketing Surveillance of medication.

Chapter 3 (papers 16 to 21)

In Chapter 3 there are variety of papers covering new concepts in Hospital Pharmacy Management strategies on a range of different topics.

The first of which, paper 16, relates to the integration of an existing computer dispensing system with an electronic prescribing system that was being developed. The objective of the integrating of the two computer systems was to improve dispensing and prescribing efficiency and to achieve greater patient medication safety. The aim of this study was to show that these benefits were achieved.

The study firstly involved a survey of 379 patient prescriptions (654 medications) over a two-week period prior to the introduction of the new integrated system. This data was compared to that obtained in a second two-week survey, using the same methodology, which involved 375 patient prescriptions (635 medications) that was conducted several months after the new integrated system was introduced.

The findings of this study were:

- The number of prescribing errors per patient was reduced from 2.98 to 0.2 errors per patient, a 93% reduction
- The number of prescribing errors per medication was reduced from 1.72 to 0.12 per medication, a 93% reduction.
- The number of dispensing errors per patient was reduced from 1.27 to 0.027 per patient, a 97.9% reduction.
- The number of dispensing errors per medication was reduced from 0.76 to 0.17 per medication, a 97.8% reduction.
- The median out-patient prescription waiting time was reduced from 27 to 13 minutes, a 52% reduction.

Therefore, this study clearly demonstrated the medication safety benefits of having a fully integrated computer software prescribing and dispensing system. In particular, it

demonstrated that a significant reduction in prescribing and dispensing errors was achieved.

Financial Management of drug expenditure is a very complex and difficult area of hospital pharmacy practice, presenting many difficult challenges and often requiring innovative creative solutions. A task often made more difficult by the continuous drive by State and Federal Governments for resource efficiency. However, a major step forward occurred when the Pharmaceutical Reform of the PBS to allow approved public hospitals to dispense PBS medication for outpatients, patients being discharged from hospital and oncology day patients.

The next four papers examine medication financial management and provides innovative concepts and approaches in the management of this difficult area of practice. An area of practice that is often not well documented.

Paper 17 examines the complex interactions between varied and various hospital stakeholders, especially medical staff, and outlines the Complex Matrix of communication and negotiation needed in a Victorian public hospital. In particular it aims to explain and understand the cultural aspects and influences of these interactions. Of particular importance, the paper considers how key medical staff could be more involved in the decision-making process for the management of medication and in the creation of a constructive culture of co-operation.

The paper aims to illustrate and put forward a formal model of how medication can be managed, especially in relation to the Hospital`s Drug Formulary and Therapeutics Committee.

This included specifying two levels of drug formulary selection criteria, the use of a Financial and Drug Utilisation subcommittee and the process of requiring individual patient progress reports for selected high cost drugs for patients who meet carefully specified patient selection criteria. Using the term “Prescribing Authorisation”, rather than “Prescribing Restrictions”, and closely involving medical staff in all these decision-making processes are also discussed.

The paper introduces the concept of Duplex Budgeting. That is a process of sharing joint budget responsibility, were the Pharmacy Department continued to provide overall management of the Drug Budget, but many sections of this budget are broken up into a series of Sub-Budgets, which are also concurrently managed by a variety of specified key stakeholders.

The paper also introduces and promotes the term “efficient drug utilisation”. The aim being to encourage the use of the cheapest alternative drug from a group of drugs used for the same indication, where there was evidence of no difference in efficacy and safety. To be effective this required the hospital Therapeutics Committee to manage the concept and to negotiate acceptable proposals with key stakeholders. The experience gained in this project was a precursor for the Therapeutics Equivalence Program discussed in papers 19 and 20.

In conclusion, the paper provides details and guidance on the drug budget and its associated management systems in public hospitals, information that is often not widely known or published. The paper also provides details on these processes as an example that others may wish to follow. Many of the concepts can also be considered to be innovative, especially at the time when the paper was first published.

Paper 18 provides guidance on the successful introduction of the PBS into Australian public hospitals. The paper outlines the various issues that needed to be addressed and aimed at providing advice and guidance to any Australian public hospital wishing to take part in this Pharmaceutical Reform process. The introduction of the PBS into three Victorian public hospitals on January 2002 was perhaps one of the most significant events in the history of Australian public hospital pharmacy practice. This Pharmaceutical Reform process has now been adopted by most public hospitals right across Australia. The reforms covered PBS medication dispensed to outpatients, patients being discharged from hospital and day oncology patients. Its introduction enabled a number of unsatisfactory anomalies to be resolved. In particular, it enabled the inequality of access for many high cost drugs to be resolved. The paper only illustrates a fraction of all the work done behind the scenes

over many years. Nevertheless, the paper provided valuable and comprehensive guidance for many hospital pharmacists in Australia.

The introduction of the PBS into Australian public hospitals also enabled the Pharmacy Departments in these hospitals to achieve significant financial savings which, in turn, provided the opportunity to enabled greater resources to be put into medication safety projects and clinical pharmacy services. The PBS was initially developed for use in community practice, therefore many innovative changes were needed to enable the successful introduction of the PBS into Australia public hospitals. The most notable of these being the changes to computer dispensing software and the redesign of prescription forms. An additional consequential benefit achieved was that the format of the outpatient and discharge patient prescription form was standardised for all hospitals involved in the reform process. A significant benefit in the goal of promoting the safe prescribing of medication.

Papers 19 and 20 introduce the subject of a Therapeutics Equivalent Program (TEP), which builds on the previously outlined strategy to improve and promote efficient and safe drug utilisation.

The introduction of the PBS into Victorian Public Hospitals enabled very significant savings in medication costs for Monash Health. However, there was ongoing pressure to further reduce medication costs for the hospital. The concept of Therapeutics Equivalence offered the opportunity to achieve these savings without the need to institute mandatory arbitrary prescribing restrictions. However, to be successful the support of prescribers is needed. The arbitrary introduction of TEP without this support has been reported in the literature, but success with these studies appears to have been limited.

The first paper describes the processes used to gain the collaborative support of the Monash Health medical staff. The study demonstrated that the support of medical staff can be achieved by involving them in the development and introduction of TEP. The achievement of this goal was not considered a possibility by many administrative staff.

It is important to recognise that TEP is not dependent on the availability of generic competitive products. Rather it adopts the concept of creating competition between products when no such competition previously existed. This is achieved by comparing medications that have the same pharmacological or therapeutic receptors and are used for the same indication, when evidence of equivalent safety and efficacy is available. The information in these two papers provides guidance on a different strategy to achieve very significant medication savings.

Paper 19 covers the time frame of the 2006/07 to 2009/10 Financial Years. During this period a saving of $3.16 million was achieved via the TEP. The patient separations over this time period increased by 10.4%, however the savings achieved increased by 65.5%. In doing so it provides solid support for the effectiveness of the TEP based on the voluntary support of the hospital`s medical staff.

Paper 20 demonstrated the continued success of the TEP over the 2010/11 to 2014/15 Financial Years in which a further savings of $7.18 million was achieved. This paper also examines the factors influencing the effectiveness of the TEP and outlines the learning achieved from TEP over the total study period, including the influence of market dynamics.

The total savings achieved via the TEP over the 2007/8 to 2014/15 Financial Years was $10.54 million. This innovative approach to a complex problem has demonstrated that success can be achieved with a carefully planned TEP. These two papers provide a path and guideline for others to consider.

The significant savings achieved from such Programs enabled expenditure on other areas of practice that would otherwise not have been possible, especially medication safety services.

Paper 21 aimed to develop a simple version of “Queuing Theory” in order to ensure adequate Pharmacy Department staffing would be available at times of peak workload in the outpatient section of the Department. The objective was to minimise patient waiting time and to ensure adequate staff were available to reduce the risk of medication dispensing errors. This systematic approach to workload and patient

numbers worked well. The study of historical work patterns and the manual counting of patients did assist in the organisation of workload. It also assisted in the planning of the days to employ extra staff and the employment times for part time staff. The mathematical model helped staff to understand the prescription queuing effect and the need for timely planning. The mathematical model complexity limited its full application at the time. However, this mathematical model could be successfully linked to current pharmacy dispensing software and barcode scanning systems.

Chapter 4 (papers 22 to 24)

The papers in Chapter 4 examine the development of hospital pharmacy department outreach programs.

Paper 22 is based on work that was done under a National Co-ordinated Care Trial grant allocated to Monash Health. Part of this funding budget was allocated locally to a Pharmacy Strategy Group, which I co-ordinated and led. The aims of this Group were to consider and develop models of care to minimise medication risks and to promote safe and efficient use of medication, with a particular focus on how to improve and promote relationships between clients and the healthcare provider. This work led to the identification of five potential service products which were examined and developed, namely:

1.Education Outreach Program

The aim of this service was to examine the use of the "Academic Detailer" concept to provide medication educational support to community medical practitioners. Two topics of education were chosen; namely; the "Eradication of Helicobacter pylori in peptic ulcer disease" and "Promoting of the rational use of NSAIDs". This service was well accepted by the GPs visited and 75% indicating they would take action on the advice provided and 96% requested a further visit. It also appeared to have some influence on the frequency of NSAID prescribing, but the small size of the sample and the number of confounding factors, limited the interpretations that could be made on the results achieved. This sub-study provided further evidence of the benefits that this type of service can provide.

2.Drug Information Services

This was not a new service but since the service at Monash Health was being well utilised, further evaluation was not thought to be a high priority for this study. However, the high utilisation of this service by both health practitioners and patients suggested the service should continue and be supported.

3.Special Medication Review and Counselling

The aim of this service was to enable GPs in the trial the opportunity to refer patients, who they thought were at high risk of medication misadventure, to a clinical pharmacist. The role of the clinical pharmacist was to review the patient`s medication and to determine if there were any useful strategies that could be employed to reduce the risk of medication problems. A similar service to that provided by a ward clinical pharmacist. The aim was to give patients advice on their medication and to empower the patient to take greater control of the management of their medication. Unfortunately, only one GP took up this offer. A lack of understanding of this service by GPs and various logistic difficulties, seemed to be the underlining causes of this service not being well utilised. However, this pilot study did provide useful guidance on the potential benefits of medication reviews. This evaluation also clarified the need for structural changes to be made to such a service to enable it to work more effectively. This included focusing on patients being discharged from hospital. The next two papers explore this concept in greater detail. A similar model was also adopted later in a community pharmacy project where the GP referred patients to an accredited pharmacist.

4.Medication Check UP

The aim of this service was to provide a clinical pharmacist to support GPs, in the trial, for patients who had difficult medication issues. This was similar to the clinical pharmacy services provided in a number of public hospital outpatient clinics. Unfortunately, it was not possible for the clinical pharmacist to be located in a clinic at a GP practice in this study, but it was thought this would be the most effective model. However, this model is now increasingly being introduced into GP practices.

There was only limited take up of this service by GPs in the trial, but those that did use the service were very enthusiastic about the benefits they received from this service.

It was thought that the lack of funding resources limited the promotion of the aims of services 3 and 4 to GPs and that this factor, along with the limited number of

pharmacists involved in the study, inhibited the uptake of these services by GPs. Nevertheless, these pilot studies did lay the groundwork for the introduction of such new innovative services at a later time.

5.Data Analysis

The CCT was given access to an extensive patient computer data base. The Pharmacy Strategy Group thought that the analysis of this data base may provide an opportunity to be able to detect patients who may be at risk of medication misadventure. The consent of patients was obtained before this study was carried out.

However, although this was an extensive data base, it nevertheless had a number of major deficiencies, in particular non-PBS drugs and those PBS drugs costing less than the PBS co-payment, were excluded. Various search strategies, for example, potential drug interactions or medication contraindications, were conducted. However, the limits of the data base restricted the benefit of such studies. Therefore, only limited work was done on this service. However, it did provide valuable experience and an understanding of how such data bases can be used effectively. This knowledge was very valuable in the work conducted in paper 24.

The next two papers expand on the learnings from the above study and examines the Hospital Outreach Medication Review Service (HOMR) provided to GPs for patients who were thought to be at high risk of medication misadventure.

Paper 23 aimed to evaluate the attitudes of patients and GPs to the HOMR service. The GPs and patients involved in the study were routinely provided with a survey form.

There were 487 patients interviewed in 2012 and 45% responded to this anonymous survey. This study found that there were 99% of patients who thought the HOMR visit was beneficial to them and 84% felt that it increased their knowledge and understanding of their medication. There were 88% of patients who felt the clinical pharmacist provided them with useful suggestions on how to manage their

medication and 92% felt all their questions had been answered. There were 94% who agreed with the suggestions provided. Patients were also happy for their information to be passed onto their GP and they were comfortable with the HOMR team pharmacist visiting their home.

There were 115 GPs (21.6%) who returned their standardised survey form. In general, all responding GPs were positive about the benefits of this service. There were 96% who agreed with the recommendations made in the HOMR report and 48% indicated they would adopt all the recommendations and a further 46% said they would adopt some of the recommendations.

The findings reported in this paper indicated the positive acceptance by both patients and their GPs. In doing so, it has provided positive support for the further development of this service.

Paper 24 examined the impact of the HOMR service on hospital unplanned patient readmissions and Emergency Department attendances. Patients were required to provide verbal consent to participate in this study. The same HOMR patient selection criteria used in the previous paper were used in this study. This study also used the extensive Monash Health computerised patient data base. This data base was developed over a number of years following the introduction of the CASEMIX hospital funding model into Victorian Public Hospitals.

A total of 398 patients who had a HOMR visit during 2012 were included in the study. The unplanned hospital and Emergency Department re-admissions of these patients were monitored for 12 months before and 12 months after the patient`s HOMR visit or contact with the hospital. A control group of 118 patients were also analysed.

In order to eliminate a number of confounding factors, it was necessary to eliminate those patients whose treatment required routine regular admissions to hospital, such as dialysis and oncology patients.

The analysis of patients was divided into three age groups, namely 50 years or less, 51 to 65 years and those patients more than 65 years of age.

No differences were found between the study and control groups, over all age groups, in the number of patients readmitted to the Emergency Departments over the study period.

However, in the case of unplanned hospital ward re-admissions it was found:

1. For those patients with an age of 50 years or less, there was an increase in the number of unplanned re-admissions.

2. For those patients between the age of 51 to 65 years, there was a 25% reduction in unplanned hospital ward readmissions, compared to the control group. This was found to be statistically significant.

3. For those patients with an age of more than 65 years of age, there was also a reduction in unplanned hospital ward readmissions compared, to the control group. However, these figures did not reach statistical significance.

It is difficult to draw a definitive conclusion from this data and it is not clear why there are such differences between the three age groupings.

It is suggested that the younger patients, 50 years of age or less, may be able to better manage their medication and that an external intervention by a clinical pharmacist may not have an additional impact.

In the 51 to 65 years age group, it possible that the additional advice and discussions may have been of benefit in empowering patients to take greater control of their medication and in doing so they were able improve the management of their medication.

This possible benefit may have also had a benefit to some patients in the more than 65 years age group. However, the complexity of the patient`s disease or the

progress of their disease may limit the potential benefit obtained from a HOMR intervention.

This is a difficult area to study due to the number of potential confounding factors, such as language and cultural aspects. Nevertheless, this study does indicate that the HOMR service may assist in reducing unplanned hospital readmissions for some patients. The GP and patient surveys also indicate the HOMR service is well accepted and that it provides a perceived benefit. This work therefore suggests the HOMR service should continue. Further studies in this area of practice, to confirm or expand, the understanding of these potential benefits should be encouraged.

Chapter 5 (papers 25 to 28)

The next Chapter covers papers involving collaborative multidisciplinary research. This type of research is an important component of hospital practice and the involvement of the hospital`s Pharmacy Department enables the specialised skills of hospital pharmacy practice to be utilised. In my role as a Director of Pharmacy I undertook to promote this type of collaboration.

Paper 24 evaluates the intermittent subcutaneous use of apomorphine injection in the treatment of Parkinsonian Motor Oscillations. This work enabled the benefits of this treatment to be confirmed and led to the availability of apomorphine injection in Australia for this indication.
The open study initially involved 8 patients, but two were later withdrawn. One due to unrelated angina and the other due to logistical problems. However, 6 patients continued on the apomorphine treatment with a sustained improvement in the control of their motor fluctuations. Patients were empowered to determine the frequency of their apomorphine subcutaneous injections.

The success of this study enabled this treatment option to be made available to other suitable patients in Australia. This in time led to apomorphine injection being available on the Australian market via the Highly Specialised Drug Program, under section 100 of the National Health Act 1953, which meant the product was able to be afforded by all suitable patients.

Paper 26 examined the effectiveness of vincristine in delaying the progress Motor Neuron Disease in SODI1 G93A Transgenic Mouse.
Vincristine was given by intraperitoneal injection to 6 mice and the sodium chloride placebo intraperitoneal injection was given to 4 mice. These injections were given every two weeks. The mean survival of the vincristine group was 132 +/- 4.1 days compared to 117.8 +/- 2.1 days for the placebo group, that is a death rate 3.8 times that of the vincristine group. While the numbers in the study are small, the results perhaps indicated the need for further studies to investigate this concept. The work does also illustrate the importance of the co-operation of a hospital pharmacy department in enabling the safe conduct of such studies.

Paper 27 examines the influence of an estimated glomerular filtration rate in determining gentamicin and tobramycin area under the curve and clearance.

The focus of the study was to consider whether the dosage guidelines for aminoglycoside antibiotics listed in the Australian Therapeutic Guidelines for Antibiotics (version 14, 2010) were optimal.

Aminoglycoside clearance was determined from linear regression using a one-compartment model. All analysis was performed on IBM SPSS version 20.

The data analysis utilised patient data in the Pharmacy Department`s Aminoglycoside Levels and Daily Dose Indicator (ALADDIN) program from April 2010 to December 2012.

The study involved the review of 496 aminoglycoside treatment episodes (319 patients) involving 1377 daily intravenous infusions for patients who were 18 years of age or older. There were 216 treatment episodes involving tobramycin and 280 involving gentamicin. Patients receiving amikacin were excluded due to the small number of patients involved. The predominant clearance route of aminoglycosides is via the kidneys and therefore the estimation of the patient`s glomerular filtration was thought to be important. To this end, the traditional Cockroft-Gault equation was compared to the Modification of Diet in Renal Disease Study (MDRD) and the Chronic Kidney Disease-Epidemiology Collaborative (CKD-EPI). This found that the CKD-EPI equation, adjusted for body surface area, showed the highest correlation and best predictive model of aminoglycoside clearance.

It was found that following the dosage guidelines for aminoglycoside, as listed in the Australian Therapeutic Guidelines (version 14, 2010), resulted in only 29.6% of patients on gentamycin and 33% of patients on tobramycin achieving their target Area Under the Curve (AUC) on the initial infusion for all treatment episodes. It was concluded that the dosage guidelines for aminoglycosides in this publication could be improved, especially in regard to giving consideration to the patient`s renal function.

Paper 28 examines the novel finding of Deferasirox, at therapeutic doses, being associated with dose-dependent hypercalciuria".

The study involved 152 patients receiving an iron chelating drug in 2014. The vast majority (81.5%) of these patients were suffering from beta thalassemia. The mean age of patients was 34 years of age and 42% were males.

These patients were matched with controls selected from patients who were enrolled in the Australia Diabetes, Obesity and Lifestyle (AusDia) study. The investigations involved a wide range of tests conducted with synchronous urine and biochemistry collection samples. One-way ANOVA was used to determine differences in hypercalciuria severity.

The urine calcium to serum creatinine ratio was calculated for patients. This ratio was used to grade the severity of hypercalciuria. The ratio of 0.4 or less mol/mol was considered normal, 0.5 to 1.5 mol/mol was graded as moderate and greater than 1.5 mol/mol was defined as severe.

The dose of the iron chelating drug used was standardised to mg/kg/day. There were 18 patients who received deferoxamine (desferrioxamine) with a mean dose of 44.1 mg/kg/day and 134 patients were received deferasirox with a mean dose of 23.2 mg/kg/day.

The study found hypercalciuria was present in 91.9% of patients being treated with deferasirox and in 83.4% of those patients receiving deferoxamine, in the presence of normal serum creatinine. A significant positive association between the weight-adjusted deferasirox dosage and the severity of hypercalciuria, after adjustment for confounding factors, was found. This association was not found with deferoxamine, however only a small number of patients were in this group. No hypercalciuria was found in the 124 control patients.

There were 11% males and 8% females who had no hypercalciuria, 72% males and 64% females had moderate hypercalciuria and 17% males and 28% females were

considered to have severe hypercalciuria. It was concluded that therapeutic doses of desferasirox could exacerbated hypercalciuria in a dose dependent association. This was therefore thought to be an important factor to consider when patients taking this medication displayed urolithiasis and/or significant bone mineral density loss. This suggests a benefit in further research to examine the long-term safety of deferasirox treatment.

This section of the Thesis outlines the findings and achievements on a wide range of related topics covered in the 28 papers comprising the Thesis. Each of these achievements have their own importance and are reflective of a life-long career, often illustrating the logic behind the development of new services in a Victorian Public Hospital Pharmacy Department. The underlying theme being patient medication safety and is centred on clinical pharmacy and related practice, including its expansion and development into other areas of practice. There is also a theme of innovation, promotion of quality of practice and medication prescribing efficiency which produced expenditure savings that enabled medication safety services to be further developed. The importance of multidisciplinary research and the benefits of involving pharmacists in such research is illustrated.

In conclusion, the Thesis covers a wide range of related subjects, which when combined have aimed to improve patient medication safety through the evolution of, and innovation in, hospital pharmacy practice over a sustained period of 45 years.

List of Publications

Chapter One

Examination the Emergence of Clinical Pharmacy Practice in Victorian Public Hospitals

1. Larmour I (1980); Clinical Activities of Ward Pharmacists - A Five Year Perspective - Part 1 - Guidelines of Practice AJHP, 10, 95-101.

2. Larmour I (1980); Clinical Activities of Ward Pharmacists - A Five Year Perspective - Part 2 - The Importance of the Pharmacists Role AJHP, 10, 131-136.

3. Larmour I, Allinson Y, Manser A et al (1984); Clinical Ward Pharmacy Quality Assurance AJHP, 14, 54-60.
    a. Citations 2

4. Larmour I, Allinson Y, Manser A et al (1984); Clinical Ward Pharmacy Survey - Victorian Hospitals 1982 AJHP, 14, 65-70. Citations 6

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Reference Details of Papers Listed in the Submitted Papers

Please note, the reference details of the papers listed in the in the submitted papers have not been separately listed.

Appendix - Published Papers

Chapter One

Examination the Emergence of Clinical Pharmacy Practice in Victorian Public Hospitals

1. Larmour I (1980); Clinical Activities of Ward Pharmacists - A Five Year Perspective - Part 1 - Guidelines of Practice AJHP, 10, 95-101.

Clinical Activities of Ward Pharmacists – A Five Year Perspective – Part 1 – Guidelines of Practice

IAN LARMOUR,
Deputy Chief Pharmacist,
Prince Henry's Hospital, Melbourne, Victoria

October, 1978

ABSTRACT

"The clinical activities of ward pharmacists after five years experience at Prince Henry's Hospital, Melbourne are reviewed. A series of two articles are based on a paper presented at the 1978 Victorian State Branch Conference of the Society of Hospital Pharmacists of Australia".

Six clinical roles for the ward pharmacists are identified – Evaluating drug therapy orders; Noting potential problems and selecting relevant parameters to monitor; Monitoring these parameters; Co-ordinating the collection of ADR reports; Providing drug information and the collection of drug utilisation review statistics.

The first article deals with the general guidelines of practice, with particular emphasis on the first five roles and the work flow of the ward pharmacists.

INTRODUCTION

The philosophies of clinical pharmacy practice have been widely discussed in recent years, and the general principles have been well documented by Brodie (1). However the details of practice have not been thoroughly elucidated. The purpose of these two articles is to attempt to define the clinical activities of ward pharmacists after five years experience at Prince Henry's Hospital.

Prince Henry's Hospital, Melbourne is a 409 bed general teaching hospital associated with Monash University. It has a number of surgical and medical specialist units and a large outpatient population.

A ward pharmacy scheme has now been operating for five years, beginning with a trial evaluation in one ward in 1973 (2). This scheme was then gradually expanded to cover all wards by mid 1975.

While it is our belief that the clinical activities of ward pharmacists are an integral part of the control and supply of medication, the latter aspect will not be dealt with in great detail in this article.

On admission a patient drug profile is prepared for each patient. This profile is updated as required, and is used to record the patient's medication needs which are subsequently supplied by the pharmacist. It also includes relevant details on the patient, their medical condition and other appropriate information.

On admission the ward pharmacist is expected to briefly interview the patient, where possible, in an attempt to confirm the patient's "Drug History", including their current medication prior to admission and any previous "allergic" or "adverse" drug reactions (Table 1).

In an attempt to provide uniformity and simplicity, the format for this patient drug interview is included on the back of the pharmacy drug profile sheet.

The pharmacist also provides drug administration instructions to patients on discharge when required and when possible.

The overall goals of the scheme are to:–

(a) Promote efficient, safe and cost effective drug usage.

(b) Detect adverse trends or reactions due to a patient's drug therapy in order to initiate corrective action as soon as possible.

(c) Document adverse drug reactions and the effectiveness of drug therapy in order to improve future patient care.

(d) Minimise the risk of adverse or toxic effects by detecting drug interactions, contra-indications, IV incompatibilities and evaluating dosage regimes.

CLINICAL ACTIVITIES

There are six clinical roles which may be defined for ward pharmacists. In summary they are:–

1st Role –
Evaluating drug therapy orders.

2nd Role –
Noting potential problems related to drug therapy, and selecting relevant parameters to monitor.

3rd Role –
The monitoring of these parameters which may be divided into two groups;

1. Routine Parameters
   (a) Serum electrolytes
   (b) Serum creatinine and urea
   (c) Blood glucose
   (d) Liver function tests
   (e) Drug blood levels
   (f) Haematological reports
   (g) Microbiology reports
   (h) Nursing notes
2. Specific Parameters for particular patients of which there are two subgroups.
   (a) Specific drugs or drug groups
   (b) Specific disease states

4th Role –
Co-ordinating the collection of adverse drug reaction reports.

5th Role –
Providing drug information.

6th Role –
Collecting drug utilisation review statistics.

TABLE 1

Function	Check List	Details or Potential problems to consider	Course of action when problems exist
1. Record patient details	Age, sex, diagnosis or problem list	Relevance to drug therapy	
2. Patient interview	(a) Previous history of or "Allergic" reactions to drug therapy	(a) Details of reaction	(a) Record details on profile and drug administration sheet. Notify prescriber. N.B. (Cross-allergic reactions between drugs).
	(b) Previous medication	(b) Drugs name(s), strength(s) & dosage(s) bioavailability problems	(b) Check medication &/or prescription brought into hospital with patient. Notify prescriber if discrepancies exist
	(c) Consumption of alcohol, tobacco, analgesics & illicit drugs	(c) Relevant to drug therapy	
3. Record patient drug profile and evaluate ordered drug therapy	(a) Check dosage regime (dosage evaluation)	(a) Dose, & frequency in normal range, correct or appropriate route **Relevance of:** (i) Renal function (ii) Hepatic function (iii) Disease state (iv) Abnormal response due to genetic variations. e.g. slow acetylators. (v) Drug pharmacokinetic properties (see table 2)	(a) Notify prescriber, monitor drug plasma levels and as appropriate: (i) Monitor serum creatinine & urea levels (ii) Monitor LFT's (iii) Select parameters to monitor
	(b) Check drug interaction potential	Consider: (b) (i) Clinical significance (i) Significant (ii) Theoretical (ii) Mode of action (iii) Methods of avoiding interaction: (i) Administration schedule	(b) (i) (i) Notify prescriber (ii) Select parameters to monitor and as for (i)
		(ii) Alternative drugs (iv) Symptoms of interaction	
		(v) Effect on ward urine tests & colour, faeces, colour, effect on lab tests	(v) Notify relevant personnel
	(c) Check IV therapy	(c) (i) Incompatibilities with (i) Other drugs (ii) Infusion solution (ii) Drug interactions (as above) (iii) Method & rate of administration & drug concentration (dose) & adverse effects	notify prescriber
	(d) Check indications & contra-indications (including potential teratogenic effects)	Contra-indications: (d) (i) Reason for contra indication & significance (ii) Alternative drugs Indications: (i) Mode of action in producing therapeutic effect (ii) Duration of effect (iii) Onset of action	notify prescriber
	(e) Check potential for side effects & adverse drug reactions	(e) (i) Type, symptoms & incidence of reaction (ii) Clinical significance (iii) Risk factors, e.g. serum K & digoxin	(e) (i) Select parameters to monitor (e) (ii) Notify prescriber (iii) Select parameters to monitor

The first article of this series of two, will deal with the general aspects behind these first five roles.
The second article will provide details of the significance of these roles in a ward situation.
The sixth clinical role will also be discussed in this second paper, along with examples.

CLINICAL ROLES

A summary of the work flow of a ward pharmacist is shown in (P97), which should occur with every patient admission and then with every medication order.

1st Role –

After recording the various details of the patient on admission, and after the patient interview, where possible, the ward pharmacist's first clinical role is to evaluate the drug order. That is, to check for initial problems in the drug order and to suggest corrective action where required. This is described in more detail in Table 1 where the functions of the ward pharmacist are listed in column one. Column two shows a proposed check list for the pharmacist to follow, while the details of potential problems are listed in column three, with column four listing the

TABLE 3

(A) SUMMARY OF GENERAL PARAMETERS
- (a) BIOCHEMISTRY REPORTS
  - (i) SERUM ELECTROLYTES, UREA & CREATININE
  - (ii) BLOOD GLUCOSE
  - (iii) DRUG BLOOD LEVELS
  - (iv) LFT's - ALKALINE PHOSPHATASE ASPARTATE AMINO-TRANSFERASE, GAMMA-GLUTAMYL TRANSPEPTIDASE, ALBUMIN & BILIRUBIN
- (b) HAEMATOLOGY REPORTS
  - (i) HAEMOGLOBIN, PLATELET COUNT, LEUCOCYTE COUNT, DIFFERENTIAL WBC (DOSAGE ADJUSTMENT, BLOOD DYSCRASIAS AND ANAEMIAS)
  - (ii) COOMBS TEST, HEINZ BODIES, METHAEMOGLOBIN, SULPHAHAEMOGLOBIN, EOSINOPHILIA
  - (iii) PROTHROMBIN TIME & PTT
- (c) MICROBIOLOGY REPORTS
- (d) NURSING NOTES
  - (i) ROUTINE URINE TESTS
  - (ii) IV THERAPY
  - (iii) TEMPERATURE & BP CHARTS
  - (iv) OTHER NOTES

(B) SUMMARY OF MAJOR SPECIFIC PARAMETERS (EXAMPLES)
- (a) SPECIFIC DRUGS
  - (i) DIGOXIN
  - (ii) MAOI's
  - (iii) WARFARIN & HEPARIN
  - (iv) GENTAMICIN & TOBRAMYCIN
  - (v) CYTOTOXIC DRUGS
  - (vi) CORTICOSTEROIDS
  - (vii) PARENTERAL NUTRITION
- (b) SPECIFIC DISEASE STATES
  - (i) DIABETES MELLITUS
  - (ii) EPILEPTICS
  - (iii) RENAL DYSFUNCTION
  - (iv) HEPATIC DYSFUNCTION
  - (v) BLOOD DYSCRASIAS
  - (vi) GENETIC DYSFUNCTION E.G. PORPHYRIA, G6DP DEFICIENCY, SLOW & FAST ACETYLATORS

The platelet count is also important when drugs, which cause a decrease in platelet adhesion, such as aspirin, are being used. Another point of interest is that the leucocyte counts can help to indicate the effectiveness of antibiotic therapy. In addition to the points already mentioned, the differential WBC can be influenced in other ways by drug therapy, e.g. Eosinophilia may be important in helping to determine whether an adverse drug reaction is taking place.

Other haematological indicators which may be of importance include –

The erythrocyte sedimentation rate which may be influenced by infection as well as by recent Dextran intravenous infusions, neoplasms, renal insufficiency, pregnancy, age, auto-immune and collagen diseases, e.g. rheumatoid arthritis or disseminated lupus erythematosus.

A positive Coombs test with other symptoms, for example, may indicate a drug induced haemolytic anaemia, e.g. Methyldopa[27]. The importance of Coombs tests in aiding the detection of adverse drug reactions has been described by Hansten[28]. Heinz bodies, methaemoglobin and sulphahaemoglobin with other symptoms may indicate a drug induced haemolytic anaemia especially in Glucose-6-Phosphatase Dehydrogenase (G6PD) deficient patients[29].

The problems that can occur with anti-coagulant therapy, especially those due to drug interactions, make it important to monitor the Prothrombin time in the case of oral anticoagulants, especially in patients with liver disease, and the Partial Thrombo-plastin Time (PTT) in the case of Heparin.

(g) Microbiology Reports, particularly bacterial sensitivity results, are important in determining the choice of antimicrobial agents, together with the dosage and method of drug administration.

A knowledge of the distribution of anti-microbial agents within the body and the site of the infection, is also important in many cases.

e.g. CNS infections.

All these reports should be monitored as they arrive in the ward each day where possible; but it is important to remember that many abnormal results are due to causes other than drug therapy.

(h) The Nursing Notes can also provide useful information as listed in Table 3A.

(i) Temperature charts —

e.g. Spikes following the administration of IV infusion solutions could indicate that the infusion solution was contaminated by micro-organisms, or it could provide supplementary evidence of an adverse drug reaction.

Similarly the influence of antimicrobial drug therapy on an infection may be reflected in the patient's temperature chart.

(ii) Ward Urine Tests —

Urine pH and its effect on drug excretion

e.g. Sulphonamides and High Dose Metho-trexate treatment with the aim of avoiding renal damage.

Urine pH is also relevant to the antimicrobial activity of some drugs, e.g. Hexamine Hippurate.

Haematuria, the presence of glucose and ketones in the urine and proteinuria may be related to drug therapy, e.g. proteinuria may be early indication of renal damage with Penicillamine[30].

The interference of drug therapy with these routine ward urine tests including their influence on urine colour, should also be considered by pharmacist.

(iii) General

There are other details that can also provide useful information with respect to drug therapy.

e.g. (1) Haematemesis and melena may be drug related or may influence the choice of drug,
(2) Blood pressure with respect to drug control,
(3) Rashes may be drug related,
(4) Patient's weight and height when required in determining Body Surface Area (BSA) (for dosage calculations). Changes in the patient's body weight may also reflect their degree of hydration or dehydration especially with respect to the use of diuretic drugs. Body weight alone is also relevant when calculating, or checking, drug dosage in many cases.

These nursing notes should be reviewed at least twice weekly.

(5) The IV administration notes must also be reviewed each day when IV additives or Parenteral Nutrition solutions are being used.

2. Specific Parameters are the second group of parameters and these can be divided into two subgroups –
   (a) Specific Drugs or Drug Groups.
   (b) Specific Disease States.

   The objective here is to select the patients at greatest risk to enable a concentration of effort on these patients.

   Table 4 lists examples of specific drugs or drug groups that may be monitored more closely, together with some of the parameters which may be selected for monitoring. Examples of the importance of this checking process are found in the literature for many drugs such as Digoxin[31] or Phenformin in Lactic Acidosis[32].

   The choice of drugs for specific monitoring naturally will be determined by the types of drugs used in the particular ward, which itself is determined by the type of patients and their diseases. It is also a matter of personal interpretation in many cases, but it should be influenced by the reported risk of adverse drug reactions occurring with a particular drug. e.g. antimicrobials and their ability to cause nephrotoxicity[33].

TABLE 4

2. SPECIFIC PARAMETERS
(a) SPECIFIC DRUGS OR DRUG GROUPS (EXAMPLES)

(i)	DIGOXIN	— DIGOXIN BLOOD LEVELS, SERUM K AND CREATININE
(ii)	DIURETICS AND K SUPPLEMENTS	— SERUM K AND CREATININE, DRUG INTERACTIONS, E.G. Li_2CO_3
(iii)	MAOI's	— FOOD & DRUG INTERACTIONS, BP
(iv)	HYPOCLYCAEMIC AGENTS	— BLOOD GLUCOSE, URINE GLUCOSE & KETONES, DRUG INTERACTIONS, SUGAR CONTENT OF PHARMACEUTICALS
(v)	WARFARIN	— PROTHROMBIN TIME, DRUG INTERACTIONS
(vi)	HEPARIN	— PTT, IV INCOMPATIBILITIES AND DRUG INTERACTIONS
(vii)	CHLORPROMAZINE	— LFT'S PARKINSONISM & TARDIVE DYSKINESIA SYMPTOMS
(viii)	ANTIMICROBIALS	— WBC, TEMP. CHART, BACTERIAL SENSITIVITIES, ESR, BLOOD LEVELS OF ANTIBIOTICS
(ix)	AMINOGLYCOSIDE ANTI-BIOTICS, E.G. GENTAMICIN, TOBRAMYCIN	— AS FOR (viii) PLUS SERUM PLASMA CREATININE AND UREA; OTOTOXICITY & VESTIBULAR DISTURBANCES
(x)	CORTICOSTEROIDS	— BLOOD GLUCOSE, SERUM K AND DRUG INTERACTIONS
(xi)	CYTOTOXICS	— BLOOD DYSCRASIAS
(xii)	HIGH DOSE METHOTREXATE THERAPY	— AS FOR (xi) PLUS URINARY pH AND FOLINIC ACID RESCUE
(xiii)	ANTIHYPERTENSIVE DRUGS	— BP, Na CONTENT OF PHARMACEUTICALS, DRUG INTERACTIONS
(xiv)	CNS DEPRESSANTS	— CONSCIOUS STATE & DRUG INTERACTIONS
(xv)	ANTIEMETIC DRUGS	— INCIDENCE OF VOMITING & NAUSEA, DRUG INTERACTIONS
(xvi)	CARBAMAZEPINE	— DRUG BLOOD LEVELS, FLUID RETENTION, SERUM ELECTROLYTES
(xvii)	ANALGESICS	— EFFECTIVENESS, FREQUENCY OF USAGE, RESPIRATORY DEPRESSION, DRUG CHOICE & DRUG INTERACTIONS
(xviii)	PARENTERAL NUTRITION	— SERUM ELECTROLYTES, LFT's, BLOOD & URINE SUGAR, BODY WEIGHT, WCC, Hb, SERUM TRACE ELEMENTS & FOLATE, FLUID BALANCE CHART, SERUM TRANSFERRIN, CHOLESTEROL & TRIGLYCERIDES

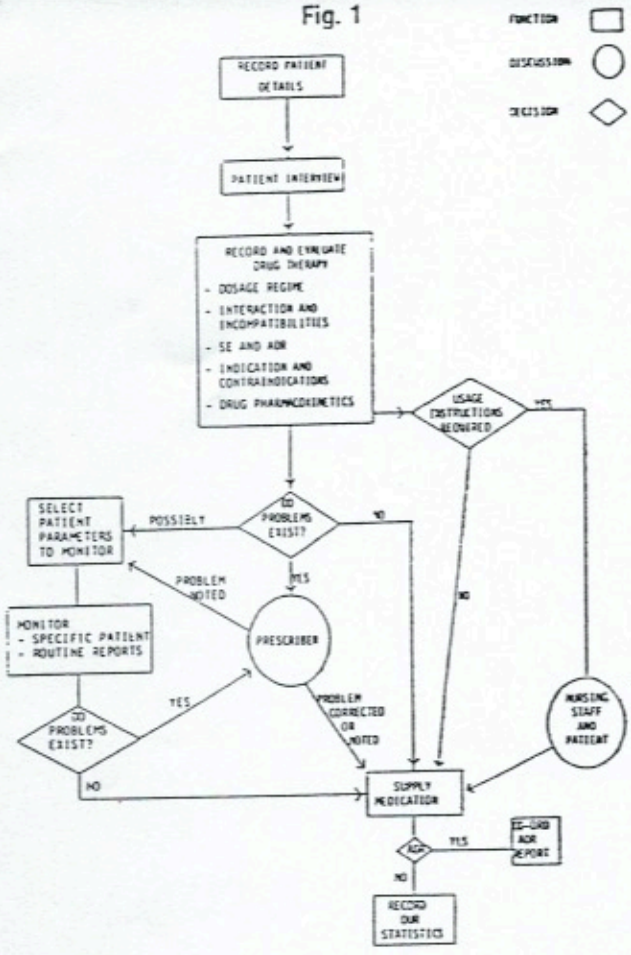
   Table 5 lists examples of specific diseases and the types of potential problems or parameters that should be monitored. These also are self limiting and the list is by no means complete. An important example is the influence of genetics on drug therapy which has been described elsewhere[34,35,36].
   Naturally there is a degree of overlap between disease specific and drug specific parameters, e.g. diabetes mellitus and oral hypoglycaemic agents[37] as there is between specific parameters and routine parameters.
   Naturally this list of parameters is very comprehensive but the more important parameters may be summarised in Table 3B.
   (A) The Routine Parameters and
   (B) Major Specific Parameters.
   But it is important to realise that the monitoring of parameters only gives the ward pharmacist an insight into the progress of the patient and enables them to be aware of the potential or real problems related to the patient's drug therapy.
   It must be stressed that perhaps the most important source of information to the ward pharmacist on these problems is ward or division rounds and meetings.
   These rounds or meetings also provide an excellent venue for the discussion of potential problems that have been detected by the ward pharmacist. Less formal discussions with medical nursing and paramedical staff are also essential. A weekly informal discussion on possible adverse drug reactions with the ward medical staff should also be encouraged.

TABLE 5

(b) SPECIFIC DISEASE STATES (EXAMPLES)

(i)	DIABETES MELLITUS	— AS FOR HYPOGLYCAEMIC AGENTS
(ii)	CONGESTIVE CARDIAC FAILURE	— DIGOXIN BLOOD LEVELS, DIURETIC THERAPY AND SERUM K & CREATININE, DEGREE OF HYDRATION
(iii)	BACTERIAL INFECTIONS	— AS FOR ANTIMICROBIALS PLUS PHARMACOKINETIC PROPERTIES OF ANTIMICROBIALS
(iv)	RENAL DYSFUNCTION	— DRUG PHARMACOKINETIC PROPERTIES AND DOSAGE ADJUSTMENT, DRUG CONTRAINDICATIONS
(v)	HEPATIC DYSFUNCTION E.G. ALCOHOLIC CIRRHOSIS	— DRUG PHARMACOKINETIC PROPERTIES, DOSAGE ADJUSTEMENT & DRUG CHOICE, DRUG CONTRAINDICATIONS
(vi)	EPILEPSY	— DRUG BLOOD LEVELS, INTERACTIONS & CONTRAINDICATIONS
(vii)	BLOOD DYSCRASIAS	— POSSIBLE INFLUENCE OF DRUG THERAPY
(viii)	SKIN RASHES	— POSSIBLE INFLUENCE OF DRUG THERAPY
(ix)	THROMBOEMBOLIC DISEASES	— PROTHROMBIN TIME OR PTT, DRUG INTERACTIONS
(x)	GENETIC DYSFUNCTION	
	(I) PORPHYRIA	— DRUG THERAPY CONTRAINDICATIONS E.G. BARBITURATES
	(II) SLOW & FAST ACETYLATORS E.G. ISONIAZID, HYDRALLAZINE, PHENELZINE, PROCAINAMIDE DAPSONE & MANY SULPHONAMIDES	— DRUG BLOOD LEVELS, THERAPEUTIC RESPONSE AND SYMPTOMS OF TOXICITY

Fig. 1



proposed course of action to be taken when relevant.

The drug pharmacokinetic properties which are most relevant to ward pharmacists are listed in Table 2. There is a large volume of drug pharmacokinetic data available from many literature sources, including useful reviews of drug half-lives and the effects of hepatic and renal dysfunction [3]. It is not possible for the pharmacist to remember all this detailed information, but they must know where they can find relevant and accurate information quickly. This also applies for information on drug interactions, but it is important to have a standard checking procedure. An interesting example of such drug interaction checking procedure has been described by Fish and Cooper [4]. But the effectiveness of such checking procedures ultimately depends on the quality of the reference sources used and on the diligence and alertness of the ward pharmacist. But it is important to consider the individual variations that can occur, together with the clinical significance of the drug interaction as discussed by Hassar [5].

2 Role –

The second clinical role is to note potential problems in relation to the patient's drug therapy and to select parameters that may indicate that a potential problem is in fact becoming a real problem. These matters must also be discussed with medical and nursing staff. Having fulfilled these prior duties, the pharmacist's next step is to supply the medication.

DRUG PHARMACOKINETIC PROPERTIES RELEVANT TO WARD PHARMACISTS

1. Distritution of the drug within the body, e.g. antibiotic penetration of CNS.
2. Routes of excretion and their importance, e.g. the percentage of drug excreted unchanged by the kidneys and the percentage undergoing biotransformation in the liver, and the methods of adjusting dosage in renal or hepatic dysfunction. It is also important to know the biological activity of metabolites when a drug is largely metabolised by the liver, especially in patients with severe renal dysfunction.
3. Biological half-life and the influence of disease states.
4. Degree of protein binding and the influence of other drugs and disease states, e.g. uraemia.
5. The relevance of bioavailability and pharmacogenetics.
6. The relevance of drug blood levels in relation to therapeutic effectiveness, dosage regimes, disease states, and toxicity.
7. The relevance of route of administration on onset of action and duration of therapeutic effect.

3rd Role –

The third role is to review and monitor these parameters in conjunction with ward medical staff, in order to establish their significance to the patient's current drug therapy and thus to detect problems as quickly as possible. A similar approach has been described by Cooper [6].

These parameters can be divided into two sub-groups.

1. Those that should be routinely monitored for all patients (Routine reports).
2. Those required for specific patients as determined by the pharmacist and the prescriber. (Specific patient).

The objectives of such monitoring can be defined as–:

(a) Detect adverse trends due to drug therapy in order to minimise the risk of drug toxicity.
(b) To determine whether adverse trends in a patient's condition could be related to their drug therapy.
(c) In conjunction with the prescriber, determine the relevance and effectiveness of drug therapy.

PARAMETER MONITORING

1. Routine Parameters –

The following reports (Table 3A) should be reviewed for abnormal results, when they are available and when it is relevant.

(a) Serum electrolytes which can indicate dehydration or oedema, while serum potassium is particularly relevant when digoxin is used in conjunction with potassium depleting drugs, e.g. certain diuretics and carbenoxolone.

(b) Serum creatinine and urea levels are an indicator of renal function, which is relevant to drug dosage and its adjustment, depending on the degree of renal failure, the drug under consideration, serum albumin levels and whether the patient is receiving dialysis treatment or not.

But it must be remembered that in many elderly patients the serum creatinine may be within normal limits even though they may have a deterioration in renal function. This is because creatinine production is reduced in the elderly with a smaller lean body mass. In such cases renal clearance is a more accurate indication of renal function. The guidelines behind such dosage adjustments have been well described in the literature[7][8][9] and is particularly important with antimicrobial agents [10] [11]. e.g. Gentamicin

The role that a pharmacist can play has been described in more detail by Berbatis and Rothwell [12]. In addition the importance of renal haemodynamics, and its various influencing factors, on the apparent volume of distribution and plasma protein binding of drugs and the variations in drug action thus caused, have been described by Duchin and Schrier [50].

Serum creatinine and urea can also provide a warning of possible drug related renal function deterioration. But it is important to consider other factors, e.g. decreased plasma volume due to low serum albumin.

(c) Blood glucose can indicate the effectiveness of drug therapy in controlling diabetes mellitus.

It can also indicate drug interference either directly or via a drug interaction. The interference of drug therapy on laboratory tests should also be considered.

(d) **Liver Function Tests (LFT's)**

The LFT's routinely used at Prince Henry's Hospital are as listed in Table 3A.

Abnormal results may indicate hepatic dysfunction which may influence –

(i) Drug dosage or the choice of drug (which is related to the % of drug metabolised in the liver), e.g. the problems relating to the use of Diazepam in patients with cirrhosis[13]. Low serum albumin levels can also influence the amounts of free and protein bound drug and may lead to changes in the therapeutic response of the drug, although such changes are difficult to predict[14][15][16].

The effect of liver disease on drug metabolism is related to the drug under consideration and the various diagnostic categories and stages of liver disease. But hepatic clearance is complicated by the influence of hepatic blood flow and the fraction of unbound drug as well as hepatocellular metabolic activity, thus making it difficult to predict the dosage requirements for a patient with a specific liver disease. Hence the need for the close monitoring of unbound drug blood levels, especially for those drugs with a narrow therapeutic index.

Another extremely important factor to consider is the use of Warfarin in patients with liver dysfunction where the Vitamin K clotting factors may be abnormally low. The use of sedatives in patients with hepatic encephalopathy should also be avoided. The problems associated with drug therapy in patients with liver dysfunction have been discussed in more detail elsewhere [17][18].

(ii) Deterioration in LFT's may also indicate an adverse effect due to drug therapy. This subject has been reviewed by Tolman[19] and Zimmerman[20].

(iii) Other aspects, e.g. supporting evidence of alcohol abuse and the need to treat withdrawal symptoms. It is of interest to note that an elevation of Gamma Glutamyl Transpeptidase (GGT) can be drug related, e.g. many anti-epileptic drugs produce a mild elevation[21] and a high elevation of GGT can occur with a high alcoholic intake[22].

These enzymes can be elevated in a number of other disease states, but the intention here is merely to point out their possible significance to a patient's drug therapy.

(e) **Drug blood levels** are obviously important in determining the effectiveness of drug therapy in that it can show –

(i) Whether a therapeutic blood level is being obtained. This is particularly important for drugs such as Theophylline[23] and anti-epileptic drugs[24].

(ii) Whether toxic drug levels are present? especially for drugs where saturation of metabolising enzymes occurs at therapeutic doses, e.g. Phenytoin[25].

(iii) Determine whether hepatic or renal dysfunction is causing abnormally high drug blood levels.

(iv) The relevance and influence of potential drug interactions.

(v) The existence and importance of genetic variations in drug metabolism, e.g. slow acetylators.

N.B. The therapeutic and toxic levels listed for particular drugs may not apply when patients are concurrently receiving other drugs with similar pharmacological properties.

(f) **Haematology reports** are important in aiding the detection of adverse drug effects[26]. The main parameters of interest are listed in Table 3A.

Haemoglobin can possibly indicate drug induced anaemias and it is also important when calculating the dosage of iron dextran infusions.

Platelets and leucocyte counts can indicate drug induced blood dyscrasias, e.g. Thrombocytopenia, Leucopenia or Aplastic Anaemia, and are particularly important when cytotoxic drug dosages are being calculated.

4th Role -

This is particularly important since the ward pharmacist's fourth clinical role is to co-ordinate the documentation of adverse drug reactions (ADR) in conjunction with medical staff. The pharmacist carrying out the previously mentioned roles is in an excellent position to be aware of the occurence of these adverse drug reactions and should therefore strive to ensure that such events are adequately documented for future use. Such information should also be properly disseminated to all the hospital's medical staff at suitable time intervals.

It should be pointed out that the ward pharmacist is also in a position to play a vital role in helping to decrease the risk of ADR's occurring, by -

(a) Monitoring drug dosage regimes, especially when high doses are used.
(b) Dissemination of drug information on the type and incidence of ADR's, together with information on the patients at greatest risk.
(c) Detecting and preventing drug interactions, contra-indications and IV incompatibilities.
(d) Watching for early signs of ADR's where feasible. (i.e. monitoring ADR's).

The role the pharmacist can play in detecting ADR's has also been described elsewhere ([38],[39],[40]) and is a form of extensive patient monitoring.

5th Role -

The ward pharmacist's fifth clinical role is that of providing patient orientated drug information, including special dosage and usage instructions to the patient and/or the nursing staff as required. This does not mean the pharmacist merely plays a passive role awaiting urgent referrals or requests, but rather they must also play an active role, whereby they seek out and research potential drug therapy problems by monitoring the various parameters discussed. These problems must then be brought to the attention of the relevant medical staff. The pharmacist must also be prepared to volunteer to search out relevant drug information from the literature and to ensure that any such information supplied is accurate and well based with reliable reference sources.

Hull & Eckel([41]) have described their experience in this role: but I must re-iterate the importance of developing a mature, friendly and mutually co-operative relationship with all ward staff. The ward pharmacist's drug information role in patient counselling, especiallly on discharge medication, should not be neglected. This information must be very basic but should cover dosage instructions, relevant side effects, home storage of drugs, actions and drugs to avoid together with information on the effects that their medication may have on urine and faeces colour and any other relevant instructions. The pharmacist must also participate in patient medication administration training schemes where relevant.

The ward pharmacist must also develop judgement to distinguish relevance from irrelevance and must realise that working in the wards is a dynamic learning experience as well as a service.

The second paper in this series will appear in the next issue of the A.J.H.P. with the List of References.

TRAVENOL LABORATORIES AWARD

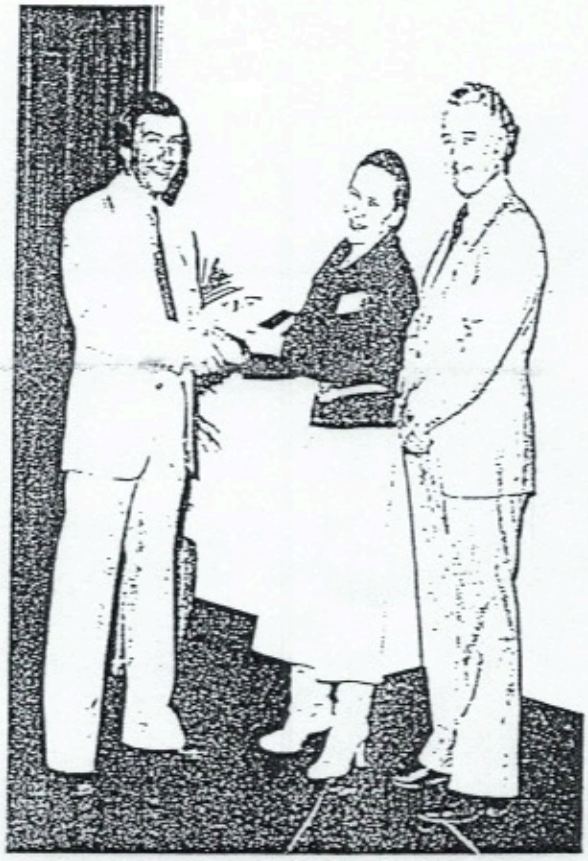
The Travenol Laboratories Award was officially presented to this year's winner —

Miss Christine Odgers.
Deputy Chief Pharmacist.
Flinders Medical Centre.
BEDFORD PARK, STH. AUSTRALIA.

during the I.V. Seminar Programme in South Australia on June 27/28, 1980.

In making the presentation Mr. Jeff Goodman, Divisional Manager — Baxter Travenol Products, spoke of the importance the pharmaceutical industry, research projects and international travel was to Travenol. Mr. Frank Ryan, Federal President S.H.P.A., thanked Travenol on behalf of the Society for its continued support in this major Award and the I.V. Seminar programmes.

Chris left Australia in July and will spend time on a number of major hospitals in the U.S.A., U.K., and Europe before returning home in September.



L to R: Mr. J. Goodman, Divisional Manager, Baxter/Travenol; Miss Christine Odgers; Mr. Frank Ryan; Federal President, S.H.P.A.

STOP PRESS!

Winner of Pharmacia Essay Award -

Successful recipient is Joyce Bostock of Mater Hospital, Brisbane.

More details next issue.

2. Larmour I (1980); Clinical Activities of Ward Pharmacists - A Five Year Perspective - Part 2 - The Importance of the Pharmacists Role AJHP, 10, 131-136.

Clinical Activities of Ward Pharmacists – A Five Year Perspective –

Part 2 – The Importance of The Pharmacist's Role

by

IAN LARMOUR
Deputy Chief Pharmacist, Prince Henry's Hospital, Melbourne, Victoria

ABSTRACT A second article in a series of two based on five years' experience at Prince Henry's Hospital, Melbourne.

This article aims to illustrate the importance of the clinical activities carried out by ward pharmacists. The problems encountered during a 30 day survey period are listed. The sixth clinical role is also discussed with the presentation of examples of surveys conducted at the hospital.

While the first article dealth with the general guidelines behind the first five clinical roles, this second article will concentrate on the operational aspects of the Ward Pharmacy Service at Prince Henry's Hospital, Melbourne.

BACKGROUND

A modified decentralised unit dose distribution system (2-3 days supply of medication) operates in three wards on the sixth floor, with these wards being serviced from a satellite pharmacy on this floor. It is hoped to extend this system throughout the hospital over the next five to six years. The remaining wards are supplied using specialised ward stocks and the issue of individual unit packs of medication as required by patients. The ward pharmacist is totally responsible for the dispensing, storage and control of all medication used in the wards that they cover.

Each patient has a medication order and administration sheet at the end of the bed, except for the psychiatric ward where it is kept in the nursing station.

Each ward pharmacist does a drug chart round twice daily.

The number of beds covered by each ward pharmacist varies, and all have additional duties within the Pharmacy Department. A standard format is shown in *Table 6*.

Since the turnover of patients is a more accurate indication of work loads than beds alone, the daily average admission, discharges and transfers are used since each of these activities represents a specific task for the ward pharmacist.

These figures alone do not completely describe the work load of the ward pharmacist since the type of patient and thus the number of the daily medications per patient and the frequency with which such medication is changed, also influences the ward pharmacist's work load. For instance in Group 4 the beds covered include those of the Intensive Care and Coronary Care Units.

The type of drug distribution system is also relevant as is shown by the lower number of beds covered in group 5, which is a modified unit dose distribution system, and technicians are not used.

Group 6 has one ward with the modified unit dose system but the Psychiatric Unit tends to produce a lower work load at our hospital.

Each ward pharmacist is generally rostered to a group of wards for a period of 3 to 6 months at one time.

Table 6

ALLOCATION OF WARD PHARMACISTS

Group	1	2	3	4	5	6
Beds Covered	76	76	77	62	40	93
Classification Notes	Surgical	Surgical	Medical	Specialist i.e. ICU, CCU, Neurol, Neuro-Surgery	Renal & Medical (Mod Unit Dose)	Surgical & Paediatric, Psych. Med. (Mod Unit Dose)
*Ave. Daily Admissions	5.3	5.8	6.2	3.8	3.0	6.4
*Ave. Daily Discharges	5.4	5.8	6.0	2.4	3.4	6.2
*Ave Daily Transfers	2.1	1.5	3.3	4.9	1.8	0.6
*Ave. Adt. Total	12.8	13.1	15.5	11.1	8.2	13.2
Wards	2NSW	3NSW	4NSW	5NSW	6NS	6W, 7W, 10W, 2E

*Statistics collected over a three month period.

They are then rostered to other sections of the department for a short period of time before being rostered back to ward duties.

The ward pharmacist also receives support from the Pharmacy Drug Information Centre and the Intravenous Additive Service. Each ward pharmacist, in addition to their clinical roles, is responsible for the supply, control, security and proper storage of all ward medication. However these aspects will not be dealt with in the article.

While ward pharmacists do receive many direct enquiries about drug therapy from ward medical and nursing staff, it is essential that the ward pharmacist play an active rather than a passive role.

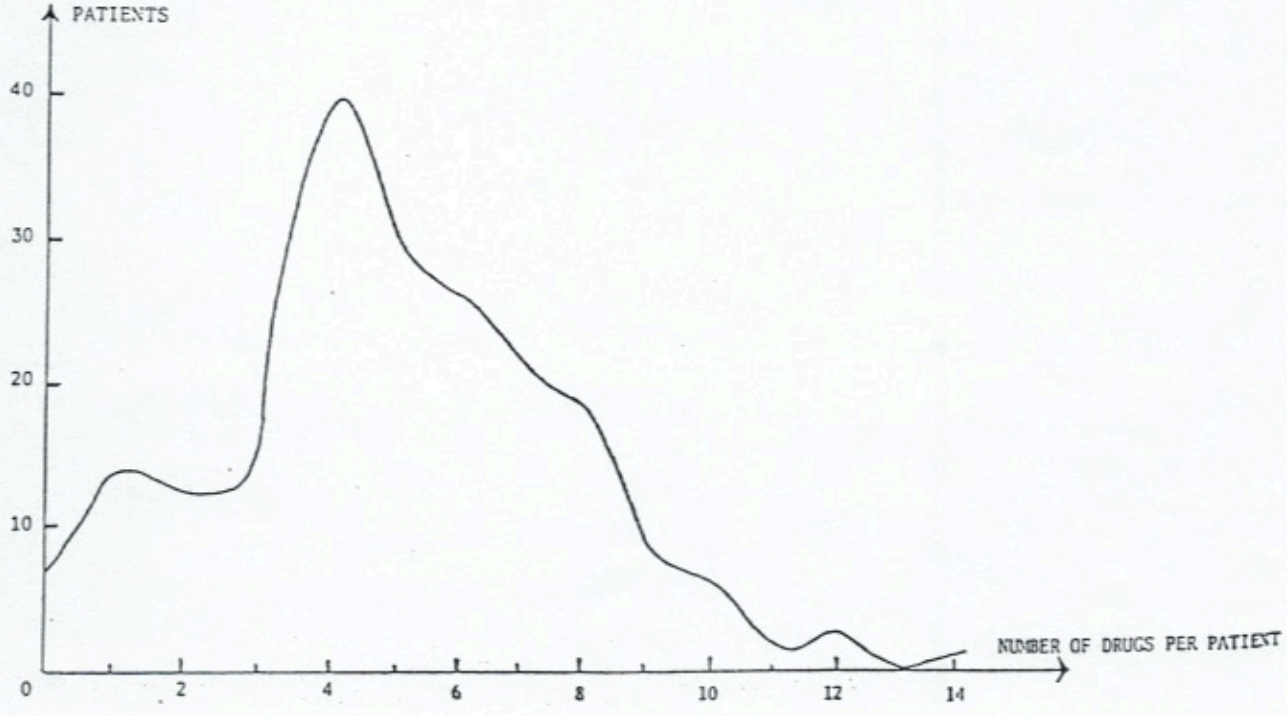
That is, the pharmacist must actively review and monitor a patient's drug therapy and progress in order to detect real or potential problems associated with such therapy.

It is important to realise that the pharmacist cannot act in isolation and regular face to face communication with medical and nursing staff is essential. This includes attending ward, unit or division rounds and meetings at least once weekly. This is in addition to the normal day to day contact with such personnel.

The co-operation of the medical staff is particularly important and at Prince Henry's Hospital this co-operation has been excellent. But communications are a two way process and the pharmacist must attempt to understand all the relevant aspects of a patient's disease state and its influence on their drug therapy.

FIGURE 2

NUMBER OF PATIENTS
vs.
NUMBER OF DRUGS PER PATIENT



ROLE SURVEY

The experience at Prince Henry's Hospital over the past few years has shown that the pharmacist in the ward, as a member of the health care team, can provide a valuable contribution to patient welfare.

Firstly in providing an efficient drug distribution system which has minimised administrative red tape and has allowed effective communication to occur between pharmacy, medical and nursing staff.

Secondly, there have been many cases where the ward pharmacist has made a positive contribution to improving a patient's drug therapy. Unfortunately many of these cases have not been adequately documented.

Therefore it was decided that the contribution of a ward pharmacist to patient drug therapy in a single ward for a randomly selected month (June '78) should be carried out.

These results have thus been documented and are intended as an example of a typical month rather than a major study.

The ward selected was a 22 bed medical ward for a period of 30 days, during which time 83 patients passed through the ward, with a daily bed average of 86.1%.

The patient turnover statistics were:

568 patient days
47 admissions
62 discharges
20 transfers (15 in, 5 out)
Beds occupied at the start of the period — 21
Beds occupied at the end of the period — 16
The ADT daily ave. (as discussed earlier) was 4.3 and the ave. stay 8.5 days.

The average number of drugs per patient was 5.1 with a standard deviation of 2.7, with a range of 0-14 drug orders. (But on previous occasions up to 20 drugs for the one patient have been observed).

The average number of drug order changes (not including discharge medication) per day were -

New drug orders 10.4/Discontinued drug orders 3
Dosage changes 1.3/Stat. doses 1.3/Pre-med. Orders 0.1

pharmacist and are in addition to the medication supplied for standing drug orders. As expected with a medical ward there are very few pre-medication orders. The number of stat doses tends to rise dramatically when oncology patients are admitted to the ward.

The actual distribution of drugs per patient is better demonstrated by the graph in *Figure 2*, which shows most patients actually had between 4 and 8 drugs prescribed for them at any one time.

There were a number of problems related to drug therapy that were detected over the period, as shown in *Table 7*.

(a) Adverse drug reactions

There were two probable ADR's in two patients that occurred as defined under the World Health Organization definition which describes an ADR as a "noxious unintended reaction that occurs at doses normally used in man for prophylaxis, diagnosis and therapy".

There was one further ADR in which a drug was suspected as being involved and two cases where an ADR may have contributed to the cause of the patient's admission to hospital.

The percentage of patients in this survey which had probable adverse drug reactions was 2.4%. This is lower than the results reported in most studies (42, 43, 44, 45, 46, 47, 48) which quote rates from 7 to 28% of patients experiencing ADR's. While it is not intended to compare this brief survey with the more comprehensive studies carried out on this subject, possible reasons for the lower rate are -

(A) the small size of the sample and the survey was not aimed exclusively at detecting adverse drug reactions.

(B) the figure only represents probable ADR's and does not include reactions which did not have a clear association with the patient's drug therapy. Another variation is the interpretation of what actually constitutes an adverse drug reaction, especially with respect to minor side effects.

and

(C) Hopefully the influence of the pharmacist in detecting unusually high drug dosages, drug interactions and contra-indications.

But the reason for mentioning adverse drug reactions is to point out that they do occur and that the ward pharmacist is in an excellent position to co-ordinate the documentation of such reactions. The monitoring of ADR's could be more thorough in determining the true incidence of ADR's to specific drugs if more personnel and resources were available, especially EDP support.

It is interesting to note that many studies on ADR's have listed a significantly higher incidence in patients where a number of predisposing factors exist (42, 45, 46), especially the older the patient's age, and the higher the number of drugs.

In both the cases found in this short survey these two factors were present.

(b) Drug interactions — five theoretical drug interactions were detected and monitored, all of which, but one, proved not to be a problem. In the other case the medication was adjusted before problems were encountered.

Three significant drug interactions were detected and corrected before they had a chance of causing a problem.

(c) Three listed contra-indications were detected. In two cases the medication was ceased and alternative drugs used. In the third case the matter was investigated and the drug continued under close supervision.

(d) One IVincompatibility was detected and corrective action taken.

(e) Prescription problems — On 16 occasions the prescription required correction, checking or monitoring as listed in Table 7(e).

(f) Patient problems requiring discussion — On eight occasions matters were discussed with the prescriber on a variety of matters not mentioned elsewhere, the most significant subject being dosage adjustments as per Table 7(f).

(g) Direct specific drug information requests, other than those of minor importance, were made on twelve occasions on a variety of subjects listed in Table 7(g).

TABLE 7

SUMMARY OF DRUG RELATED PROBLEMS ENCOUNTERED OVER PERIOD

(a)	ADVERSE DRUG REACTIONS (ADR)		
	(i) DURING HOSPITAL STAY		
	PROBABLE	2 PATIENTS	
	POSSIBLE	1 PATIENT	
	% PATIENTS WITH PROBABLE ADR	2.4%	
	(ii) CAUSE OF ADMISSION		
	POSSIBLE	2 PATIENTS	
(b)	DRUG INTERACTIONS		
	THEORETICAL (MONITORED)	5	
	SIGNIFICANT (CORRECTED)	3	
(c)	CONTRAINDICATIONS	3	
(d)	INTRAVENOUS INCOMPATIBILITIES	1	
(e)	PRESCRIPTION PROBLEMS		
	(i) ILLEGIBLE, INCORRECT DOSAGE OR DRUG NAME		6
	(ii) UNUSUAL DOSAGE REGIMES CHECKED		3
	(iii) POTENTIAL PROBLEMS REQUIRING SPECIFIC MONITORING		7
	TOTAL		16
(f)	PATIENT PROBLEMS REQUIRING DISCUSSION		
	(i) DOSAGE ADJUSTMENT	4	
	(ii) GENERAL	3	
	(iii) ALLERGY HISTORY NOT CHARTERED	1	
	TOTAL	8	
(g)	SPECIFIC INFORMATION REQUESTS AND DISCUSSIONS (EXCLUDING MINOR REQUESTS)		
	(i) CHOICE OF MEDICATION	3	
	(ii) DOSAGE REGIME/PROTOCOL	1	
	(iii) METHOD OF ADMINISTRATION	1	
	(iv) ADJUSTMENT OF DOSAGE REGIME IN RENAL FAILURE	1	
	(v) SIDE EFFECTS	4	
	(vi) AVAILABILITY	1	
	(vii) IDENTIFICATION	1	
	TOTAL	12	

TABLE 8
SURVEY OF DRUG PRESCRIBING

11 MOST COMMONLY PRESCRIBED DRUGS	% PATIENTS PRESCRIBED THESE DRUGS
DIGOXIN	35.5%
NITRAZEPAM	25.8%
FRUSEMIDE	22.6%
POT. CHLORIDE SLOW RELEASE	22.6%
GLYCERYL TRINITRATE	19.4%
HEPARIN	16.1%
PARACETAMOL/PROPOXYPHENE	14.5%
SALBUTAMOL	14.5%
AMILORIDE	11.3%
PROPRANOLOL	9.7%
SORBIDE NITRATE	9.7%

TOTAL OF 96 DIFFERENT DRUGS PRESCRIBED OVER PERIOD

TABLE 9
CONCURRENT ANTIBIOTICS

GENTAMICIN SOLE DRUG		18 CASES
1 OTHER ANTIBIOTIC		30 "
2 OTHER ANTIBIOTICS		26 "
3 OTHER ANTIBIOTICS		2 "
CEPHALOTHIN	in	36 CASES
AMPICILLIN	"	12 "
PENCILLIN G	"	8 "
CLINDAMYCIN	"	22 "
OTHERS	"	10 "

An analysis of the relative frequency of drugs prescribed in the ward was carried out. There were 96 different drugs prescribed over the period investigated, and the incidence of the 11 most commonly prescribed drugs are shown in Table 8. The distribution of patients according to sex was 66% male and 34% female.

The number of occasions on which a ward pharmacist can make contributions other than in that of drug supply does vary with the type of patient in the wards covered.

It also depends on the experience, confidence and ability of the pharmacist; which really emphasises the need for the training of pharmacists to be patient orientated.

This does not mean training pharmacists to be pseudo medical practitioners but rather, pharmacists who are able to deal with the real problems associated with drug therapy.

6th Role

Finally, I would like to examine the sixth and vital clinical role that the ward pharmacist can play: that is in collecting drug utilisation review statistics (49). That is the process of monitoring and recording events associated with the actual use of the prescribed medication to evaluate or establish standard protocols.

Two major examples of this role that have been carried out at Prince Henry's Hospital in recent years are:-

1. Gentamicin Survey
   and
2. IV Additive Solution Usage Survey

The Gentamicin Survey requires that whenever a patient is prescribed Gentamicin, the pharmacist must fill out a specific form for the purpose and must follow a definite course of action.

This is an ongoing programme and the sheets are retrospectively analysed every six months.

The ward pharmacist is expected to contact the prescriber when trough levels exceed 2ug/ml (or peaks of 10ug/ml — 15 mins. after IV injections or 60 mins. after IM injections) with a view to dosage adjustment.

The prescriber is also contacted when the Gentamicin therapy exceeds 1 to 2 weeks duration. This is done in liason with the Microbiology Department.

The result of a recent survey —

76 patients were monitored over 6 months.

The blood levels were normal in 44 patients, with no levels taken in 11 patients (all less than 4 days therapy).

Trough 2ug/ml in 21 patients.

Peak 10ug/ml in 8 patients

Dosage reduced in 15 patients

Duration of therapy.

Most courses of therapy were less than 14 days (67 patients), 7 between 14 and 30 days and 2 greater than 30 days.

Gentamicin was often used with other anti-microbial drugs as shown below:-

Gentamicin used alone in 18 cases

1 other antibiotic in 30 cases

2 other antibiotics in 26 cases

3 other antibiotics in 2 cases

The most commonly concurrently used antibiotics are also listed in Table 9 with Cephalothin being the most commonly used (36 cases).

In 11 patients the trough levels progressively rose to consistantly exceed 2.5ug/ml. The only common feature available was that in all cases another antibiotic was used.

These were — Cephalothin in 6 cases
Ampicillin in 3 cases
Penicillin G in 2 cases

In several of these cases a rise in serum creatinine was also documented, possibly indicating renal deterioration. But I must point out there were a number of other variables associated with these patients.

This type of information is used by the Therapeutic Sub-Committee and the Infection Committee in the performance of their duties: especially in relation to the incidence of bacteria resistant to Gentamicin. These statistics can also help to determine the ADR incidence for specific drugs.

The second example is that of a survey on the use of IV infusion solutions as a method of administering drug therapy. The survey presented is that carried out recently over a 5 day period. Several other such surveys have also been carried out over the past few years at Prince Henry's Hospital.

Here the ward pharmacists are given a sheet which they fill out during the normal course of their duties. A total of 572 IV infusion solutions (not including Parenteral Nutrition Solutions) were used over the survey period, of which —

35.6% had one drug added
and
5.1% had two drugs added
i.e., a total of 40.7% of all infusion solutions used over the period contained at least one drug additive.

The drug additives most commonly used were:

Pot. Chloride	55.6%
Heparin	17.6%
Cytotoxics	8.4%
Aminophylline	6.1%
Lignocaine	3.9%
Others	8.4%

This type of information is used to:-

(a) Enable the Pharmacy Department to estimate stock movement and usage patterns
(b) Enables the Pharmacy Department to develop and plan its IV additive services
(c) Enables the Therapeutic Sub-Committee to evaluate costs, IV therapy practices and to disseminate such information via the Pharmacy Bulletin.

In summary there are six clinical roles that can be identified for the ward pharmacist.

1st Role Evaluating drug therapy orders
2nd Role Noting potential problems related to drug therapy and selecting relevant parameters to monitor
3rd Role The monitoring of these parameters
4th Role Co-ordinating the collection of ADR reports
5th Role Providing drug information
6th Role Collection drug utilisation review statistics

In order to carry out these roles satisfactorily the ward pharmacist should have the following qualities:

(a) Knowledge that is relevant to patient orientated drug therapy
(b) Personality, the ability to communicate maturely and effectively
(c) Judgement to distinguish relevance from irrelevance
(d) Willingness to learn, and
(e) Experience

CONCLUSION:

In conclusion these two articles have attempted to show that the pharmacist does have a very real practical clinical role to play in the wards as part of their normal duties.

It is difficult to estimate the dollar value of these services, but if it helps to reduce the discomfort of patients, enables debilitating side effects or adverse drug reactions to be minimised or avoided, decreases a patient's stay in hospital, avoids litigation, aids the medical practitioner, particularly resident medical officers, in the resolution of patient problems and occasionally helps to save a life, then surely the scheme must be justified economically.

The development of schemes such as the one described, must become the top priority of all Victorian hospital pharmacists, if we are to make the maximum contribution to patient drug therapy. This is not to say that other areas of practice should be neglected but rather they should be integrated to produce a common goal.

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Further information may be obtained from Dr. K. Raymond, Victorian College of Pharmacy Ltd, 381 Royal Parade, Parkville, 3052. Telephone 387 7222.

Closing date of application is 19 December 1980.

The College acknowledges the assistance of Travenol Pty Ltd in the creation of this scholarship.

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Clinical Ward Pharmacy Quality Assurance

Ian Larmour, Yvonne Allinson, Allan Manser, Gordon Spalding, Kathryn Brett, Suzanne Swan

Introduction

Late in 1981 the Victorian Branch of the Society of Hospital Pharmacists of Australia (SHPA) formed a working party to examine methods of developing quality assurance in clinical pharmacy practice, especially clinical ward pharmacy practice. The primary objective for this group was to present a paper on the subject at the 1982 Victorian State Branch Conference.

The purpose of this article is to summarise the findings of this working party in the hope of providing guidance and suggestions on ways in which clinical pharmacy quality assurance can be developed in Australian hospitals.

The 1970s saw the development of clinical ward pharmacy practice and it is timely for the 1980s to be the decade of quality assurance, where these achievements are consolidated and improved while, at the same time, achieving greater uniformity in the type and quality of service provided.

Quality assurance for clinical ward pharmacy practice presents difficulties in that:

1. There are few clear end points which can be assessed accurately; i.e. it is a service rather than an end product as you have with manufactured items, and
2. ward pharmacists work in an autonomous manner outside the department.

Thus, to a large extent, quality assurance in this context rests on the integrity and ability of the ward pharmacists and it is important to realise that quality assurance is the responsibility of every pharmacist, not just those who are in administrative positions.

The working party defined quality assurance in this situation as meaning 'confidence that defined tasks are carried out efficiently, safely, effectively and in accordance with the highest standard of professional ethics and knowledge'.

One of the first tasks of the working party was to gather information on the extent and nature of clinical ward pharmacy practice within the state of Victoria. The results of this survey are to be published in a separate article. However, the survey did illustrate that quality assurance programs in this area, were only in their formative stages and that there were considerable differences in the type of ward service provided by the various hospitals.

The working party adopted the following premise for a successful clinical ward pharmacy quality assurance programme, viz:

1. Pharmacists must be adequately educated and trained to be able to carry out the required tasks, and
2. ward pharmacists must be fully apprised of what their duties are in detail, and they must know what standard is expected of them.

Once these two aspects are catered for, motivating procedures have some chance of success in encouraging and maintaining quality assurance. But of course there is the further proviso that pharmacists must have the time available to carry out these tasks, that is, the tasks should not be unrealistic in regard to the time available. However, what is important is that the tasks that can be done, are in fact done well; that is, lack of time should not be an excuse for substandard practice, no matter what the extent of the involvement. What it does mean is that priorities have to be set on an individual basis in each hospital.

The working party outlined five areas on which a clinical ward pharmacy quality assurance program should be built:

Undergraduate and postgraduate education
Continuing education
Peer review
Inservice education
Department administration.

Undergraduate and postgraduate education

The quality of clinical pharmacy practice is very difficult to assess as previously discussed. Therefore,

Ian Larmour, BPharm, FSHP, Yvonne Allinson, BPharm, Grad Dip Hosp Pharm, Gordon Spalding, BPharm
Pharmacy Department, Prince Henry's Hospital, Melbourne.
Allan Manser*, BPharm, FSHP
Director of Pharmacy, Woden Valley Hospital, Canberra.
Kathryn Brett, BPharm
Pharmacy Department, Preston & Northcote Community Hospital, Vic.
Suzanne Swan, BPharm
Pharmacy Department, Dandenong & District Hospital, Victoria.
(*Previously Pharmacy Department, Royal Melbourne Hospital, Vic.)

Address for correspondence:
Ian Larmour
Director of Pharmacy
Prince Henry's Hospital, St. Kilda Road
Melbourne, Victoria 3004

one of the most important guarantees of quality is in having staff who have been adequately educated and trained in the skills that are required by competent clinical ward pharmacists.

Appropriate education provides the building blocks for the development of clinical skills. This view was reflected by practising pharmacists in the survey undertaken by the working party. Only 31% of pharmacists working in the wards had postgraduate qualifications, however, 87% of respondents indicated that they believed more training was needed. The majority of respondents also indicated that they felt this extra training should be carried out jointly in the hospital wards and at the Victorian College of Pharmacy, and most felt the traineeship year could be used more effectively in providing some of this training.

The working party felt that there were three aspects to clinical ward pharmacy training, viz;

— The pharmacy undergraduate should receive the basic education in clinical practice at the Victorian College of Pharmacy.
— The knowledge obtained by the student should be developed into clinical pharmacy skills in the ward environment.
— The need for ongoing continuing education and inservice education programs.

However, since most practising clinical ward pharmacists have not received formal clinical training, there is also a need to consider postgraduate education programs. Therefore the question of formal education was considered in two parts:

1. undergraduates (or future graduates), and
2. postgraduates.

1. Undergraduates

a) Undergraduate education

The undergraduate needs the skills to interpret information and data accurately and thoroughly, including the reliability and validity of that information. Subsequently they must develop the ability to make judgements and the skill to communicate effectively.

To achieve this, future graduates need a thorough background knowledge of pharmacology, pharmacokinetics, medical terminology, disease states, therapeutics and the complications of drug therapy. The working party established a list of primary and secondary subjects which were thought necessary in providing the basis of clinical pharmacy training (Table 1).

Table 1.

Primary subjects
Pharmacokinetics
Pharmaceutics, e.g. characteristics of dosage forms
Pharmacology
Clinical pharmacology, e.g. ADR and therapeutic monitoring etc.
Therapeutics
Secondary subjects
Communications
Disease States
Physiology
Epidemiology
Literature evaluation

The Victorian College of Pharmacy course has recently been updated and it is still too early to evaluate the changes which have been made. From a review of the curriculum it appears most of the relevant subject areas are included, although the subjects of clinical pharmacology and epidemiology may not be well covered. In addition, the scope and depth of the new subjects, e.g. pharmacy practice and clinical pharmacy and therapeutics, are as yet unknown. The working party believes that these subjects may provide the basis for further improvements in the program to develop clinical pharmacy education. Some of the objectives of clinical pharmacy training are covered in Table 2.

Table 2. Objectives of clinical pharmacy training

Students need the knowledge to engender the ability to:
1. interpret and understand the relevance of laboratory results to drug therapy;
2. detect early signs of drug induced toxicity;
3. detect and understand the significance of drug interactions;
4. detect patients at greatest risk of drug-induced toxicity and to act appropriately;
5. evaluate the safety and efficacy of dosage regimes for individual patients;
6. understand the relevance and effects of disease states on drug therapy, including indications and contraindications;
7. provide accurate, thorough and timely drug information, including advice in the selection of drug therapy.

It is possible that these subjects could be developed to allow the undergraduate student to obtain preliminary training and experience in the ward. The working party felt that this undergraduate experience could be a precursor to the further clinical pharmacy training undertaken in the traineeship year. (This is discussed in more detail under work experience below).

The Victorian College of Pharmacy has recognised the need to make changes and this must be an ongoing review with permanent active liaison developed

between the Victorian College of Pharmacy and the Society of Hospital Pharmacists of Australia (Victorian State Branch) to provide advice and guidance in the area of clinical pharmacy practice.

b) Work experience

A major criticism of the undergraduate course is that it still lacks patient contact. This could be achieved by clinical ward pharmacists providing a teaching service to students in the wards of hospitals, thereby enabling students to apply academic knowledge in a practical situation and thus begin the process of developing clinical skills.

Work experience during the trainee year also varies greatly between hospitals. Only a few hospitals offer trainee programs with regular rotation to inpatient ward services. There is a need to produce more uniformity and a general upgrading of the traineeship experience. This could be achieved by a more structured clinical learning program in the trainee year, with students being supervised by hospital pharmacy staff in conjunction with the Victorian College of Pharmacy e.g.:

(i) College electives could be taken in the trainee year, and/or
(ii) lectures could be held to integrate course work and pharmacy practice, for example, the practical applications of clinical pharmacokinetics.

In many ways the traineeship year offers a unique opportunity to mesh together academic knowledge and clinical practice. All too often, trainees forget basic knowledge because they don't understand how it relates to practice.

The article by E. Dean Martin[1] is a helpful guide to the types of topics, questions and assignments which may be of benefit during the trainee year.

2. Postgraduates

Clinical pharmacy is now an established service, yet, from the survey undertaken, pharmacy graduates still feel that further education is necessary in order to develop their skills to the fullest extent. While dedicated and competent pharmacists working in clinical areas are likely to develop the required skills eventually, the time taken to attain the expertise could be dramatically shortened by appropriate postgraduate education.

In Victoria, two postgraduate courses are available –

a) Fellowship Course of the SHPA
b) Graduate Diploma in Hospital Pharmacy, Victorian College of Pharmacy

Both these courses serve a current need and when improvements in clinical ward pharmacy teaching at the undergraduate level have been achieved, these courses could become more advanced and specialised. However, postgraduate courses are often not available or suitable to all, therefore, it is necessary to consider supplementary methods of upgrading knowledge; one of the major objectives being to encourage each other in the pursuit of new knowledge and skills.

Continuing education

Continuing education can be defined as educational processes outside the academic institutions and pharmacy departments.

1. State specialty practice groups

Small special interest groups of pharmacists could be established to hold regular informal workshop discussions on specific areas of practice; the purpose being to provide a forum for the exchange of ideas amongst practising ward pharmacists and other interested pharmacists.

This may relate to problems encountered or to the different techniques and methods used in practice and may cover a variety of topics, for example:

— how to take a good medication history;
— how to monitor specific drugs;
— how to monitor adverse drug reactions (ADRs);
— how to apply pharmacokinetic principles to therapeutic drug monitoring and dosage calculation.

2. Weekend seminars

Weekend seminars on clinical ward pharmacy topics could be held at intervals. These would aim to improve the depth of knowledge that the pharmacist already possesses.

It is envisaged that these seminars would consist of a series of lectures given by experts in the field.

Examples of major topics which could be covered are:

— dialysis
— oncology services
— liver diseases
— heart diseases

3. Lecture series

The lecture series run by professional societies such as the SHPA could be more structured to incorporate lectures on a set list of disease states or therapeutics topics to be covered in a cyclical man-

ner, for example, every three years. This would ensure the regular updating of pharmacists' knowledge in areas thought to be important to current clinical pharmacy practice.

Peer review

Peer review is a cornerstone in the implementation of a clinical pharmacy quality assurance program and in simple terms may be defined as staff appraisal of their work value and each other's.

The working party saw a peer review group as providing a friendly, constructive environment in which to motivate self improvement by promoting discussion and the sharing of knowledge. This should be seen as being distinct from administrative assessment.

One of the first steps is to decide who should be members of the peer review group. The size and composition of the group will vary depending on staff numbers. In small hospitals it may be the Chief Pharmacist alone. In the medium to large sized hospitals it may be a number of staff. An example of such a group may be:

the Chief Pharmacist (or Deputy)
the Senior Pharmacist in charge of the wards
and staff pharmacists.

The working party saw the inclusion of at least one staff pharmacist as essential in order to ensure the group is not seen as an assessment panel. Whether the staff pharmacist should be directly appointed by the Chief Pharmacist or elected by the staff is a matter for individual hospitals. Appointments should be for a fixed term (e.g. one year) and should be rotated if possible. All members of the clinical ward pharmacy peer review group must have had considerable ward experience.

It was also felt that it was essential for several discussion sessions on the format and objectives of the department's peer review program to be held with the staff prior to the implementation of such a program.

Mechanisms of peer review

The working party felt there were two major mechanisms by which a peer review program could be introduced, viz. clinical ward pharmacists' meetings and ward visits. Each has the aim of encouraging pharmacists to learn from each other, and to provide support as required.

1. Clinical ward pharmacist meetings

Although probably not relevant to the smaller hospitals, a similar function could still be achieved through normal staff meetings or set discussion times. From the results of the working party's survey, only eight hospitals reported that they held regular clinical ward pharmacists' meetings. However, the working party felt that such meetings form an essential component of clinical ward pharmacy services in the larger hospitals and strongly recommends the introduction of such meetings as the first step to the introduction of a peer review program.

The recommendations of the working party on the format of these meetings are as follows:

(a) The meeting should be held weekly, at a time and place where the maximum number of staff can attend.
(b) Attendance should be compulsory for the current ward pharmacists and for trainee pharmacists, but the meeting should also be open to all other interested staff.
(c) A roster for presentations by pharmacists should be prepared, with some meetings being set aside for general discussions on the day-to-day running of the ward pharmacy system; e.g. drug distribution reports, incident reports, problems with interviewing or counselling patients, examination of the system's shortfalls etc.
(d) The meeting should be chaired by a member of the peer review group. This member should also be responsible for the administration involved in organising the meeting.
(e) The basis of presentations by pharmacists should be educational and should emphasise the role of the ward pharmacist; e.g.
    — case presentations
    — drug utilisation review (DUR) reports
    — reports on clinical trials
    — ADR reports
    — specific drug or disease topics of interest.
(f) The peer review group should provide guidance and comments on the presentations as necessary, and in private if appropriate.

The objectives of these meetings are to create discussion and improve communication between staff, in addition to the training and educational aspects.

2. Ward visits

The aim of such visits is to observe, check, encourage and to provide guidance. The working party believes some notice, e.g. one week, should be given to the pharmacist concerned, and the visits should be conducted on a one-to-one basis. The pharmacist

should be informed directly at the time of any shortcomings. Conversely, positive features displayed by the ward pharmacist should be recognised and used as an example for other ward pharmacists.

Items that would be checked on a visit include:

(a) stock control, e.g. ensure that there are no problems with stock rotation or storage, excessive stock, expired stock, and drug distribution records.

(b) communications – check the pharmacist has an effective interaction with the patients, nursing, medical and other paramedical staff on the wards.

(c) patients' drug profiles – check these are up to date. For example, do they contain notes on admission drugs, drug sensitivities, diagnosis, drug related problems, and any relevant laboratory reports?

(d) patient reports – The ward pharmacist should be asked for a brief verbal report on selected patients. The report should include comments on the patients' medication history, their clinical response and any related pharmaceutical problems.

(e) medication charts, e.g. have drug charts been annotated to provide clarification or advice? Have drug interactions or contraindications been detected? Are dosage regimens safe? etc.

Other functions that the peer review group could be involved in include: supervision of inservice education, trainee teaching programs, and in conjunction with the Chief Pharmacist, establishing standards.

Inservice education

Inservice education (i.e. education programs within the pharmacy department) must be an integral part of any department that seeks to maintain the highest level of professional expertise, especially with respect to clinical ward pharmacy services.

The working party divided ward pharmacist inservice education into two areas, namely inservice training and ward orientation.

1. Inservice training

The components of inservice training should include:

(a) regular attendance at relevant ward rounds or meetings by the ward pharmacists;

(b) encouragement of staff to attend hospital lectures and seminars (as well as the continuing education programs and conferences run by professional organisations);

(c) weekly staff meetings; some of these should be set aside for educational purposes, e.g. journal club presentations, visiting speakers from medical and paramedical departments or units, and films or video tapes on relevant subjects;

(d) ward pharmacists' meetings;

(e) provision of adequate drug information resources, e.g. special subject files and journals;

(f) a trainee pharmacists ward experience program should be operating.

2. Ward orientation

A ward orientation program is essential to ensure the skills and expertise required for specific ward areas do not have to be learnt from scratch by each new ward pharmacist. There is also a need for a more intensive program for pharmacists who have no previous ward pharmacy experience.

The major aspects of a ward orientation program should include:

a) Pharmacist with no previous ward experience

The program should begin with an interview with the Chief Pharmacist. This should provide background information on the position, explaining the tasks to be performed and the general standards expected, including the statistics to be collected. The pharmacist should also do preliminary reading of job descriptions and relevant articles in order to obtain a background knowledge of the ward service provided.

b) Documentation of procedures

In order to maintain continuity of standards of service, it is important that each clinical ward pharmacist position be adequately documented. This means that, in addition to the job description documents, each ward area should have a procedures document or handbook. This should contain a common core of useful clinical and therapeutic information, together with details on aspects which only relate to the particular ward area; e.g.

— disease states likely to be encountered;
— special aspects in the treatment of these patients;
— peculiarities with drug therapy, such as unusual doses and/or drugs and special precautions etc.;
— special procedures, such as may be expected for an intravenous oncology admixture service;
— general information on the day-to-day running of the ward.

A reference list of useful articles and textbooks is also recommended. The information in this document or handbook should be updated at the end of

each ward pharmacist's tenure in a particular ward area.

c) Ward changeover

A changeover period is recommended (e.g. one week) to enable time for briefings and several visits to the ward area with the current ward pharmacist. Visits should cover points such as:

— introduction to medical and nursing staff etc.;
— attendance at ward meetings or rounds;
— the location of histories and laboratory reports, etc.

This period also allows time for discussion between the current and future ward pharmacists on the areas covered in the procedures document.

Department administration

While the success of a quality assurance program is the responsibility of all staff members, it is important to realise there will be no such program unless leadership is provided from the top. There are a number of methods by which pharmacy administrators can initiate and encourage a successful quality assurance program for clinical ward pharmacy services.

1. Staff selection

One of the most important tasks is the selection of the right type of people to carry out the required tasks.

The working party drew up a thumbnail sketch on the type of characteristics required, viz:

(a) They must have appropriate training, knowledge and, if possible, experience. Obviously people have to start somewhere, thus a pharmacist's inexperience should not preclude them from clinical ward duties. But it does mean inexperienced staff must undertake a more intensive orientation program.
(b) They should possess an ability, and indeed a desire, to learn from experience.
(c) They should be able to communicate effectively with all levels of hospital staff.
(d) It is essential that they have the ability to apply knowledge to make judgements on what is relevant and on how to solve problems.
(e) Their temperament should be of a stable nature, and they should be reliable, honest, observant and display initiative and motivation.
(f) They should be interested in their ward role and the patient's well-being.

If staff are chosen well, much of the remainder will fall into place.

2. Motivating environment

It is important to establish an environment which encourages objective self improvement and motivates people to attain a high standard.

Examples of how this may be achieved are:

(a) organise and establish a department peer review group or equivalent, as discussed earlier;
(b) encourage continuing education and ensure these programs are operating effectively;
(c) regularly review the objectives and performance of the service.

3. Work experience

The working party felt it was extremely important to allow ward pharmacists to work in a particular ward area for a period of three to six months to enable them to develop their skills and to enable them to establish sound communication links with ward medical and nursing staff.

4. Communication of duties and standards required

It is important that staff are fully aware of the objectives of the service, the duties involved and the standard required. This may be achieved by:

(a) establishing a ward pharmacy orientation program as previously mentioned, and ensure it works;
(b) interviewing staff to provide guidance and assistance with problems, e.g. when a pharmacist takes over an unfamiliar ward area or as part of the orientation program and then periodically as required;
(c) ensuring job descriptions are written and up to date. These should be explicit and easy to read. This also includes procedures to be followed for specific tasks when appropriate; e.g. the procedure for monitoring and reporting adverse drug reactions, or, patient medication history interview procedures.

Often the greatest problem facing ward pharmacists is a lack of time, and therefore priorities may need to be set out clearly. Each hospital must allocate its own priorities, and these are also likely to vary with the type of ward being covered.

For example, groups of patients believed to be at greatest risk should be specified and more intensive monitoring procedures should be documented for these patients.

This may be disease related, e.g. renal or hepatic dysfunction – dosage and drug selection; or it may be drug related, e.g.

warfarin – prothrombin levels, drug interactions;
digoxin – serum potassium, renal function, serum digoxin levels;
aminoglycoside antibiotics – dosage, renal function, ototoxicity, serum drug levels.

5. Staff evaluation

This is an important role for the Chief Pharmacist; it is also an extremely difficult task as the ward pharmacists are working on their own outside the department.

Evaluation is a matter of personal judgement but it may involve the following points:

— Are tasks done properly, thoroughly and accurately, or are actions timely or are priorities known?
— Are tasks approached with sincerity and with a serious concern for the patient?
— What initiative is displayed when handling problems and set tasks?

The working party defined a number of possible approaches to this problem, but again it is a matter of personal choice.

Possible methods are:

(a) direct discussion and interviews as previously mentioned; this may involve the Chief Pharmacist, Deputy Chief Pharmacist or Senior Pharmacist.
(b) passive feedback from other pharmacy or hospital staff, but ensure this information is accurate and unbiased; such information should never be more than an alert for more intensive observation from a distance.
(c) informal discussions with the pharmacist and general observations.
(d) periodic visits to the wards, independent of peer review ward visits and different in nature. Perhaps a brief visit to all wards by the Chief Pharmacist or Deputy Chief Pharmacist and the relevant Senior Pharmacist with random inspections of patient medication administration charts, drug trolleys and satellite pharmacies. Basically a flag waving exercise which also affords the opportunity to meet and talk with other ward staff.
(e) Another possible mechanism is to review computer printouts. For example: daily chemical pathology computer printouts on drug blood levels for hospital patients can be checked and where sub-therapeutic or toxic levels occur, the relevant ward pharmacist can be asked to explain what action was, or is, being taken.
(f) Following on from this, apart from computer printouts, there are a number of other statistics and reports, collected manually by ward pharmacists, that can be reviewed, e.g.

— drug stock lists;
— response to a drug recall;
— stock expiry date check lists;
— patient workload statistics;
— clinical activity statistics such as drug interactions detected, intravenous incompatibilities found, dosage regime problems detected;
— the completeness of clinical drug trial records where appropriate;
— the completeness of patient drug profiles. Are details such as the patient medication history or drug hypersensitivities listed?
— the thoroughness of drug utilisation review surveys or questionnaires;
— adverse drug reaction reports. Are there any? If so, are they accurate?
— the quality of written replies to drug information questions.

Conclusion

The working party has attempted to provide guidelines on how quality assurance in clinical ward pharmacy can be achieved. However, they are not necessarily the only way of approaching the problem, and naturally not every method or aspect of the working party's findings will be applicable to all hospitals.

In addition many of these methods cannot be developed overnight, but rather must be gradually developed over a number of years. The onus is on all members of the profession to ensure that an efficient program, which meets the needs of their particular hospital, is implemented. It is not easy, but it is essential if our profession is to achieve the highest possible recognition from others.

It is also important to point out that peer review should never be considered, nor used, as a punitive tool, but rather it should be a positive, helpful process aimed at encouraging self improvement.

It is the challenge of commitment to the profession that faces us today. Not the minimum standard of practising a technique, but rather incorporating the highest standards of professional ethics and knowledge into our daily practice.

We have a legal responsibility to ensure our patients' medication is accurate, timely and safe. We have a moral obligation to ensure that the risks of drug toxicity are minimised and that patients know how to use their medication effectively. It must be remembered that if we do not do our job well, it is ultimately the patient, our client, who suffers.

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Clinical Ward Pharmacy Survey – Victorian Hospitals 1982

Ian Larmour, Yvonne Allinson, Allan Manser, Gordon Spalding, Kathryn Brett, Suzanne Swan

Introduction

The concept of clinical ward pharmacy services is no longer in its infancy. It is being practised by efficient professional pharmacists in a number of hospitals and has been done so for a number of years. However in these times of constant change it is often difficult to know 'the state of the art' throughout Australia.

The Clinical Pharmacy Quality Assurance working party, set up by the Victorian State Branch of the Society of Hospital Pharmacists of Australia (SHPA) for the 1982 Victorian State Branch Conference, was faced with this problem. It was therefore decided to undertake a survey on the subject, in Victorian hospitals.

Method

A questionnaire (Appendix 1) was sent to 52 Victorian hospitals with pharmacy departments in early 1982. Hospitals were divided into groups according to the size of the pharmacy department staff, viz: those with more than 10 pharmacists, those with 3-10 pharmacists and those with 2 or less pharmacists. Replies to the questionnaire were received from 39 (75%) hospitals, 35 of which had clinical ward pharmacy services.

Response by hospital type:

No. pharmacists	No. hospitals	% response
> 10 pharmacists	8	100%
3–10 pharmacists	16	100%
≤2 pharmacists	15	54%

Ian Larmour, BPharm, FSHP
Yvonne Allinson, BPharm, Grad Dip Hosp Pharm
Gordon Spalding, BPharm
Pharmacy Department
Prince Henry's Hosptial Melbourne
Allan Manser*, BPharm, FSHP
Director of Pharmacy
Woden Valley Hospital, Canberra
Kathryn Brett, BPharm
Pharmacy Department
Preston & Northcote Community Hospital, Victoria
Suzanne Swan, BPharm
Pharmacy Department
Dandenong & District Hospital, Victoria.
(*Previously Pharmacy Department
Royal Melbourne Hospital, Victoria)
Address for correspondence:
Ian Larmour
Director of Pharmacy
Prince Henry's Hospital
St. Kilda Rd., Melbourne, Victoria 3004

Results

The respondents to the questionnaire indicated a total of 102 ward pharmacists positions throughout the state of Victoria, although the hours spent per week on ward pharmacy duties often varied greatly. The distribution of these positions by hospital type is shown in Table 1. Respondents indicated that an estimated 172 different pharmacists filled these positions over a period of one year. Of these, 54 (31%) had post graduate qualifications.

However 34 (87%) of respondents indicated that they believed pharmacists needed additional training in order to perform at their best as clinical ward pharmacists. It would seem that this lack of additional training would make it extremely difficult for inexperienced pharmacists to develop the necessary skills.

Respondents were asked to specify when they believed this training should take place. Of the 36 replies to this multi-choice question, 13 (36%) felt it should occur at the undergraduate level, 28 (78%) felt it should take place in the traineeship year, 30 (83%) specified inservice training and 30 (83%) specified postgraduate courses. It will be seen from these results that it was generally considered that the additional training should take place in several areas, with the most popular combination being the traineeship year, inservice education and postgraduate education. The majority of respondents (74%) felt this additional training should be carried out jointly in the wards and at the Victorian College of Pharmacy, although several also mentioned that part-time correspondence courses such as the SHPA Fellowship Diploma also had an important part to play. Only 19% of respondents believed the extra training should take place in the ward environment alone (Table 2) and no respondents felt this training should be carried out at the Pharmacy College alone.

Of the 35 hospitals with clinical ward pharmacy services, 20 (57%) indicated that trainee pharmacists worked under supervision in the ward areas for part of their traineeship year, which seems unusually low, but it should be remembered that many of the smaller pharmacy departments do not have trainee pharmacists on their staff.

Of the 35 hospitals with clinical ward pharmacy services, 12 hospitals had a staff of 2 or less phar-

Table 1. Location of clinical ward pharmacist positions in Victoria, 1982

Question	Total	>10 pharmacists	3-10 pharmacists	≤2 pharmacists
Clinical ward pharmacist positions	102	43	43	16
Total pharmacists filling positions per year	172	88	67	17
Clinical ward pharmacists with postgraduate qualification	54	24	23	7

Table 2. Additional training

Question	Undergraduate course	Traineeship year	Inservice training	Postgraduate course
(a) When should training be undertaken? (36 replies – multiple answer)	13	28	30	30
		Pharmacy college alone	Wards Alone	Both pharmacy college and wards
(b) Where should this training be carried out? (36 replies – single choice)		—	7	29

macists. In these hospitals the questions on ward pharmacist meetings and the allocation of pharmacists to the wards were largely irrelevant. However, of the 23 hospitals with larger departmental staff establishments, only 39% had regular ward pharmacy meetings, with the majority of these meetings being held regularly every 1 or 2 weeks (Table 3).

In the 24 larger hospitals, 16 indicated that ward pharmacists were allotted ward pharmacy duties on the basis of a roster, 2 indicated that a roster for selected staff was used, while the remainder indicated that staff were selected for these duties (Table 4).

The length of ward tenure varied with 9 (26%) hospitals indicating that ward pharmacists spent less than 3 months in one roster to a ward area, while 11 (31%) other hospitals indicated that ward pharmacists spent greater than 3 months in a particular ward area per roster, while the remaining hospitals, including the smaller hospitals, indicated that the ward pharmacist's appointment was permanent (Table 4).

Of the 11679 beds located in the 35 hospitals, 7756 beds (66%) were covered by clinical ward pharmacy services and there was little difference between the 3 groups of hospitals (Table 5). Of all hospitals, 13 (33%) indicated that all beds were covered by clinical ward pharmacists, a further 15 (38%) covered between 50-90% of beds, and 7 (18%) covered between 10-50% of beds (Table 6).

Table 3. Ward pharmacist meetings (35 hospitals)

Question	Total	>10 pharmacists	3-10 pharmacists	≤2 pharmacists
(a) Are regular ward pharmacist meetings held?				
YES	9	4	5	—
NO	14	4	10	—
Not Applicable	12	—	—	12
(b) Frequency of meetings (9 hospitals)	Weekly	2 weekly	Monthly	Every 3-4 months
	5	2	1	1

Table 4. Allocation of staff

Question	Roster	Roster/selected staff	Selected	Written application	Not applicable
(a) How are staff allocated to wards?	16	2	5	1	11
	<3 months	≥3 months	Permanent	No reply	
(b) Average tenure per ward pharmacist	9	11	14	1	

Table 5. Total beds covered by ward pharmacists

Department size	Total beds	Total beds covered by ward pharmacists	%
Total (35 hospitals)	11 679	7 756	66.4%
Pharmacy department size:			
>10 pharmacists (8 hospitals)	3 831	2 655	69.3%
3-10 pharmacists (15 hospitals)	5 363	3 392	63.3%
≤2 pharmacists (12 hospitals)	2 486	1 709	68.8%

Table 6. Percentage of beds covered in individual hospitals by ward pharmacists

Percentage covered	100%	80%	70%	60%	50%	40%	30%	20%	10%	0%	Total
Number of hospitals	13	5	5	3	2	3	2	1	1	4	39

Summary

Percentage of beds covered	100%	90-50%	10-49%	0%
	13	15	7	4

Table 7. Average number of beds covered by each ward pharmacist per hospital per day

Beds covered	20	30-39	50-59	60-69	70-79	80-89	90-99	100	120	150	161	229	320	Total
Number of hospitals	2	5	5	4	4	4	3	3	1	1	1	1	1	35

Summary

Beds covered	< 50	50-100	> 100
Number of hospitals	7	23	5

Table 8. Average time/bed covered by ward pharmacists per hospital per day

Minutes	< 1	1-1.9	2-2.9	3-3.9	4-4.9	5-5.9	7-7.9	9-9.9	12	No Response	Total
Number of hospitals	3	5	7	6	5	5	1	1	1	1	35

Summary

Minutes	< 2	2-3.9	4-5.9	≥ 7	No Response
Number of hospitals	8	13	10	3	1

The average number of beds covered by ward pharmacists in each hospital varied considerably (Table 7). In summary, of the 35 hospitals with clinical ward pharmacy services, the average number of beds covered by ward pharmacists was between 50-100 in 23 (66%) of hospitals, less than 50 beds in 7 (20%) hospitals and greater than 100 beds in 5 (14%) hospitals (Table 7).

The average time spent per bed per day also varied considerably (Table 8). A summary of the average time per bed showed that in 8 (23%) hospitals the ward pharmacists spent less than 2 minutes per bed, in 13 (37%) hospitals the ward pharmacists spent from 2 to 3.9 minutes per bed, in 10 (29%) hospitals they spent from 4 to 5.9 minutes per bed and in 3 (9%) hospitals they spent greater than 7 minutes per bed per day.

These figures mirror considerable variation in the type and scope of services provided. However it must be remembered that the demand for services and the type of service required does vary according to the type of patient being treated. E.g. Nursing home and standard maternity patients generally require less intensive services than medical or intensive care unit patients.

It should also be pointed out that within some hospitals there was considerable variation in the number of beds covered and time spent per bed by the various ward pharmacists and again this variation may reflect the type of patient being treated in the relevant ward.

Hospitals were asked to specify what services they provided in 'all', 'most' or 'some' wards covered by clinical ward pharmacists. The response to this question is shown in Table 9 (All responding hospitals with the service), Table 10 (Departments with greater than 10 pharmacists), Table 11 (3-10 pharmacists) and Table 12 (2 or less pharmacists)

Table 9. All hospitals with pharmacy ward services (35)

Duties	% of hospitals responding: Wards All	Most	Some	None
a) Drug chart review (e.g. drug interactions, dosage regimes etc.)	91	6	3	—
b) Drug distribution	88	6	6	—
c) Modified unit dose drug distribution	37	9	20	34
d) Unit dose drug distribution	6	3	9	82
e) Provide drug information	85	9	6	—
f) Actively monitor adverse drug reactions	29	9	25	37
g) Therapeutic drug monitoring	20	17	23	40
h) Pharmacokinetic service for drug dosage	6	3	23	68
i) Drug utilisation review surveys	23	3	37	37
j) Monitor patient parameters (e.g. renal function, serum electrolytes etc.)	29	14	37	20
k) Prepare intravenous drug admixtures for the ward(s)	14	12	20	54
l) Directly involved in clinical trials	6	3	17	74
m) Attend ward rounds and meetings regularly	14	3	29	54
n) Record patient drug profiles	41	9	25	25
o) Conduct patient interviews (e.g. medication history, hypersensitivities etc.)	9	9	28	54
p) Patient counselling for discharge prescriptions	29	9	31	31
q) Dispense discharge prescriptions	54	9	17	20
r) Involved in patient education programs	12	6	22	60
s) Involved in education programs for ward staff or medical students	20	3	43	34

The figures in these tables represent the percentage response to the appropriate question and the data in the tables is basically self explanatory.

The aspects of services most commonly listed as being provided to all wards were drug chart review, drug distribution and providing drug information. The types of services most frequently mentioned as not being covered in any ward were classic unit dose drug distribution, direct involvement in clinical drug trials and pharmacokinetic service for drug dosage.

Table 10. Pharmacy departments with > 10 pharmacists (8 hospitals)

	% of hospitals responding			
Wards	All	Most	Some	None
Duties				
a) Drug chart review (e.g. drug interactions, dosage regimes etc.)	100	—	—	—
b) Drug distribution	100	—	—	—
c) Modified unit dose drug distribution	50	—	25	25
d) Unit dose drug distribution	—	—	12	88
e) Provide drug information	75	25	—	—
f) Actively monitor adverse drug reactions	52	12	24	12
g) Therapeutic drug monitoring	25	12	38	25
h) Pharmacokinetic service for drug dosage	12	—	12	76
i) Drug utilisation review surveys	12	12	52	24
j) Monitor patient parameters (e.g. renal function, serum electrolytes etc.)	25	25	25	25
k) Prepare intravenous drug admixtures for the ward(s)	—	12	36	52
l) Directly involved in clinical trials	12	12	52	24
m) Attend ward rounds and meetings regularly	38	—	50	12
n) Record patient drug profiles	76	—	12	12
o) Conduct patient interviews (e.g. medication history, hypersensitivities etc.)	12	12	12	64
p) Patient counselling for discharge prescriptions	25	25	50	—
q) Dispense discharge prescriptions	12	—	50	38
r) Involved in patient education programs	12	—	25	63
s) Involved in education programs for ward staff or medical students	12	—	76	12

Table 11. Pharmacy departments with 3-10 pharmacists (15 hospitals)

	% of hospitals responding			
Wards	All	Most	Some	None
Duties				
a) Drug chart review (e.g. drug interactions, dosage regimes etc.)	86	14	—	—
b) Drug distribution	80	13	7	—
c) Modified unit dose drug distribution	26	14	20	40
d) Unit dose drug distribution	7	—	7	86
e) Provide drug information	80	7	13	—
f) Actively monitor adverse drug reactions	20	7	33	40
g) Therapeutic drug monitoring	13	20	27	40
h) Pharmacokinetic service for drug dosage	—	7	33	60
i) Drug utilisation review surveys	20	—	33	47
j) Monitor patient parameters (e.g. renal function, serum electrolytes etc.)	27	20	40	13
k) Prepare intravenous drug admixtures for the ward(s)	20	20	13	47
l) Directly involved in clinical trials	—	—	13	87
m) Attend ward rounds and meetings regularly	7	—	40	53
n) Record patient drug profiles	40	20	26	14
o) Conduct patient interviews (e.g. medication history, hypersensitivities etc.)	7	7	40	46
p) Patient counselling for discharge prescriptions	27	7	33	33
q) Dispense discharge prescriptions	73	13	7	7
r) Involved in patient education programs	7	7	20	66
s) Involved in education programs for ward staff or medical students	20	—	47	33

Table 12. Pharmacy departments with ≤ 2 pharmacists (12 hospitals)

	% of hospitals responding			
Wards	All	Most	Some	None
Duties				
a) Drug chart review (e.g. drug interactions, dosage regimes etc.)	92	—	8	—
b) Drug distribution	92	—	8	—
c) Modified unit dose drug distribution	42	8	17	33
d) Unit dose drug distribution	8	8	8	76
e) Provide drug information	100	—	—	—
f) Actively monitor adverse drug reactions	25	8	16	51
g) Therapeutic drug monitoring	25	16	8	51
h) Pharmacokinetic service for drug dosage	8	—	16	76
i) Drug utilisation review surveys	34	—	33	33
j) Monitor patient parameters (e.g. renal function, serum electrolytes etc.)	34	—	41	25
k) Prepare intravenous drug admixtures for the ward(s)	16	—	16	68
l) Directly involved in clinical trials	8	—	—	92
m) Attend ward rounds and meetings regularly	8	8	—	84
n) Record patient drug profiles	16	—	33	51
o) Conduct patient interviews (e.g. medication history, hypersensitivities etc.)	8	8	25	59
p) Patient counselling for discharge prescriptions	33	—	16	51
q) Dispense discharge prescriptions	58	8	8	26
r) Involved in patient education programs	16	8	25	51
s) Involved in education programs for ward staff or medical students	25	8	16	51

Conclusion

While it is difficult to collect data on the extent and type of clinical ward pharmacy services, the working party believes the data collected is useful as a 'bench mark' in defining and documenting the role of clinical ward pharmacists throughout the state of Victoria. The survey also highlights the call from all hospital pharmacists for the support and assistance of academic pharmacy institutions to help in the development of relevant educational programs to enable pharmacists to meet the needs of their changing professional role.

The working party was pleased to observe the growth in clinical ward pharmacy practice throughout Victoria despite the difficulties created by the current financial times.

Acknowledgements

The data presented in this paper is based on information supplied by the responding hospitals and the working party members would like to express their gratitude to these hospitals for their co-operation.

Appendix 1

Clinical Ward Pharmacy Questionnaire

Victorian Clinical Pharmacy Working Party 1982

1. Hospital name_____ Number of beds_____

   Occupancy_____

2. Total number of pharmacists allocated to ward service at any one time_____
3. Total number of wards_____
4. Total number of wards covered by ward pharmacists_____
5. Please fill in the following details for each ward pharmacist position.

	Number of Beds Covered	Time Spent in Ward Related Duties on Average Weekday	Number of Visits to Wards Each Day	Supplementary Notes if Required (e.g. Oncology Unit Dose)
Ward Pharmacist (a)				
Ward Pharmacist (b)				
Ward Pharmacist (c)				
Ward Pharmacist (d)				
Ward Pharmacist (e)				
Ward Pharmacist (f)				
Ward Pharmacist (g)				
Ward Pharmacist (h)				

6. Do trainee pharmacists work in the wards? Yes/No
   If 'Yes', please list brief details of involvement.

   _____

   _____

7. How are ward pharmacists allocated to wards?
   (Tick relevant section)
   - (a) Roster
   - (b) Written application from pharmacists
   - (c) Selected
   - (d) Other
     (Please list)_____

     _____

8. For what length of time are pharmacists allocated to particular wards?

   _____

9. How many of your staff are likely to carry out ward duties over a 12 months period?

   _____

10. How many of these pharmacists have obtained, or are obtaining post-graduate qualifications?

    _____

11. Do you believe pharmacists require special training to work in the wards?
    Yes/No
    If 'Yes', where are these skills best taught?
    (Please tick relevant section(s))
    - (a) Under-graduate
    - (b) Traineeship year
    - (c) Inservice training
    - (d) Post-graduate

    Should these skills to taught –
    - (a) At the Pharmacy College
    - (b) In ward areas
    - (c) Both
    - (d) Other
      (Please list)_____

      _____

Questionnaire Cont.

12. Are ward pharmacist meetings held? Yes/No
If 'Yes', how often?

_____

13. Which of the following duties are performed by ward pharmacists.

	All	Most	Some	None
(a) Drug chart review (e.g. drug interactions, dosage regimes etc.)				
(b) Drug distribution				
(c) Modified unit dose drug distribution				
(d) Unit dose drug distribution				
(e) Provide drug information				
(f) Actively monitor adverse drug reactions				
(g) Therapeutic drug monitoring				
(h) Pharmacokinetic service for drug dosage				
(i) Drug utilization review surveys				
(j) Monitor patient parameters (e.g. renal function, serum electrolytes etc.)				
(k) Prepare intravenous drug admixtures for the ward(s)				
(l) Directly involved in clinical trials				
(m) Attend ward rounds and meetings regularly				
(n) Record patient drug profiles				
(o) Conduct patient interviews (e.g. medication history, hypersensitivities etc.)				
(p) Patient counselling for discharge prescriptions				
(q) Dispense discharge prescriptions				
(r) Involved in patient education programs				
(s) Involved in education programs for ward staff or medical students				

14. Other comments

_____

_____

_____

_____

_____

_____

_____

_____

_____

Please return questionnaire to Mr I. Larmour, Pharmacy Department, Prince Henry's Hospital, St. Kilda Road, Melbourne.

Ian Larmour
Working Party Convenor
15th February, 1982.

5. Allinson Y, Dolphin R, Larmour I, Spalding G (1985); The Application of Peer Review to Clinical Pharmacy AJHP, 15, 4-7. Citations 3

The Application of Peer Review to Clinical Pharmacy

Yvonne M. Allinson, Roger G. Dolphin, Ian Larmour, Gordon J. Spalding

Clinical ward pharmacy services are now a well established and accepted facet of hospital pharmacy practice. However, it is essential that such services operate in conjunction with a department quality assurance program, with the central component being peer review. This paper outlines the steps taken to implement such a program in a pharmacy department. Emphasis is placed on the need for staff to be informed and involved in the decision making process. The concept of peer review is examined and three mechanisms of operation are described, viz. ward pharmacist meetings, ward visits and a clinical training program for trainee pharmacists. The program is well accepted by the staff and proves to be beneficial.

Introduction

Clinical ward pharmacy services are now a well established and accepted facet of hospital pharmacy practice. However, it is equally important that such services operate in conjunction with a quality assurance program. This is to ensure that:

1. patients receive the highest and safest quality of care that we can provide;
2. we are deserving of the trust put in us by the general public;
3. resources are used in the most cost-effective manner;
4. a foundation is provided to the claims that we make regarding our clinical role.

Quality assurance was the theme of the 1982 Society of Hospital Pharmacists of Australia (SHPA), Victorian State Branch Conference, and one of the areas of practice covered was clinical ward pharmacy.[1] It was recognised that the implementation of such a program for clinical ward pharmacists presented a number of special problems, partly because there are few definite end points, and partly due to the autonomous nature of their role. It was concluded that the mainstay of such a program hinged on the development of an effective and well accepted peer review program.

Yvonne M. Allinson, BPharm, Grad Dip Hosp Pharm
Roger G. Dolphin, BPharm, Grad Dip Hosp Pharm
Ian Larmour, BPharm. FSHP
Gordon J. Spalding, BPharm
Pharmacy Department
Prince Henry's Hospital
St. Kilda Road
Melbourne, Vic. 3004

Address for correspondence:
Ian Larmour
Director of Pharmacy Services
Prince Henry's Hospital
St. Kilda Road
Melbourne, Vic. 3004

This paper outlines the approach taken by the Pharmacy Department at Prince Henry's Hospital, Melbourne in the development of a peer review program, which is basically orientated to the needs of the clinical ward pharmacy services which have operated in the hospital since 1973.

Prince Henry's Hospital is a 409 bed acute teaching hospital associated with Monash University. The Pharmacy Department has a staff of eighteen pharmacists including six clinical ward pharmacist positions. These positions are rostered on a rotational basis with each ward tenure being three to six months and all wards are covered by the service.

Development

The initial step was to discuss the concept of peer review with all pharmacists, on a group and individual basis, in order to seek their opinions and to explain the concept. The concept adopted was that peer review meant 'staff appraisal of their work value and that of each others', and the aim was to develop a friendly constructive environment to motivate self improvement and to encourage the communication of information between staff in order to reach and maintain the defined level or quality of service. The objects of the program were to:

1. establish, monitor, review and maintain standards of practice;
2. develop the clinical skills of pharmacists by the provision of background knowledge and the documentation of techniques;
3. encourage staff to share their knowledge and experience;
4. examine the defined role of clinical ward pharmacy services and to detect real or potential problems in the system;
5. provide the necessary assistance to overcome any difficulties.

It is important to mention that peer review was also considered to be distinct from administrative assessment.

The next step was the formation of a department Peer Review Committee (PRC) to consider the mechanisms by which a clinical pharmacy quality assurance program could be implemented. Staff were asked to consider the composition of such a committee and it was decided that committee members should preferably be experienced clinical ward pharmacists. The Director of Pharmacy Services then invited a senior pharmacist and two staff pharmacists to participate on the committee for a twelve month period, on the understanding that at the end of this period, one member would remain on the committee to ensure continuity for the following year and that two new members would be added to the committee.

This was to ensure fresh ideas would be obtained and that representation would be shared. It was decided that the Director of Pharmacy Services would be an ex officio member of this committee and each committee member would have defined tasks to carry out routinely.

Mechanisms of peer review

The PRC directed their efforts into three areas:

1. upgrading the existing ward pharmacist meeting;
2. development and implementation of guidelines for peer review visits to the wards;
3. development of a clinical training program for the department's five trainee pharmacists.

1. Ward pharmacists meetings

Weekly ward pharmacist meetings had been held for many years and the task of the committee was really only to define the role of the meeting and to streamline its operation.

(a) Role of ward pharmacist meetings

The role of these meetings was defined as:

(i) educational i.e. to provide an incentive for all pharmacists to improve and share their knowledge;

(ii) clinical role examination and development i.e. to discuss job descriptions and duties in order to improve the service or to establish a means by which shortcomings could be overcome;

(iii) liaison within the department i.e. to keep others informed of current trends in patient treatment or ward systems and to discuss drug-related problems;

(iv) feedback from the drug information centre i.e. the feedback on interesting questions and answers (which also requires participation by the department's trainee pharmacists);

(v) administration i.e. to discuss and to provide advice on department clinical pharmacy service policies.

(b) Conducting the meeting

A meeting time of 0830 hours each Wednesday was chosen as it allowed all current ward pharmacists, other pharmacists not currently working in the wards and trainee pharmacists to attend.

The meetings are held in a conference room outside the department because of the availability of audio-visual aids and because it enables uninterrupted discussion. The meeting is now chaired by a member of the PRC on a four monthly roster basis and another member is rostered to record the minutes of the meeting. Each pharmacist is required to give two presentations over the year, with a roster being prepared by the PRC at the start of the year. The choice to topic is left to the pharmacist but is subject to defined guidelines and may take the form of:

(i) case presentations — unusual or typical cases found in particular wards;
(ii) adverse drug reaction reports;
(iii) clinical drug trials — especially where a clinical ward pharmacist is involved;
(iv) drug profiles (particularly for new drugs);
(v) therapeutic drug monitoring;
(vi) drug utilisation reviews;
(vii) drug therapy and protocols, including the comparative merits of different medication.

The presentation should emphasise the role of the ward pharmacist and the PRC members provide advice and assistance on these presentations to the pharmacists as required.

Some examples of recent topics are as follows:

— amiodarone — its use and problems;
— the interaction of quinidine and digoxin;
— drug therapy and elective surgery;
— case history of antithymocyte globulin in renal transplant rejection;
— case history — methyldopa, adverse drug reaction;
— case history and drug therapy — Hodgkins Disease.

Presentations usually take twenty minutes with approximately five to ten minutes for discussion. After the discussion period the senior pharmacist in charge of inpatient services may raise any administrative problems.

In addition, every third week is set aside solely for general discussion. In these meetings a wide variety of topics are discussed e.g. new drug treatment,

new procedures, new clinical drug trials, difficulties in the system, drug related queries or other new knowledge that should be shared with others. It is in these meetings that liaison with the drug information centre takes place. This includes a five to ten minute presentation made by a rostered trainee pharmacist on an interesting drug information enquiry which the trainee has helped to answer. This is part of the trainee pharmacists clinical training program and the aim is to develop their communicating skills in a group setting; training which is relevant to their participation in clinical ward pharmacy meetings and ward or medical unit meetings. Each trainee pharmacist receives assistance and guidance from a member of the PRC.

On occasions, in these general discussion meetings, there is a set topic discussed. This discussion is led by a PRC member after a short presentation. Some recent examples are:

(i) patient interview techniques, where specific guidelines were presented and the various techniques that can be used were discussed;

(ii) ward pharmacists handbook, where the contents of this book were reviewed and the inclusion of additional information was discussed;

(iii) adverse drug reaction reporting, in which the previous twelve months' reports were reviewed and specific guidelines on the detection of adverse drug reactions were developed and discussed;

(iv) therapuetic drug monitoring, where the techniques and pitfalls were discussed and guidelines developed.

2. Ward visits

The second major thrust of the PRC was the development of a peer review ward visit program. This means that one member of the PRC, together with the relevant clinical ward pharmacist, visits the wards covered by that pharmacist. The concept of these visits is that they provide a one to one informal discussion on the performance of the pharmacist concerned and should be a mutual learning experience. The role of the peer review pharmacist is not only to observe and check, but also to provide encouragement and guidance.

The visits are a review exercise and it is important to remember that unless a task is defined in department policy, there may be no absolutely right or wrong way of carrying it out, but the aim is to create discussion of these matters with a view to improving the overall standard of our clinical ward services.

Each ward pharmacist has at least one peer review ward visit towards the end of a tenure in a particular ward area. Ideally the reviewing pharmacist will have worked in this ward at some earlier time.

In order to remove the element of mystery or fear, a check list was prepared and circulated to all pharmacists. This check list provided a uniform framework for these visits since they were conducted by three different pharmacists. This check list is subject to annual review and includes such aspects as:

— the pharmacist's endorsements on medication charts;
— the quality of patient drug profiles;
— stock control and statistical procedures;
— patient and drug monitoring procedures, including notations made on the patient's drug profile and in the pharmacist's log book;
— drug information answers;
— knowledge of patient counselling;
— adverse drug reaction reporting together with patient reports.

However, the peer review pharmacist is not limited by this check list if other interesting points or problems are observed. Notes are made during the visits, mainly to enable accurate collating of results of all the reviews at a later date. These recorded notes are seen by the pharmacist under review and they include any comments that they may wish to make. Peer review ward visits generally take seventy-five minutes and are conducted at a mutually convenient time with one or two days notice.

The results of the initial visits were tabulated and presented to all staff pharmacists for discussion. This report documented the findings and comments obtained and highlighted those areas of practice that were being done well, and also those areas of practice where there was a need for improvement or which required further discussion. Anonymity was maintained in this public document. A number of recommendations relating to the details of practice came out of these discussions and are currently being implemented or examined in greater detail.

3. Trainee pharmacists clinical training program

This program was a secondary consideration for the committee and whilst not strictly peer review of clinical ward pharmacists, it is nevertheless relevant to the subject. This is because, firstly the PRC has an educational role; secondly, the trainee program provided teaching guidelines for the clinical ward pharmacists, and finally, hopefully it will help to produce better trained clinical pharmacists.

The details of this program were presented in a poster at the 1983 SHPA Federal Conference and therefore only a brief outline will be given in this paper.

The department has operated a ward orientation and experience program for its trainee pharmacists for many years. In this program, the trainee pharmacists were rostered on rotation to inpatient services for two week periods. In a full year this amounted to eight to ten weeks in the wards, with all ward areas being covered. However, the PRC decided that the existing program should be more fully developed.

Initially teaching guidelines for the clinical ward pharmacists were developed and discussed. Then each ward pharmacist was asked to produce a list of questions that related to the drug therapy and disease states encountered in their ward area, including common abbreviations, terminology and a list of useful reference sources. These lists of questions and references were then reviewed by the members of the PRC and standardised in quality, content and format. The documents were then reviewed at a clinical ward pharmacists meeting.

When the trainee pharmacists start their roster in a particular ward area, they are presented with a list of questions that they must commence to answer before beginning work in that area.

There are eleven sets of questions and each generally requires three to four hours work. The answers are then reviewed by the appropriate pharmacist and additional information is requested when relevant. The pharmacist is then expected to continue the teaching and questioning process, according to the defined guidelines, during the remainder of that week. Feedback from our trainee pharmacists indicates that they find this system extremely useful and interesting.

Evaluation

While the program has been operating for nearly two years it is still too early to provide a complete evaluation of the program's effectiveness, and of course evaluation must be an ongoing process. Nevertheless, many positive benefits have come out of the program to date.

1. Staff development

The program, and its build-up, has created interest and has stimulated staff to examine their role and performance in the wards, and with this has grown a confidence in both their ability and the importance of their role.

2. Staff acceptance

All pharmacists were interviewed by PRC members to elicit their perception of the program. The feedback was very positive and all believed the program was beneficial and should continue. This acceptance was clearly demonstrated by the friendly, rational and constructive dialogue that occurred without personality clashes during the peer review ward visits.

3. Education

A number of topics have been covered and each has promoted interest and discussion.

4. Problem detection

A number of problems or difficulties have been detected and most have been resolved and some are under further investigation and discussion. All pharmacists and trainee pharmacists were involved in the review of the problems which, in some cases, led to the development of practice guideline documents. The clinical ward pharmacists have reported that they have found these documents of value.

5. Communication

The introduction of the peer review program has promoted discussion and a greater sharing of knowledge.

6. Improved standards

There has been an obvious and gradual improvement in the quality of presentations made at meetings, as there has been in the confidence and technique of the presentor. The regular evaluation of the peer review ward visits indicate that many problem areas are being handled more thoroughly. There is also a general feeling that the clinical ward pharmacists are better equipped to handle their ward role. The program has also proved to be an extremely valuable training method for new pharmacists coming into the ward service and has supplemented the department's ward orientation program.

Conclusion

Peer review is a difficult challenge, but it is important for pharmacists to review their ward activities. Which tasks are most useful? Is our service really what we think it is? Only by asking these questions and only by examining our performance can we be sure that our goals are reached and are justifiable to others. Discussions with department pharmacists indicate that they have found the program to be a very productive exercise rather than a threatening experience and are keen for the program to continue.

Peer review is now a requirement in the Australian Council on Hospital Standards — Accreditation Guide for Hospitals and Extended Care Facilities, but more relevantly, peer review provides a mechanism by which we can provide inservice education and training, achieve our goals in practice and ensure staff are being employed in the most useful manner — a critical factor in the current climate of economic restraint. But the most important aspect is that it improves the quality of patient care.

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My Medication, Your Information

Ian Larmour

The causes of patient non-compliance are diverse, but the lack of appropriate drug information and education is one factor. The aim of the study was to find out what patients wanted to know about their medication, with the objective being to tailor the Pharmacy Department's patient education and counselling program to more closely meet the needs of patients. The study's ultimate goal was for patients to receive the maximum benefit from their drug therapy and therefore to improve both drug therapy and drug therapy economics. A total of 84 out-patients were interviewed and their opinions and comments were sought on a number of subjects including drug information content and delivery, counselling needs, patient compliance, labelling, adverse drug reactions and language difficulties. The results of this survey are discussed. Labelling appeared satisfactory (except in the case of supplementary labels), language difficulties were fewer than expected, and the incidence of adverse drug reactions higher than expected. The use of a Dosett® container was the most popular of the aids to compliance that were discussed with the patients. Most patients believed drug therapy counselling should be done by both medical practitioners and pharmacists. The information requested by patients varied considerably. The information most commonly sought was in relation to the purpose of the medication, adequate directions, drug interactions, actions to avoid and minor side-effects. The results of the survey have enabled a revision of the Department's approach to patient medication counselling.

Introduction

Medication is an essential component in the treatment of many diseases. The patient's prognosis depends on accurate diagnosis, rational prescribing and the correct dispensing of medication. However, outside the hospital environment, the decision on whether the dispensed medication is taken or not, rests with the patient.

Patient non-compliance with medication has been extensively studied and has shown non-compliance rates varying from 4% to 90% ($\bar{x}$ 36.9% ± 21.8%).[1-9]

Unfortunately, in most cases, the different methodologies used in these studies prevents an accurate comparison of results, but it can be concluded that non-compliance is a substantial problem. The methods that have been used to measure non-compliance include: patient interviews, the counting of unused doses, monitoring of prescription repeats, analysis of urine and blood for the presence of the drug or its metabolite and the monitoring of specific disease parameters such as blood pressure. Studies of the behavioural characteristics of non-compliant patients indicate a positive correlation with a number of factors, including family stability and the patient's perception of the seriousness of their disease and their susceptibility to the disease. Factors which show a negative correlation include clinic waiting time and the complexity of the prescribed medication.[1,14]

The causes of non-compliance have also been extensively studied.[1,6-8,10-12]

Mathews and Hingston[13] found a lack of distinct demographic characteristics for non-compliant patients.

There are, however, a number of direct factors that can cause non-compliance:

1. complicated dosage regimen;
2. large numbers of different concurrent medication;
3. language problems;
4. poor eye-sight and forgetfulness, especially in the elderly;
5. illegible labels or unintelligible wording on labels or pamphlets;
6. patients not understanding the purpose or importance of their medication;
7. suspicions or doubts about the safety of medication.

The non-compliant patients should not be regarded as a kind of misfit. Instead, they should be regarded as examples of where the system has failed to provide the patient with the information that they need and can understand, to enable them to make a rational decision on whether to take their medication or not.

Ian Larmour, BPharm, PhC, FSHP
Director of Pharmacy Services
Prince Henry's Hospital
St. Kilda Road
Melbourne, Vic. 3004

Address for correspondence:
Ian Larmour
Director of Pharmacy Services
Prince Henry's Hospital
St. Kilda Road,
Melbourne, Vic. 3004

Parkin et al.[15] and Hulka et al.[16] have reported that problems of non-compliance arise from the misunderstanding of dosage instructions.

It has been demonstrated that patient compliance can be improved by effective patient counselling by a pharmacist,[4,8] indicating the importance of an effective patient counselling program. To achieve this, it is necessary to attempt to understand the needs of the patient.

The aim of this study was to ask patients to specify what information and assistance they would find beneficial, with the aim being to incorporate these features into the department's counselling program and hopefully assist in the promotion of autonomous compliance.

Patient feedback was also sought on other aspects of the outpatient dispensing service and thus the survey also provided a type of quality assurance review.

The project also provided a valuable training program for the Department's trainee pharmacists and enabled them to gain experience in patient-pharmacist communications.

Prince Henry's Hospital, Melbourne, is a 407-bed acute teaching hospital with a large outpatient clinic population. The patients interviewed were randomly selected (using a random numbers table), from most clinics over a period of several months (Table 1).

Table 1. Clinics from which patients were randomly selected

Clinic	No. of patients interviewed	Clinic	No. of patients interviewed
Accident	1	Menopause	4
Anticoagulant	2	Neurology	5
Cardiology	5	Neurosurgery	1
Dental	1	Oncology	3
Dermatology	6	Ophthalmology	2
Diabetic	5	Orthopaedic	2
ENT	2	Plastic Surgery	2
Endocrinology	6	Psychiatric	4
Gastroenterology	3	Renal	4
Hypertension	3	Respiratory	5
Lipid	1	Rheumatology	6
Medical Unit A	1	Staff	1
Medical Unit B	2	Thoracic	1
Medical Unit C	4	Vascular Surgery	2

The patient's clinic was recorded according to the clinic attended prior to the interview. Many of the patients interviewed also attended several other outpatient clinics during the year.

Each patient was interviewed using a standard questionnaire to aid uniformity and, where appropriate, patients were shown examples of labels and patient aids. The questionnaire was designed[17,18] to encourage patients to give their answers spontaneously. The subject was introduced with an open question, but, where relevant, the interviewer would compare the patient's answer against a check list and would then ask additional questions if any points were not initially covered by the patient. The interviews were carried out by five trainee pharmacists under the direction and guidance of the Director of Pharmacy Services.

Results

A total of 84 randomly selected patients were interviewed. This represented 0.5% of all patients who obtained medication from the pharmacy department over the survey period. The age and sex of the interviewed group is shown in Table 2. There is an expected skew towards the patients who are over 50 years of age or older, with males and females being fairly evenly distributed. Approximately 46% of the patients interviewed routinely attended more than one clinic due to the co-existence of two or more medical problems, and 38% of patients were prescribed more than three concurrent medicines.

Table 2. Sample population characteristics

84 patients: 46 (54.8%) male
38 (45.2%) female

Age distribution:

Age group (years)	< 35	35-49	50-65	> 65
Patients	18 (21.5%)	9 (10.7%)	28 (33.3%)	29 (34.5%)

Number of clinics attended by patient:

Number of clinics	1	2	3	> 3
% patients	(53%)	(19%)	(15%)	(13%)

Number of concurrent medicines:

Number of medicines	1	2	3	4
% patients	(19.1%)	(20.2%)	(22.6%)	(6%)
Number of medicines	5	6	7	
% patients	(10.7%)	(9.5%)	(6%)	

Time on current medication:

Time	0 (new)	1 month	2-6 months	7-12 months	1-9 years	⩾ 10
% patients	8.3%	10.7%	15.5%	11.9%	29.8%	23.8%

Of the patients interviewed, 19% had been receiving their medication for a month or less and 23.8% claimed they had been on the same medicine for 10 or more years, with 46.4% of patients receiving their current medication for one year or less.

1. Suitability of labelling

All patients were shown examples of the computerised prescription labels and the standard coloured supplementary labels which are routinely used. The response of patients is shown in Table 3. These results were very encouraging except in the case of the supplementary labels, where 22.6% of patients found them hard to read. Predicably it was the older patients who had most difficulty with these labels.

The main complaint about the supplementary labels was that the size of the letters was too small and thus hard to read (21.4% of patients) and several patients with poor eye-sight could not read the labels at all. Some patients (7%) complained that the supplementary

labels were too lengthy and confusing. A number of patients also complained that the bright colours used on some supplementary labels made them hard to read.

Bright colours are used in these labels to attract the patient's attention, but in view of these findings it may be a self-defeating exercise. However, the labels in question also had very small printing and possibly the combination of these two factors made the label difficult for some patients to read. It may also have been due to the lack of contrast between the colour of the label background and that of the lettering.

Two patients made specific complaints about the standard supplementary label No. 8 'Avoid excessive skin exposure to direct sunlight while you are undergoing treatment with this medicine'. The label has very small black letters on a bright green background and the patients found the directions lengthy and unclear.

Therefore, it would seem that directions on supplementary labels should be short, simple and in the largest possible lettering. The characters should appear distinctly on a pale, bland background colour. The size of the printing used is of course limited by the length of the directions and the size of the label. Thus, it would seem appropriate to use a larger label size for these supplementary labels.

Table 3. Medication labels

Main label	
Easy to read?	98.8% Yes
Easy to understand?	95.2% Yes
Supplementary	
Easy to read?	77.4% Yes
Easy to understand?	95.2% Yes
Are they helpful?	94.1% Yes

2. Language problems

The language difficulties encountered are shown in Table 4. Surprisingly, language was a problem for only 9.6% of the patients interviewed, with only 3 patients having extreme problems. In these cases, there was usually a relative who could assist. However, although the sample size in this study was relatively small, it seems that language does pose a problem that cannot be ignored.

Several points are worth noting. Firstly, there was a broad range of languages (7) involved and secondly, patients may also be illiterate in their native tongue, thus limiting the usefulness of foreign language labels and pamphlets in some cases.

3. Indicators of compliance

This study did not attempt to assess the extent of patient non-compliance with medication, although patients were asked several low-key questions on the subject in an attempt to obtain some indication of the extent of non-compliance. However, these questions were really a lead into other questions. The first question related to variation of dosages:

Table 4. Language problems

	Patients	%	Languages
No difficulty	76	90.4%	—
Great difficulty	3	3.6%	Italian (1) Polish/Russian (1) Turkish (1)
Some difficulty	5	6%	Greek (2) Italian (1) Arabic (1) Polish/German (1)

Total number of patients experiencing difficulty with the English language 8 (9.6%).

'At times some patients choose to vary the dosage; do you find it necessary to do this?' If the patient gave a positive response, he/she was asked to give a reason for adopting this course of action. A total of 22 (26.2%) patients answered 'yes' to this question.

Of these, 7 (8.3%) were not prepared to comment further. However, 8 (9.5%) patients were able to give a legitimate reason for varying their dosage, viz, insulin dosage varied with home monitoring of blood sugar (2), analgesic dose was 'prn' (2), salbutamol inhaler was used 'prn' (1), medical practitioner advised patient (1) and one patient varied the dose according to his mealtimes.

The explanations given by the remaining 7 (8.3%) patients indicated true non-compliance:

- One patient tried to reduce the dose, against her medical practitioner's advice, because she felt the dose was too high.
- Another patient also indicated that she would cut down the dose if she thought she was getting too big a dose, but also stated that she may increase the dose of her hypnotic if it was not working.
- One patient stated that she stopped taking her tablets when she felt better.
- One patient admitted to varying his dose of propranolol tablets but offered no explanation.
- Three patients admitted to omitting doses because the medication made them feel drowsy.

Of the latter three patients, two stated they reduced their dose or stopped taking the medication if it made them feel tired, and the third stated that he deliberately avoided taking his midday dose of oxazepam if he was going out, since it made him feel 'drowsy and dopey'.

The attitudes of the latter group may reflect the negative influence of the large-scale publicity given to drug abuse over recent years. Therefore, the counselling pharmacist should attempt to give patients a much more balanced view by emphasising the positive benefits of correctly prescribed medication.

In the case of non-compliance caused by drowsiness, it could be argued that the dosage regimen did not meet

the needs of the patient. Perhaps patient compliance could be encouraged by careful consideration of the patient's life-style when determining dosage instructions. There is also a need for simple, uncomplicated labels on the medication container.

Due to different methodologies, it is difficult to compare these results with those of other papers. However, Boyd et al.[19], in a detailed study of patient compliance, reported that 25% of patients knowingly skipped a dose and 40% of patients used incorrect dosing intervals.

The second question related to patients forgetting to take their medication: 'One of the biggest problems for patients is remembering to take their medication exactly as directed. Is it a problem for you?' Only 6 (7.8%) patients answered 'yes', while a further 13 (15.5%) said that it was problem sometimes. That is, nearly 23% of patients interviewed admitted that they did have some problems in this respect. In comparison Boyd et al.[19] reported that 25% of the patients they studied forgot to take doses.

About the same number, but not always the same patients, indicated that they used a system to help them remember to take their medication. These results are shown in Table 5, with the main method being to separate their daily medication requirements, or to place them in a prominent place.

Table 5. Memory aids

System to aid memory	23.8%	Yes
Methods used:		
Write notes	3.6%	
Leave in a prominent place	7.2%	
Tablets put out daily	4.6%	
Spouse reminds	2.4%	
Meal times	2.4%	
Calendar	1.2%	
Daily pill container	2.4%	

Later in the questionnaire patients were also asked: 'Do you have (or have you had) any old medication at home?' to which 29 (34.5%) answered 'yes'. They were also asked 'Do you find your medicine tends to accumulate at home?' to which 22 (26.7%) answered 'yes'. Patients who answered 'yes' to this latter question were asked why they thought it happened. Only 9 patients were prepared to comment; three said it was due to over-prescribing, two patients said they liked to have a reserve stock of medicine, two said they got additional medication from their local general practitioner and one claimed it was because he forget to take his medication. The responses to these questions were fairly uniform across the four age groups. However, the response rates may be an underestimation of the true picture due to the inherent problems in obtaining statistics on the degree of patient compliance by an interview technique. The study was not attempting to determine the extent of non-compliance, nevertheless, the patients' responses do confirm the existence of patient non-compliance and indicate that it could be a substantial problem, whether intentional or not. However, the question that has not been addressed is whether the individual patient's non-compliance is continuous, periodic or a rare event.

4. Compliance aids

Patients were then asked if there was any system or aid that they thought would be helpful for them, and they were also shown some examples. The summary of their responses is shown in Table 6, with the Dosett container being the most popular system, especially with the over 65 age group. The use of a written chart was considered to be useful by 52.4% of the group, but was least popular with the over 65 age group. The use of a daily pill container was also very popular, but was least popular amongst patients under 49 years of age. The use of a calendar was least popular with the over 65 age groups and most poplar with the 35-49 age group, and the use of a 'special booklet' was most popular with the 35-49 and 50-65 age groups. The example of a 'special booklet' shown to patients was the standard Anticoagulant booklet provided by Glaxo Australia Pty Ltd. This booklet contains general patient information about the use of warfarin tablets and provides a medication record section. The relatively low acceptance of the booklet by the patients interviewed may have been due to its lack of relevance to their specific needs.

Table 6. Attitude to patient aids

	Some help
Written chart	52.4%
Doset container	67.8%
Daily pill container	51.2%
Calendar	26.2%
Special booklet	30.9%

5. Adverse drug reaction experiences

Patients were asked whether they had experienced any unpleasant or serious reactions to their medication. A total of 27 (32.2%) patients claimed that they had. Of these, 13 cases were relatively mild reactions and 4 cases were considered doubtful drug reactions; however, 10 cases were serious adverse drug reactions and included: sensitivity to penicillin (2), insulin induced hypoglycaemia (3), methyldopa-induced shock (1), gynaecomastia due to cimetidine (1), bleeding of an ulcer while on warfarin (1), lithium toxicity (1), digoxin toxicity (1).

The more minor reactions included gastrointestinal disturbances, headaches, flushing, itching, dizziness and mild skin rashes.

These results were surprising, but obviously this survey relied upon the patient's own description and the

sample size was fairly small. Nevertheless, a positive response by 32.2% of the patients interviewed is a disturbingly high figure and may reflect some degree of justification for a patient's suspicion about his/her medication. It also stresses the need to advise patients on how to use their medication properly, with particular emphasis on what steps they may take to minimise side-effects (especially the minor ones) or drug-drug or drug-food interactions. It may also be advantageous to supply patients with information on the procedure to be followed should they encounter any untoward side-effects.

6. Type of information desired

Patients were asked to indicate what details they required about their medication. Of the patients interviewed, 87% wanted their medication directions explained; the other 13% were older patients who had been on their medication for many years.

Overall, 75% of those interviewed wanted to know about minor side-effects, while only 43% wanted to know about rare or serious side-effects.

However, 60% of the under 35 age group wanted information about serious side-effects, which contrasted with 26% of patients in the over 65 age group. Most patients (91%) wanted to know the purpose of their medication. Many desired to know the expected duration of their drug therapy and many requested feedback on how their disease was responding to drug therapy.

The question about advice regarding precautions or 'actions to avoid', e.g., caution in driving a motor vehicle or operating machinery, brought a positive response from 76% of patients. Surprisingly, only 72% of patients wanted to know about drug interactions (including drug interactions with alcohol) although the need for such advice will vary with the medication prescribed. Patients were also asked whether or not they needed information on the storage and disposal of medication, but only 56% and 44% respectively were interested in this type of information. When analysed by age group, the younger age groups (paricularly those under 35) were much more interested in receiving information on drug interactions, side-effects and precautions.

Thus the personal preference of patients regarding the type of information they require can vary considerably. However, perhaps the main needs of patients can best be met by a one-to-one discussion between patient and pharmacist. This belief is endorsed by the high preference of patients (85.7%) for verbal counselling as discussed in the next section.

In this question, as in others, patients were first asked to specify the points that they wanted to know about their medication. Each patient was then prompted from the set list of points mentioned above.

The disturbing feature about this question was that almost all patients had to be prompted to obtain a response to each of the points listed, but more significantly, the initial response rate was only 22% of the response rate recorded when the patient was prompted by the interviewer. (Mean response 21.9% ± SD 24.8%, range 0-100%).

This indicates that patients are not always sure of what information they really need, and supports the concept of providing patients with a check-list of questions to ask about their medication. Such a list was developed following the surveys done by Chilton Research and Louis Harris and Associates on behalf of the United States Food and Drug Administration (FDA) in which they identify a major problem as being that patients simply do not ask enough questions. Those specified by the FDA[20] are:

- the name of the drug;
- its purpose;
- how and when to take it;
- when to stop;
- what food, drinks and other drugs to avoid while taking it;
- what side-effects may occur.

In view of the results of this study, it would seem the following points could also be added to this list:

- how long the medication will be needed;
- what actions should be avoided while taking the medicine;
- special storage conditions, if any.

The high incidence of adverse drug reaction experiences indicates that it would be justified to include a note on the procedure to be followed if such a reaction is encountered by the patient. This should include a 24-hour emergency telephone number . Hopefully, such a patient check-list would help to overcome the information gap in communications between patient and pharmacist or medical practitioner, by encouraging patients to ask more questions.

It may also be appropriate to add a general statement advising patients to ask their medical practitioners for progress reports on the effectiveness of their medication. Other useful information could also be included, such as warning patients not to share medication, safety aspects, the importance of cautionary labels, checking for expiry dates, procedures for prescription repeats and the benefits of drinking a glass of water after taking their medication.

7. Information delivery

Patients were asked to indicate their preferences on the format of counselling and education programs (Ta-

ble 7). Most patients wanted to be counselled by both pharmacists and medical practitioners and felt that the information from pharmacists could be provided verbally over the counter. However, approximtely 45% felt that all or part of the information could be given verbally, but in private, especially for very personal, sensitive or embarrassing matters. Less interest was shown in pamphlets (31%) and films or audiovisual aids (10.7%). In the latter case, this may have been because there was no sample film shown to the patient, who therefore may not have been in a position to accurately assess the benefits, or otherwise, of such films.

Table 7. Preference for method of information delivery

	yes
Verbally, over the counter	85.7%
Verbally, in private	45.2%
Written pamphlets	31%
Films, audiovisual aids	10.7%

Current developments

The pharmacy department is currently reviewing methods by which its patient medication education and counselling program can be improved. Due to current manpower limitations, the main thrust is towards patients in greatest need. These fall into two categories:

1. Patients needing extra counselling:

(a) when new medication is prescribed;
(b) when a dosage regimen is changed;
(c) language difficulties; to help overcome this problem, a counter telephone has been installed to allow a three-way conversation between the patient, interpreter and pharmacist. The telephone interpreter service is only used when the normal hospital interpreter service is not able to handle the request.
(d) complicated drug administration directions; e.g., prednisolone withdrawal;
(e) particular drugs (e.g., warfarin, monoamine oxidase inhibitors, clonidine, β adrenergic blocking drugs);
(f) particular dosage forms (e.g., inhalers or suppositories);
(g) particular drug combinations (e.g. (i) drug interactions that can be avoided by giving the two medicines at different times, such as antacids and tetracyclines; e.g. (ii) stabilised drug interactions that can become a problem if doses are missed or if the patient decides to discontinue one of the drugs).

Counselling is done verbally, but reinforced with relevant pamphlets or charts for specific dosage forms or drugs. The main points are futher reinforced at subsequent visits and all counselling sessions are ended with a general question, e.g., 'Is there anything that you would like more information about?' or 'Are there any questions that you would like to ask?' or 'Are you having any problems with your medicine?'

2. Patients with compliance problems: i.e., patients who are thought to need compliance aids and counselling are referred to the pharmacy department by the patient's medical practitioner. The main method involves using a Dosett container in conjunction with the District Nursing Service. These are usually elderly patients who have a number of different medicines.

Future developments

In the light of this survey, our plans for the future are:

1. to conduct a detailed review of the information and the format of information provided to patients in the form of pamphlets and labelling. The relevance of the supplementary labels for particular drugs has already been reviewed by the Department Peer Revew Committee.
2. to provide patients with a check-list of points that they should know, or ask, about their medication, together with information on the course of action to be followed when problems are encountered. These pamphlets will be placed in the pharmacy outpatient waiting area and will include a number of points listed on a similar type of pamphlet already in use.
3. to initiate special counselling programs for specific types of patients and to establish clinic discussion groups.
4. to evaluate or develop video training films. The use of such films will be pursued, despite the survey showing that few patients were interested in video training films. This may be because they had no sample film to view and were thus not able to comment accurately on their usefulness. The patients did, however, indicate a strong preference for personal discussion and thus these films may be limited to general background information. Much, of course, will depend on the quality of the films used.
5. to request structural changes to the Pharmacy Department patient counselling area, in order to facilitate counselling in a more relaxed and private environment.
6. to introduce a medication guide chart, to supplement the normal labelling and pamphlets, for specific drugs or patients.
7. to conduct a patient communication and counselling inservice training course for Pharmacy Department staff. This may become a regular part of our in-service training.

Conclusion

The study showed that the labelling provided was satisfactory, except for long, complicated supplementary

labels. It also confirmed the existence of compliance problems and enabled an assessment of patient attitudes to compliance aids, the drug information required and the form in which this informatiion could de delivered. The results have been used to develop strategies to improve the relevance of our patient counselling. The perceived needs of patients can vary considerably from individual to individual, but it is difficult for patients to ask the right questions without knowing what information they require. Therefore the use of a patient check-list of questions would seem extremely relevant. The relatively high incidence of minor (15.5%) and serious (11.9%) reactions to medication is disturbing and justifies the inclusion of information about the action to be followed if problems occur. Most patients believed counselling was required from both pharmacist and medical practitioner. The delivery of information verbally over the counter on a one-to-one basis was considered satisfactory by most patients, except for matters of a private or delicate nature.

The compliance aids most favoured were the Dosett container and a written medication chart. The study indicated that only about 24% of patients used a system to help them remember to take their medication. This figure is surprisingly low and perhaps indicates that patient education should cover this aspect.

It is unlikely that any system will produce 100% compliance, but if pharmacists are to adequately serve their patients, they must develop skills which will provide patients with the information they want and can understand. Such information must be related to patients' individual needs so that they progress from thinking 'my medication, your information' to 'my medication, my information'.

Hopefully, this survey has helped the Pharmacy Department achieve this goal.

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SHPA Policy Guidelines for Hospital Pharmacy Quality Assurance Programs

The Society of Hospital Pharmacists of Australia Quality Assurance Specialty Practice Committee:
Ian Larmour (Chairman), Yvonne M. Allinson, Julie L. Andrews, Robert H. Brice, John K. Jackson, Brian D. Reed

This document aims to outline the components of a quality assurance program in a hospital pharmacy department. The details in each area of practice have not been specified as it is intended that these will be developed by each Committee of Specialty Practice and individual pharmacy departments. The examples suggested are thus intended only as guidelines for these groups.

Quality Assurance can be defined as the procedures which are used to set, promote, maintain and monitor the desired standards for services or products.

The achievement of these standards is enhanced by an integrated structure of operation and assessment procedures. To be successful it is essential that all staff are involved in all stages of the program.

In the establishment of a quality assurance program the following steps are necessary:

1. Setting of goals

The general quality assurance goals for each section of the department should be determined.

2. Criteria selection

To achieve these goals, each aspect of a section should be examined in detail to determine the critical components that must be monitored, the ways in which quality can be monitored or promoted and what prerequisites are required.

This includes:

personnel	— selection;
	— training;
	— evaluation;
	— staff type and numbers;
	— job description.
materials and products	— type;
	— specifications;
	— assessment, evaluation and monitoring.
facilities	— construction;
	— floor plan;
	— equipment needed;
	— equipment specification;
	— monitoring of equipment.
procedures	— documentation;
	— critical steps;
	— checking procedures.

The critical aspect in the criteria selection is that it should have a direct bearing on the quality of the service or the product.

3. Setting of standards

The standard required for each criterion should be established. These may be absolute or require a percentage of compliance (relative).

To be successful this requires the involvement of all relevant staff, viz. experts in the area of practice and users of the services or products, utilising the 'Peer Review' and 'Quality Circle' concepts. These standards should be actively promoted and communicated to all staff, especially new staff.

Standards are also set by State and Commonwealth legislation and professional ethics as well as other non-legislative requirements e.g. Code of Good Manufacturing Practice for Therapeutic Goods and the Accreditation Guide of the Australian Council on Hospital Standards.

4. Methods

For each selected criterion, methods should be developed to promote, achieve and monitor the desired standard.

Methods fall into three main categories:

(a) protocols of practice (inprocess controls);
(b) assessment and monitoring methods (end-point controls);
(c) staff training, education and involvement.

(a) Protocols of practice (inprocess controls)

The steps in procedures must be thoroughly documented and should be designed to enhance quality assurance and incorporate relevant criteria and their required standard. The aim is to incorporate critical steps and specifications to promote quality assurance in each area of practice.

This includes:

(i) detailed documentation of duty statements and procedures for each position or process, including the qualifications, responsibilities, training and accreditation of personnel;
(ii) checking procedures in all areas of the department, viz. methods, documentation and the responsibilities of personnel;

(iii) the documentation of manufacturing procedures and records including the use of master formulary worksheets;

(iv) documentation required for all procedures and the design of forms and records, including accountability of documents and labels;

(v) material specifications and methods of verification;

(vi) equipment to be used in procedures, including inprocess checking of equipment, together with the maintenance and monitoring of procedures and records plus the calibration and validation of equipment. This may also include disposables and clothing;

(vii) documentation of microbiological monitoring procedures including methods, materials, sample size and selection, equipment, procedures, including quarantine procedures and action to be taken when a product failure is encountered;

(viii) documentation of labelling requirements and the use of warning or supplementary labels;

(ix) documentation of patient medication counselling, education and interview procedures, including patient pamphlets or medication compliance aids or charts;

(x) documentation of storage requirements of materials and products and receipt and issue procedures;

(xi) documentation of packaging procedures and records, including container and label specifications;

(xii) documentation of analytical procedures including sample size and selection, procedures, methods, materials, equipment, quarantine procedures and the action to be taken when a product failure is encountered;

(xiii) documentation of cleaning procedures;

(xiv) documentation of drug recall procedures originating both from within and outside the department.

(b) Assessment and monitoring methods (end-point controls)

Critical points in the provision of a service or product should be selected and evaluated against the set standard.

This review should be carried out by personnel not directly involved in the process under examination, e.g. a department peer review committee.

This may involve:

(i) clerical audits

Performance should be evaluated against a set criterion for each audit type.

This is likely to be carried out periodically but should be done regularly and should cover each department section within a reasonable time frame. The results of the audit must be documented. For example:

- manufacturing records;
- equipment records e.g. maintenance and monitoring records;
- patient drug profiles;
- endorsements on patient drug charts and prescriptions;
- written drug information answers;
- drug information files (e.g. current, readily accessible, and search procedures;)
- drug utilisation reports;
- therapeutic drug monitoring reports. This may include statistical analysis of pharmacokinetically predicted doses or levels against actual results;
- adverse drug reaction reports;
- microbiological testing reports;
- analytical testing reports;
- patient waiting times;
- pharmacist intervention records;
- statistical analysis of work loads.

(ii) chemical and/or physical examination of materials or products

This type of assessment would usually be in the form of ongoing routine procedures. Individual standards and specifications should be developed for each product. For example:

- microbiological testing;
- chemical assay for product integrity;
- physical examination and identification of products and materials;
- labelling of items;
- material or product verification e.g. pH, boiling or melting point, refractory index

(iii) system testing

The use of trial prescriptions or questions on an anonymous basis can be used periodically to randomly assess the standard of the service. This method should only be used if staff are aware that it may be done at any time and should have the acceptance of staff.

(iv) the use of questionnaires or interviews

Users of products and services may be asked for their assessment and satisfaction with particular services or products by the use of carefully designed questionnaires and/or interview sheets and communication techniques.

(v) personnel evaluation

Evaluation of personnel performance and the effectiveness of training methods should be under constant review by the Department's administrators.

(c) Staff training, education and involvement

This includes:

(i) inservice education;

(ii) inservice training and orientation;

(iii) continuing education (non-departmental);
(iv) research;
(v) peer review;
(vi) quality circles;
(vii) distribution of documentation on procedures and duty statements and communication of objectives and changes.

5. Evaluation of performance

The results of all audits should be critically reviewed by department administrators, section heads, department peer review committees and relevant personnel.

Good, mediocre and bad results must all be fed back to staff for discussion and comment.

Remedial action should be implemented as necessary with particular emphasis on training and education.

6. Review of standards and criteria

Standards and criteria should be constantly reviewed and evaluated. Changes may be required for a variety of reasons. For example:

- the results of performance evaluation;
- changing work pattern;
- an increase in the sophistication of the department's services;
- changing priorities;
- reports on practice in other hospitals and/or in the literature.

7. Supplementary notes

Administrative control, support and direction are necessary for a quality assurance program. But to be successful all staff must be involved. This may be achieved via the concepts of peer review and quality circles.

(a) Peer review

Peer review may be defined as the procedure where peers review and comment on each other's performance.

It has the following objectives:

(i) motivation of staff;
(ii) promotion of open effective communication between peers;
(iii) detection and resolution of problems;
(iv) promotion and setting of standards;
(v) review and guidance;
(vi) education;
(vii) administration and organisation aspects.

It requires the delegation of authority to staff members.

In larger hospitals this requires the formation of a department peer review committee of 3 or 4 pharmacists (e.g. 2 staff pharmacists, 1 senior pharmacist and the director or deputy director of pharmacy services).

In smaller hospitals it may involve all pharmacists on the staff. For very small departments (e.g. a sole pharmacist) it may require linking in with the pharmacy departments of other hospitals of similar type or geographic convenience.

The peer review committee may be involved in all aspects of pharmacy practice and should meet at least once every one or two months. However, the committee should be responsible for organising weekly meetings for staff, e.g. ward pharmacist meetings.

Peer review is distinct from administrative assessment, which should only be used when peer review fails.

(b) Quality circles

This differs from peer review in that it would involve all staff in a particular section of the department. The emphasis is also more oriented to the quality of services in the relevant section, especially problem solving and the use of resources and facilities. However, the objectives are similar to peer review, albeit on a different scale. This enables the more timely resolution of a number of section-specific problems, and may extend into other aspects e.g. the promotion of efficiency and productivity.

These meetings of section staff should be held on a regular basis depending on need. The aim is to identify, select and analyse solutions to problems.

8. Larmour I (1992); Report of the Quality Assurance Committee of Speciality Practice, SHPA 20th. Federal Conference Canberra 22nd - 25th November 1991 and AJHP, 22, 48 - 50.

Report of the Quality Assurance Committee of Specialty Practice

The Society of Hospital Pharmacists of Australia Committee of Specialty Practice in Quality Assurance

I will in this presentation give an outline of the objectives of the Committee of Specialty Practice in Quality Assurance (QA COSP), and discuss a number of aspects of quality assurance.

QA COSP Objectives

The objectives of the QA COSP have been:

1. To raise the general awareness of the need for quality assurance (QA) within the profession.

2. To outline the components of a hospital pharmacy department QA program. Guidelines have been produced and were published in the *Australian Journal of Hospital Pharmacy.*[1]

3. To utilise the expertise of other COSPs. Since QA crosses all boundaries of hospital pharmacy practice, we have encouraged other COSPs to develop QA criteria and processes in their areas of expertise. Most COSPs (especially the Clinical Pharmacy, Drug Information and Poisons Information COSPs) have risen to this challenge.

4. To promote discussion and to develop the practical aspects of QA programs. A very successful QA seminar was held in Melbourne in 1990. The seminar was well attended and excellent and enthusiastic discussions took place.

The proceedings of this seminar have recently been published and are now available for purchase from SHPA. We hope this seminar will be the catalyst for future developments in QA within the hospital pharmacy profession.

5. To develop QA networking. The QA COSP plans to send out a questionnaire to all hospitals in an attempt to compile a database on QA activities in Australian hospital pharmacy departments, the aim being to encourage liaison between hospitals – a network of sharing experience and helping and guiding each other. It is hoped that hospitals with particular expertise in an area of QA will be prepared to offer assistance and to act as a reference source to those departments wanting to establish similar programs.

6. To promote an understanding of QA in daily practice. In the early 1980s, QA was on few people's agenda, but I believe it is true to say now that it is on everyone's agenda. This is a pleasing trend. However, the Committee believes there is still a degree of confusion on what QA really means in daily practice.

Therefore, today there are several themes that I would like to develop. I will be concentrating more on the general aspects of QA in a pharmacy department.

An Objective Definition of Quality

What is quality? Quality is a subjective term that means something different to each of us (goodness, beauty, excellence, size, the way we are treated, etc.). These subjective values may cloud our response when we talk of quality assurance. Therefore we need an *objective* definition of quality.

Phillipe Crosby, author of *Quality is Free* and *Quality Without Tears*, defines quality as 'conformance to requirements'. In our terminology, requirements are 'criteria' or 'specifications'.

Some criteria, but not all, may contain, 'threshold values' which are 'allowed variations in a particular criterion', i.e. many processes have a normal distribution of variation. If the variation is outside this distribution there is a special cause and this should set alarm bells ringing.

Having defined quality, what then is an acceptable level of quality failure? Crosby specifies 'zero defects', i.e. we should meet our specifications or set criteria 100% of the time. If you consider this unreasonable, consider how often a bank balance error, when you lose money, is acceptable to you. Or, how many of you boarded an aeroplane in the last few days, expecting it to crash?

But who sets these criteria, or specifications? There are a number of sources, such as:

1. professional ethics, developed over years of practice;

2. professional society guidelines, such as those of the SHPA;

3. legislation and regulation, e.g. Pharmacy Board guidelines, Code of Good Manufacturing Practice, etc.; and

4. department administration, hopefully with staff input and involvement.

Most of the criteria involved in the practice of our profession are well known and applied, but they are not always documented in procedure manuals. There is also, of course, the process of setting criteria for specific audits or reviews of services.

Objectives of Quality Assurance

QA is the sum total of all actions taken to achieve 'conformance to requirements' for 100% of the time. But how do we put QA into practice? The aspects I would

The Society of Hospital Pharmacists of Australia Committee of Specialty Practice in Quality Assurance: Ian Larmour, (Chairman), Michael Ryan (Convenor), Ron Batagol, Lee Belcher, Robert Brice, Karen Clark, Karen Howitt, Allan Manser.

Address for correspondence:
Ian Larmour
Manager of Pharmaceutical Services, Monash Medical Centre
Locked Bag 29, Clayton Vic 3168

like to discuss are 'Getting it right the first time' and 'Continuous improvement'.

Getting it Right the First Time

In other words, we should do everything possible to avoid the chance of a mistake, defect or problem from occurring in the first place. There are two components: planning for quality and organising for quality.

1. Planning for quality

We need the right starting point or building blocks in place if we are to get the result we want at the end. This covers areas such as:

(a) Department goals, i.e. clear directions on what the department wants to achieve. These must be communicated to staff.

(b) Personnel. This covers qualifications, experience, number and type of staff, job descriptions, staff training programs and mechanisms for staff involvement in decision making and problem resolution, etc.

(c) Facilities.

(d) Equipment, e.g. laminar flow cabinets, etc.

2. Organising for quality

This means setting up our department in a way that will ensure mistakes or defects do not occur or are detected at the earliest possible stage so as to avoid more serious problems. It involves defining processes and monitoring performance. Organising for quality covers:

(a) Routine methods:

(i) Clearly documented procedures (including task related QA criteria). The added advantage of documenting routine procedures is that it also allows more time to spend on the non-routine difficult tasks. These routine tasks range from manufacturing and dispensing through to routine expiry date checking or back order follow-up.

(ii) Documentation and records of activity, e.g. manufacturing and packaging records, interventions made by ward pharmacists or outpatient pharmacists, etc.

(iii) On-the-job training and orientation of staff.

(iv) Checking activities at critical procedure points, e.g. prescription or manufacturing sheet checking, identification and validation of raw materials and continuous or end-point monitoring of products (e.g. sterility testing) and services (e.g. prescription waiting time, stock shortages).

(v) Equipment maintenance.

(vi) Defined procedure for reporting problems, defects or mistakes (i.e. action to be taken, forms to be filled in, etc.).

(vii) Staff involvement in decision making, e.g. peer review or quality circles.

(b) Specific reviews or audits:

These are performed periodically on a regular basis. This is an important part of QA, but only one part. The aim is to evaluate the outcome of our service with the desire to further improve it. Not everything needs to be done at once, and areas to audit can be chosen according to an area of interest (perhaps concerns exist) or in a cyclic fashion, whereby there is a 5-year plan and one part is done each year, for example.

Obviously a balance is required between the need for review, and the shortage of time. We should avoid what Berwick described as an 'orgy of measurement'.[2] Thus, we need to be selective in our choice, but what we choose should be done well, and we must take action to correct problems found. If no problems are found, move on to a new area, and perhaps return for review at a later time.

Audits of reviews may be department based, or multidisciplinary, and may be:

(i) audits of documents, e.g. adverse drug reaction reports, drug information replies, patient drug profiles, etc.;

(ii) reviews of interventions made by clinical pharmacists and their outcome;

(iii) multidisciplinary drug utilisation and effectiveness reviews; or

(iii) questionnaires to users of our services (internal and external to the department).

Continuous Improvement

Continuous improvement (or 'kaizen' as the Japanese call it) is a philosophy of continually striving to improve performance. It means detecting and correcting problems, and learning from mistakes, so as not to repeat them, and is an ongoing process, the aim being to bring the error rate down over time.

But what do we do if we find a problem or a mistake? Many problems can be solved quickly by the administrative process or by having clearly documented procedures. However, many problems require detailed review and need to involve a variety of staff. It may be more time-consuming in the short term, but if the problem is solved for ever, then it will surely save considerable time and effort at a later stage. There are two aspects of continuous improvement that I want to discuss today: the individual or the system, and the problem solving cycle.

1. The individual or the system

If a mistake is made, who is to blame – the individual or the system? Was the employee properly trained? Was the procedure clearly laid out? What about fatigue? Were checking procedures carried out by others? Obviously there are many factors to be considered.

If we concentrate on the individual, the 'bad apples' theory, people tend to hide mistakes or distort information to make it look good without any relationship to quality. This creates staff dissatisfaction and may lead to further poor performance. Most importantly, the opportunity to learn from mistakes is lost.

In fact, Dr W. Edward Deming, in 1982 and 1986, in studies at the Massachusetts Institute of Technology, found that 96% of errors in the workplace were due to process or system faults, poor training, poor job design and unclear purposes. Mistakes were rarely made due to lack of will, skill or benign intention. When the individual was involved, it was most often not because of lack of motivation or effort.

Thus, the emphasis must be on the system rather than the individual, though, of course, we must consider the possibility that individuals are placed in positions beyond their capacity, when relevant.

I would also point out that the benefit of having an objective definition of quality, i.e. conformance to requirements, is that it reduces the emotional content of problems, such as 'goodness' or 'badness', thereby allowing the problem to be dealt with effectively.

2. The problem solving cycle

The importance of detecting problems or defects is not so much that they occur but rather what can be done to prevent them from ever occurring again. The cycle is merely a systematic process for documenting, analysing and solving problems and the monitoring of these solutions.

The steps in the cycle are:

(a) collect information on what happened, step by step (when, where, what, who);

(b) analyse the problem and detect possible causes (why did it happen);

(c) develop solutions (brainstorming);

(d) discuss possible solutions and select a course of action;

(e) implement the solution;

(f) monitor the solution's effectiveness;

(g) if no problem, move on. If there is a problem, start again. Remember that the aim is continuous improvement.

Staff Involvement

This is the last subject I want to cover. The QA COSP has long advocated the need for involvement of staff in QA activities such as criteria setting, procedure and service development, problem resolution and decision making, monitoring, education and orientation, as well as administrative aspects. If any administrators are still doubtful, I put it to you that you are at the mercy of anyone who works for you. Therefore, it is in your interest to train your staff and to involve them in the running of your department.

The involvement of staff in QA has been put under the headings of 'peer review' and 'quality circles', but it really does not matter what the group is called. Nor is it solely for larger departments. In larger departments, a coordinating group is needed, but in smaller hospitals it may be that all staff are involved. It does involve some delegation of authority, but there are many benefits:

1. it allows the opportunity for frank and open communication (i.e. it is okay to make suggestions) and allows problems to be aired, discussed and resolved;

2. it allows the utilisation of the expertise of all your staff, i.e. the people actually carrying out the tasks;

3. it develops teamwork and cooperation; and

4. most importantly, *involvement* develops commitment and ownership.

Conclusion

QA failure has significant implications in terms of cost to the community, but we in the healthcare professions have an extra burden of responsibility to ensure our services and products are of the highest possible standard in order to safeguard the health of our patients. We must be worthy of the trust put in us by others. In addition, our patients' (i.e. our customers') perception of quality may not solely depend on how well we do our job technically, but also on how courteously we treat them. This factor should be borne in mind by all of us as we move into an increasingly competitive environment.

We should not see QA as a separate part of practice. Rather, it should be a part of everything we do. Nor should we see QA as merely to prevent mistakes. Rather it should be seen as a means of promoting efficiency and professional service.

We must never be content with the *status quo*, but should be continually striving for improvement in everything we do. Above all else, I truly hope that the profession will embrace QA as a way of life.

References

1. The Society of Hospital Pharmacists of Australia Quality Assurance Specialty Practice Committee. SHPA policy guidelines for hospital pharmacy quality assurance programs. Aust J Hosp Pharm 1988; 18: 129–30.
2. Berwick DM. Continuous improvement as an ideal in healthcare. N Engl J Med 1989; 320: 53–6.

Questions

Question: Dr Abel, Penna says we must document clinical outcomes to the insurance companies. Why is this?

S. Abel: It relates to reimbursement. For example, for our pharmacokinetic dosing service and our nutrition support service, we charge. Therefore, we need documentation to justify the charges.

Question: Mr. Collopy, I am interested in the use of gentamicin assays as a clinical indicator. We know that there are many inappropriate drug assay requests. With the use of the indicators there may be an increase in the number of assays, to little benefit. Would dosage changes as a consequence of assay results be a better indicator?

B. Collopy: With regard to your first point, it depends on where the threshold is set. In the first instance it will be set with regard to current practice, therefore there should be little increase. The field will decide what is appropriate. As for your second question, we do intend to ask for this sort of information at a later date in the program.

9. Larmour I (1994), Survive and Thrive with Quality Assurance, Quality Assurance COSP Workshop Report, AJHP 24, 92 - 93.

Those most at risk include the elderly who are taking more than 5 drugs or who are confused; de-institutionalised psychiatric patients; the chronically or terminally ill; and those from non-English speaking backgrounds. Community pharmacists, home nursing and community health services are in a position to refer someone who is in need of assistance. Compliance is the objective.

Good communication skills and a sound knowledge of pharmacotherapeutics are major requirements of the community liaison pharmacist. Service to long-term care patients should emphasise the patient as an individual. Health and cost benefits can be demonstrated by reduction of hoarding and rationalising of therapy.

Measurement of outcomes is essential if the services of a community liaison pharmacist are to be valued. Aspects which can be documented include:

- Audits of patient drug usage
- Adverse drug reactions
- Drug interactions and interventions
- Drug costs
- Reduction in hospital visits
- Readmission rates
- Number of prescriptions
- Therapeutic drug monitoring

More difficult to quantify are better utilisation of resources and quality of life.

Who pays is determined by who values the service. The service should be seen as separate to supply of medication. Governments talk about the advantages of having community liaison pharmacists, but they must be convinced to take the next step and to supply funding. Systems should be put in place to determine those patients who are at greatest risk of failure to comply with their medication regimen.

Workshop 7

Survive and Thrive with Quality Assurance

Committee of Specialty Practice in Quality Assurance

Contact person: Ian Larmour, Chairman, Committee of Specialty Practice in Quality Assurance
COSP representatives: John Jackson (Federal Convenor), Julie Andrews, Ron Batagol, Lee Belcher, Karen Clark, Elizabeth Creber, Carmela Corallo, Karen Howitt, Allan Manser, Margaret Walker

The underlying message of the workshop was to stress the importance of 'Quality Assurance' in the survival of our profession in these times of rapid and dramatic change. Could we follow the fate of the dinosaurs?

The workshop had four components:

1. Quality Assurance COSP activities

A briefing on the activities of the Quality Assurance COSP included a report on a hospital survey conducted in 1992.

In order to give workshop participants an idea of the type of Quality Assurance projects reported and in order to promote networking, a handout was issued. A Quality Assurance checklist was also issued in order to help hospital pharmacists develop their Quality Assurance Plan.

2. Basic Principles of Quality Assurance

A summary of the basic principles of Quality Assurance was presented and covered the following basic principles:

(a) Criteria and standards

The desired level of service or product needs to be defined or specified. This becomes the criteria by which we can monitor our performance.

The standard is to achieve this criteria at all times i.e. zero defects.

The most common types of data distribution were discussed in relation to the place of statistics in our criteria, viz:

— binomial data distribution where the results are absolute i.e. right or wrong;

— normal distribution where there is a normal variation in the process e.g. wound infection rates or patient waiting times. Such normally accepted variation can be built into our criterion, in what is normally described as 'threshold' values. These threshold values are based on the standard deviation about the mean. It was explained that in quality assurance usually we only worry about the negative variation, i.e. when we do worse than expected.

(b) 'Getting it Right the First Time'

That is doing all that we can to make sure our services or products meet our criteria and standards i.e. avoiding mistakes or problems.

This requires:

i) planning for quality e.g. procedure manuals, staff qualifications and training, facilities.

ii) organising for quality e.g. on-the-job training and checking procedures to monitor our performance on a day-to-day basis.

(c) Continuous Improvement

That is striving to find better procedures, methods and systems on an ongoing basis. When problems are

found (via incident reports, routine monitoring or specific audits or reviews) the cause should be investigated and improved methods, procedures or systems developed i.e. learning from mistakes. This is the basis of the 'Problem Solving Cycle' and it was emphasised that such reviews should concentrate on:

- the system not the individual
- data analysis not opinion.

(d) Staff Involvement
The importance of directly involving all staff in quality assurance was emphasised, since this improves communication, ownership and commitment.
(e) A Way of Life i.e. Quality Assurance is not a separate component of practice but rather an integral part of all practice.

3. Pratical Examples of Quality Assurance

In order to demonstrate that specific quality assurance audits or reviews are not difficult, a series of case studies on quality assurance projects were presented, with the emphasis on methodology. These were:
(a) an outpatient prescription error survey
(b) a survey of patient drug information leaflets
(c) discharge patient counselling rates
(d) telephone surveys - customer satisfaction, staff utilisation.

4. Performance Indicators

The concept of performance indicators was explained. In summary, performance indicators are key statistics that we monitor routinely. Whenever performance varies from what is expected, then it acts as an alert for further investigation and action.

The aim of the SHPA Federal Council and the Quality Assurance COSP is to develop performance indicators that are relevant to hospital pharmacists.

A brief brainstorming session was held in order to seek the ideas and opinions of members.

The Quality Assurance COSP has defined two types of performance indicators, viz:
(a) clinical indicators i.e. those that relate to patient care
(b) management indicators i.e. those that relate to support activities.

The requirements specified for a performance indicator were that they must:

- be able to be measured
- be relatively easy to obtain
- be reproducible
- be suitable for objective review
- be useful (and important).

Excellent discussion was generated and a number of ideas were developed. This information will be used by the Quality Assurance COSP in further developing this concept.

Performance indicators are primarily designed for use by individual pharmacy departments. However, it was pointed out that it may be useful for the profession to select a small number of key perfomance indicators to use on a national basis. Such information may give valuable support to pharmacy departments in their quest for survival.

In summary, the workshop covered a wide range of topics and achieved the aims outlined below:

- to encourage the use of Quality Assurance methods
- to provide details on the basic principles of Quality Assurance
- to provide practical information and advice on the application of Quality Assurance
- to promote discussion and seek opinions on the concept of performance indicators.

Workshop 8

Evaluating the Effectiveness of Drug Distribution Systems

Committee of Specialty Practice in Drug Distribution

Chairperson: Penny Thornton, Pharmacy Department, Westmead Hospital, Westmead NSW 2145
Scope: Drug distribution systems within hospitals
Aims:
1. To identify possible outcome measures of effectiveness
2. To identify costs incurred in distributing drugs
3. To look at future developments in drug distribution

Program:
Introduction and presentation of preliminary results of Australian survey of drug distribution methods — **Penny Thornton**
Interactive session on outcome indicators — **Margaret Duguid** (COSP convenor)
Cost of drug distribution by dose form: results from the national pharmacy casemix study — **Colleen Brooks**
Costs identified in changing from traditional to patient-based distibution — **Sue Bayly** (Royal Adelaide Hospital)
Future developments: report on a feasibility study

10. Larmour I, (1996) Performance Indicators in Hospital Pharmacy Practice, AJHP, 26, 89-93 and AJHP, 26, 376.
Citations 5

ices are being provided to those people rather than through a department by department approach. It is important therefore to know your achievements and level of performance compared to others; this in turn requires a commitment to evaluation and improvement at personal, service and organisational levels.

Fundamental to the ACHS' changing approach to quality is a desire to work in partnership with healthcare facilities, to assist in achieving accreditation status, but most importantly to enhance the quality of health care. ACHS Accreditation has a number of significant advantages for participating organisations. In some States, additional funding is provided to hospitals which are accredited. Accreditation is also becoming a prerequisite for contract negotiations between private hospitals and some health funds and accreditation status may impact on the level of reimbursement from some funds. An accredited facility will have a competitive advantage, by being able to objectively demonstrate efficiency and quality of services that meet community expectations. This will also help organisations to deliver care in line with best industry practice. The ACHS is looking at providing comparative data to participating organisations on a regular basis, to assist in benchmarking.

The movement towards ongoing self-assessment and periodic reviews by the ACHS will help healthcare facilities to maintain momentum in their quality improvement programs — to become dynamic learning organisations which are continually evaluating roles, services and performance. Accreditation helps organisations to focus on areas of customer service that may require improvement with the aim of ensuring that all customers, both internal and external, are satisfied customers. ACHS Accreditation is a tangible way of demonstrating to customers that your organisation is committed to providing high quality of care and excellence of service.

However, quality in itself is a never ending story. It cannot be mandated but comes from within, hence the question will always remain — can it be done better ?

This is the ACHS' changing approach to quality and the question that I leave with you.

Performance Indicators in Hospital Pharmacy Practice

Ian Larmour, Manager of Pharmaceutical Services, Monash Medical Centre, Chairman, SHPA Committee of Specialty Practice in Quality Assurance

Quality means many different things to people, but I believe it implies:

- Safety
- Accuracy
- Efficiency
- Effectiveness
- Meeting expectations.

Successful quality programs require input and feedback from staff and clients, that is we should see ourselves as part of a team.

Importantly quality programs require:

- planning (structure i.e. building blocks)
- organising (process i.e. ensuring procedures, systems and process are implemented and followed)
- monitoring (outcome i.e. reviewing our performance).

The aim is to achieve optimal outcome which, in simplified terms, has two major components:

- achievement of the desired result (this may be an intermediate step in a process or an end point in itself);
- continuous improvement.

MONITORING FOR QUALITY

Various methods are used in monitoring for quality. In some cases it will done periodically e.g.

- service reviews (where systems should be fully reviewed to seek out and resolve major problems or inefficiencies i.e. common cause problems);
- audits of various types;
- surveys and questionnaires;
- peer review ward visits.

In other cases, the monitoring for quality will be done on a continuous basis, such as:

- in-process controls e.g. checking procedures;
- complaints management;
- monitoring incident reports produced in the department or hospital;
- product and raw material tests for product integrity; and
- performance indicators.

Thus performance indicators are but one small part of a Quality Program.

Performance indicators may be defined as: 'statistics that accurately reflect performance of key services'.

The benefits of using performance indicators are

that they:

- focus our attention on our key services; and
- provide an alert to unexpected variation, thus enabling us to investigate the matter further.

It is the first step in continuous improvement. In other words, if we find a genuine problem then it is important to ensure that we take all the necessary steps to fix the problem and to ensure it does not occur again.

I would like to briefly remind you of the 'Continuous Improvement Quality Circle'. Having received an 'alert' to a particular problem the cycle follows a process of:

— defining the problem
— analysing the problem
— seeking various solutions
— choosing a solution
— implementing the solution and
— monitoring the results.

If the problem is resolved, we can then move on to the next project. If not, then the cycle should continue. In other words, it is really just a systematic approach to problem solving.

There are a number of factors to consider when choosing performance indicators. These factors include statistics that are:

- specific to the service being monitored;
- measurable and reliable;
- achievable within our normal resources, so that monitoring can be ongoing and repeated (the frequency of monitoring may vary with the individual performance indicator that is being monitored);
- relevant and useful to us and our clients;
- interpretable.

So what are our key services? I feel that they cover:

- dispensing and supply of pharmaceuticals;
- clinical services;
- education of patients, students and others;
- the provision of drug information and advice to patients and other health professionals;
- procurement of pharmaceuticals;
- product preparation, including extemporaneous products and sterile products;
- research including involvement in clinical drug trials.

Performance indicators can take many forms, but several simplified examples are:

Structure

- hours of staff education each year

Process

- number of interventions made by ward pharmacists

Outcome

- dispensing accuracy
- prescription waiting times
- percentage of patients counselled about their medication by a pharmacist.

Performance indicators have three main applications in that they allow:

- intra-department monitoring i.e. monitoring our own performance within our departments against our historical data. They can also be used as evidence that the department is performing according to your business plan;
- monitoring the department services provided to our clients i.e. ensuring we are meeting the needs of patients, other departments and other health professionals;
- benchmarking i.e. it gives us the opportunity to not only monitor our own performance, but it also gives us the chance to compare our performance against those of our colleagues. However, it must be remembered that true benchmarking has both a quantitative (statistical) component and a qualitative (descriptive) component.

When performance indicators are compared, we must remember that we are only dealing with the quantitative component of benchmarking. But it does mean that if the results cause you concern, you can then move to the next step of seeking to carry out a qualitative review.

Our response to 'bad news' can be either a negative response e.g. 'It is all a load of rubbish! They don't know what they are doing and so on.'

Alternatively, we can make a positive response e.g. 'How can we improve our services? What do we need to do to catch up?'

In fact the smart manager would use this data to get the necessary resources to enable them to catch up.

I would advocate that the latter response is what our profession needs to pursue, if we are really serious about continuous improvement and we want to make a positive contribution to patient care.

In recent years all health professional groups have become increasingly aware of the need for national performance indicators.

Therefore, after considerable discussion at various venues, including a workshop at the last SHPA Federal Conference, the QA COSP and the Federal Council decided that we should start moving in this area.

QUALITY ASSURANCE COSP SURVEY

Subsequently, it was decided to conduct a survey of four performance indicators. In addition to collecting preliminary data, secondary objectives of the

survey were to raise awareness of the performance indicator monitoring concept and to encourage people to put the principles into practice.

The factors which influenced our choice of performance indicators were that it was thought that:

- the information would be useful for all hospitals; and
- that collecting the data required would be achievable.

The response rate to the survey was 37% with all States participating, although the response rate did vary across the various states. However, useable data (to at least one question) was only able to be obtained from 24% of the 300 hospitals surveyed in November 1994.

The first performance indicator (Question 6) was 'The percentage of discharge patients counselled about their medication by a pharmacist'.

Results

n = 53
mean = 43.8% SD = 31%
range = 0.5% to 100%
median = 40%

The survey showed that on average 43.8% of discharge patients were counselled about their medication by a pharmacist, but there was considerable variation. However, some hospitals indicated that they did not supply any discharge medication. In some cases this was because patients were being transferred to another hospital.

The second performance indicator (Question 7) was 'The incidence of totally out of stock pharmaceutical items which occurred because of a failure in the pharmacy department systems'.

Results

n = 51
mean = 0.9% SD = 1.1%
range = 0.01% to 5%
median = 0.7%

These results are noted for their extreme variation with a mean of 0.9% and an incredible standard deviation of 1.1%, indicating that there were probably many different methods being used to make the calculations.

Some respondents indicated that they included items not normally kept in stock. The intention was that it should only be applied to items which are normally kept on the shelf in the department and where the stock became totally depleted due to a failure in our systems.

It was also not meant to include items which could not be supplied by the manufacturer due to production problems.

The third performance indicator (Question 8) was 'The number of interventions made by ward pharmacists per 100 bed days'.

Results

n = 38
mean = 0.036 interventions per 100 bed days
SD = 0.02
range = 0.01 to 0.09
median = 0.03

The variation in results again was significant and perhaps indicated that different methods were being used. Surprisingly, one of the difficulties encountered was in determining the number of bed days. Some respondents thought it only applied to bed days for the wards covered by a ward pharmacist.

What was intended was that it should include all bed days. In hindsight, however, we should have perhaps specified the exclusion of some groups of patients who do not have any contact with the pharmacy department, such as simple same day surgical procedure patients.

There was also some confusion as to what constituted an 'intervention'. However, we did clearly specify the definition put forward by the Clinical Pharmacy COSP. There were many estimates and guesstimates and this data was not included.

The final performance indicator (Question 9) was 'The percentage of attempted interventions by pharmacists that were accepted'.

Results

n = 41
mean = 85% SD = 12.5%
range = 60% to 100%
median = 90%

These very positive results indicate a high level of acceptance of pharmacist input into patient care by medical staff. This data may be useful for the SHPA in developing arguments on the need for clinical pharmacy services.

FUTURE DIRECTIONS?

The survey response was reasonable, but the number of respondents who could provide useful data was a little disappointing. However, this was expected and hopefully more people will now be collecting the data. Many of the respondents did indicate that they would be collecting the data in future.

However, the survey has provided the SHPA with baseline data and for the first time individual departments have at least a rough idea of what is going on nationally. The future directions should include the following aspects:

- Repeat surveys are obviously needed — I must also say that the members of the QA COSP thought the data would be relatively easy to

collect, however when we started to collect the data ourselves, we did uncover a number of technical difficulties. These matters will be more clearly specified in any future surveys.

- Input on choice of performance indicators is requested. I wish to make it very clear that the QA COSP is very keen to hear your views on what performance indicators you believe would be beneficial to the profession. Please feel free to contact myself or any other members of the QA COSP. The other COSPs of course should also be pursuing this matter.
- Quality use of medication indicators — to date we have largely concentrated on the use of performance indicators within our own departments. This is because we believe it is important to have our own house in order before we start preaching to the world.

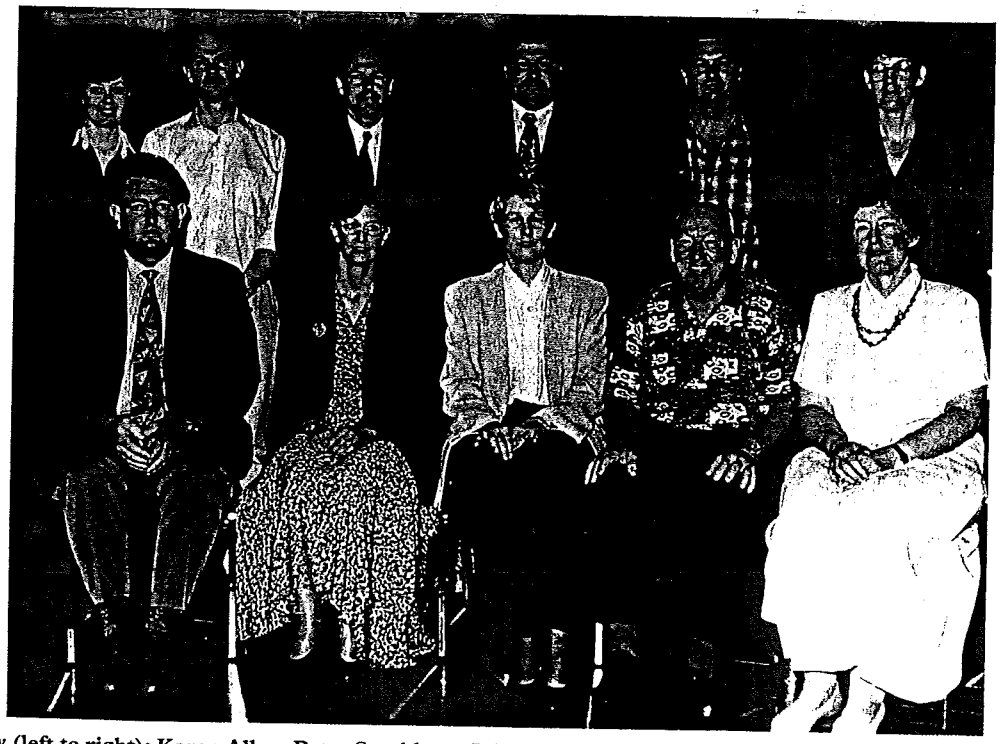
However, it is now an appropriate time for us to broaden our horizons to help develop performance indicators that are relevant to ourselves and our various clients.

Quality use of medication is an obvious area and we now need to concentrate our efforts in this direction. In fact, many of us are already doing so e.g. collecting data for the ACHS Clinical Indicators 6.1 and 6.2; monitoring hospital admissions due to adverse drug reactions; and many of us have drug utilisation evaluation programs in place.

- Effective use of performance indicators — we need to ensure that we fully develop all the processes to get the maximum value out of performance indicators, particularly in respect to continuous improvement. Obviously there is still much to learn.
- Influence of technology — one of the most frequent complaints that I hear is about the amount of time it takes to collect quality monitoring data. Therefore we need to look to technology to enable us to gain the data that we need with the minimum of effort and disruption e.g. ward pharmacists collecting intervention data on hand held computers, rather than using handwritten notes; barcoding of patient prescription labels which can be scanned on receipt and issue to the patient so that waiting times can be determined.

My final comment on our directions for the future is that I believe performance indicators should be a key element of all pharmacy department business plans and quality programs.

SHPA Federal Council



Back row (left to right): Karen Allen, Peter Stuchbery, John Jackson, George Taylor, Peter Tenni, Helen Dowling
Front row (left to right): Chris Alderman, Sue Brown, Jane Hill (Executive Officer), Neil Naismith, Ruth Giesel

11. Larmour I, Thomson W (1997) “Spend more on pharmacists and less on drugs” Letter to Editor, AJHP, 27, 335. Citations 2

LETTERS TO THE EDITOR

Spend More on Pharmacists to Spend Less on Drugs

To the Editor,

In these times of economic constraint, hospital pharmacists are increasingly being required to justify their roles. The need to demonstrate the value-added services provided by hospital pharmacists has long been recognised, but has always been difficult to quantify.

An essential part of this process is the evaluation of the economic impact of the clinical interventions made by pharmacists. Therefore the importance of the SHPA Cost Benefits Analysis Study cannot be overstated. However, readers may be interested to learn of some interesting data that we have obtained in a preliminary benchmarking exercise, which involved a number of large teaching hospitals across the country.

Data analysis is of course only one part of the benchmarking process, but it does present a number of problems, not the least of which is to find common parameters that reflect valid comparisons. This is because of variations in work unit definition, data collection and work practices across the country. During our review, we found drug expenditure, pharmacy department salary costs and the number of bed days to be the most durable parameters available to enable a degree of comparison between hospitals across the nation.

The most interesting finding was the relationship between drug costs per bed day and total pharmacy department salary costs per bed day (Figure 1).

This illustrates a strong relationship between decreasing drug expenditure and increasing pharmacy department salary costs, suggesting that more comprehensive pharmacy services do add value to the hospital's operation. Expenditure recouped under Section 100 of the *National Health Act* was excluded because these drugs are mainly used outside the hospital and their prescribing is subject to specified limitations.

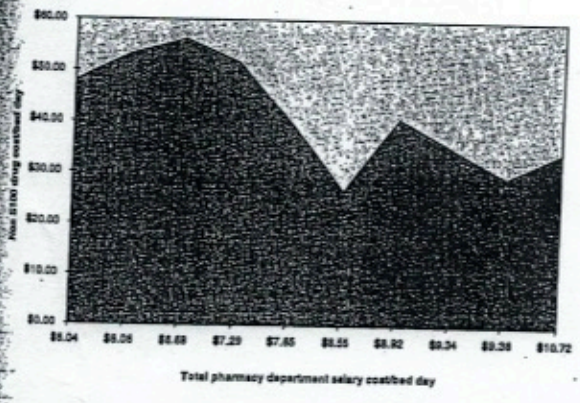


Figure 1. Total pharmacy department salary cost/bed day vs non-Section 100 drug cost/bed day

The limits to the interpretation of these data are fully recognised, nevertheless we believe readers will find the data fascinating. A qualified epidemiologist and biostatistician reviewed the data and conducted a linear regression analysis. This showed a clear relationship where drug costs (excluding Section 100 drugs) per bed day decreased by an average of $5.20 (95% confidence interval $2.38 to $8.01) for every dollar of pharmacy department salary costs spent per bed day. (The p value for the relationship is $p = 0.0068$, so the hypothesis that there is no relationship is rejected in favour of a simple linear model; residual standard error: 6.766 on 8 degrees of freedom; multiple R-squared: 0.6201; F-statistic 13.06 on 1 and 8 degrees of freedom.)

Despite any limitations in the data, we believe hospital administrators would be well advised to think long and hard before they decide to 'gut' clinical pharmacy services. The cure may be worse than, what has been described by some consultancy firms as, the Victorian disease.

Ian Larmour
Manager of Pharmaceutical Services
Monash Medical Centre

Bill Thomson
Director of Pharmacy
Austin & Repatriation Medical Centre

SPA 1997 Remuneration Survey Published

To the Editor,

The Salaried Pharmacists' Association (SPA) has published the results of their 1997 remuneration survey covering both community and hospital pharmacists.

The survey was conducted by the Association of Professional Engineers, Scientists and Managers (APESMA), Australia on behalf of SPA. APESMA has been conducting remuneration surveys of its own

MONASH MEDICAL CENTRE

A hospital of the Southern Health Care Network

13th June 1997

Damien Jolly
Senior Lecturer
Epidemiology & Biostats
Department of Public Health and Community Medicine
Melbourne University
Fax: 9347 6136

Dear Damien

Data as discussed.

Major Hospital Benchmark Data (10 Hospitals across Australia, Drug Expenditure (less Sect 100 drugs) > $5 million pa)

Hospital	Drug Expenditure (less Sect 100 Drug Expend)	Beddays	Tot Pharm Salary Costs	Drug Cost (Excl S100) per Bedday	Total Pharm Sal Cost per Bedday
1	$9,150,000	224,248	$2,000,000	$40.80	$8.92
2	$7,260,000	136,513	$827,744	$53.18	$6.06
3	$15,143,005	315,745	$1,906,873	$47.96	$6.04
4	$5,721,593	215,936	$1,846,172	$26.50	$8.55
5	$7,898,712	198,124	$1,516,494	$39.87	$7.65
6	$8,494,629	247,392	$2,650,750	$34.34	$10.72
7	$6,119,653	174,612	$1,631,165	$35.05	$9.34
8	$7,886,126	269,013	$2,522,579	$29.31	$9.38
9	$12,856,886	228,875	$1,528,094	$56.17	$6.68
10	$6,155,742	119,437	$870,251	$51.54	$7.29
	[Refunded & mainly outpatient expenditure, limited range of very high cost drugs]				

Thanks for looking at this data. MMC is Hospital 4.
My Fax Number is 9550 2595, Telephone 9550 2596.

Yours sincerely

Ian Larmour
Manager of Pharmaceutical Services

Clayton Campus: 246 Clayton Road, Clayton, 3168, Victoria, Australia
Telephone: (61) (03) 9550 1111 Facsimile: (61) (03) 9550 6111
International Country Code (61) Interstate Area Code (03) International Callers Place (613) in Front of Chosen Number

The University of Melbourne

Department of Public Health and Community Medicine
200 Berkeley Street, Carlton, Vic 3053 Australia

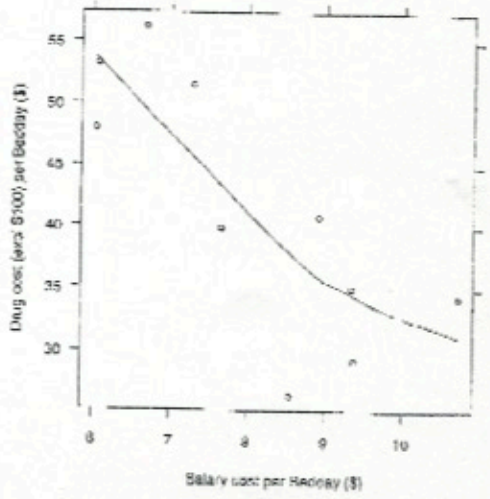
Fax Cover Sheet

Date	Monday, 16 June 1997	*Pages:* 1 (incl)
To	Ian Larmour Manager, Pharmaceutical MMC	*fax:*9550 2595 *phone*: 9550 2596
From	Damien Jolley, Epidemiology & Biostatistics Unit	*fax:* 9347 6136 *phone:* 9344 4093

Major Hospital Benchmark Data

Dear Ian: results of analysis, as discussed.

Question concerns the relation between drug expenditure per bedday and salary costs per bedday. A plot shows a clear linear relation, with drug costs decreasing uniformly with increasing salary expenditure.



We can fit a linear model to these points:

```
Call: lm(formula = drug.pb ~ sal.pb)
Residuals:
    Min      1Q  Median      3Q     Max
 -12.44  -3.947  0.7742  5.473   7.504

Coefficients:
              Value  Std. Error   t value  Pr(>|t|)   lower95
(Intercept)  83.3548   11.7866     7.0720    0.0001   60.2531
     sal.pb  -5.1950    1.4377    -3.6135    0.0068   -8.0128
             upper95
(Intercept) 106.4564
     sal.pb  -2.3771

Residual standard error: 6.766 on 8 degrees of freedom
Multiple R-Squared: 0.6201
F-statistic: 13.06 on 1 and 8 degrees of freedom, the p-value is 0.006847
```

This shows that drug costs per bedday decrease, on average, by $5.20 for every dollar per bedday spent on drugs (this figure comes from the co-efficient for "sal.pb" above; 95% confidence interval $2.38 to $8.01).

The P-value for the relation is P=0.0068, indicating that the hypothesis that there is no relation is rejected in favour of a simple linear model.

I hope this information is useful, Ian.

Cheers,

DEPARTMENT OF PUBLIC HEALTH AND COMMUNITY MEDICINE
THE UNIVERSITY OF MELBOURNE, 200 BERKELEY STREET, CARLTON, VICTORIA 3053 AUSTRALIA
TEL +61 3 9344 4093: FAX +61 3 9347 6136

12. Larmour, I, Creber E, Manser et at (1998) Hospital Pharmacists and the Challenge of Quality. AJHP, 28, 226-231. Citations 1

Hospital Pharmacists and the Challenge of Quality

Ian Larmour, Elizabeth S Creber, Allan J Manser, Emma M Wong, Mary J Wood

ABSTRACT

This review outlines an approach to quality enhancement in hospital pharmacy practice. Quality programs require planning, organisation, monitoring, correction of problems, and feedback to clients, customers and staff. Standards to be attained must be carefully selected and acceptable to all relevant staff. Peer review is useful for pharmacists working outside the department (e.g. ward pharmacists). Quality circles involve all relevant staff working in a particular area with a specific problem to be solved. Pharmacy departments should have an overall quality plan with long-term and short-term goals which compliment the hospital's quality improvement program. The financial cost of implementing quality programs in hospital pharmacy should be considered in the context of the cost of 'quality failure' to the hospital.

Aust J Hosp Pharm 1998; 28: 226-31.

INTRODUCTION

Hospital pharmacists' work is vitally concerned with quality and accuracy and frequently they must develop a departmental quality program. This paper documents the opinions and suggestions on quality by a group of interested pharmacists. The ultimate objective of all quality programs must be to achieve an improved patient outcome. However, to achieve this goal we must have the appropriate building blocks in place.

Quality means different things to different people but in hospital pharmacy practice it implies:

- safety;
- accuracy;
- efficiency;
- effectiveness; and
- meeting expectations of all clients, both internal and external.

Quality assurance is a broad generic term which covers all procedures and activities which are used to set, maintain, monitor and continuously improve the desired standards for services or products.[1] These standards are more likely to be achieved by an integrated structure of operation and assessment procedures.

PRINCIPLES

Successful quality programs require input and feedback from staff and clients, that is, we should see ourselves as part of a team.

Importantly, quality programs require:

- planning;
- organising;
- monitoring;
- correction of problems; and
- feedback to clients, customers and staff.

The aim is to achieve optimum outcomes which, in simplified terms, have two major components:

- getting it 'right the first time' and
- continuous improvement.

Getting it Right the First Time

This means planning so that we produce the desired result the first time. This may be an intermediate step in a process or an end point in itself. This requires planning and organising for quality.

Planning for Quality

Often also called quality 'structure', or the building blocks for quality. Examples of areas to address are:

- staff – numbers/qualifications/experience;
- job descriptions and work instruction documents;
- staff in-service education programs;
- incident reporting procedures and forms;
- establishing 'quality' workgroups;
- facilities and equipment;
- department and service goals;
- a quality plan (manual); and
- detailed procedure manuals which reflect what is actually done.

Ian Larmour,[1] BPharm, FSHP, MSc
Elizabeth S Creber,[1] BPharm, FSHP, Grad Dip Hosp Pharm
Allan J Manser,[2] BPharm, FSHP, MBA
Emma M Wong,[3] BPharm, Grad Dip Hosp Pharm
Mary J Wood,[4] BPharm
[1] Monash Medical Centre, Victoria
[2] The Royal Melbourne Hospital, Victoria
[3] Alfred Hospital, Victoria
[4] St Vincent's Hospital, Melbourne, Victoria

Address for correspondence:
Ian Larmour
Pharmacy Department
Monash Medical Centre
246 Clayton Road
Clayton Vic. 3168

Organising for Quality

This is often referred to as quality 'process' and relates to activities which ensure procedures, systems and processes are implemented and correctly followed. This involves:

- ensuring checking procedures (in-process controls) are carried out correctly;
- ensuring quality work groups are operating effectively; and
- ensuring complaints or errors are fully and promptly investigated and that corrective action is implemented.

Examples of the aspects covered are listed in Appendix 1 Section 1.

Continuous Improvement

This is the process of continually striving to improve services or products and to 'learn from mistakes' to ensure that they are not repeated. It requires monitoring for quality.

Monitoring for Quality

This is also called quality 'outcome' and refers to reviewing or evaluating our performance. It covers a variety of activities which should involve all pharmacy department staff or alternatively it may be multidisciplinary. It is a process of continuous evaluation, monitoring, review and assessment of activities. Examples of the areas that can be covered are listed in Appendix 1 Section 2.

One concept of special significance is that of performance indicators, often also called key performance indicators (KPIs). Performance indicators may be defined as statistics that accurately reflect performance of key services.

The factors to consider when selecting a performance indicator are outlined in Appendix 1. They should cover key pharmacy department service areas and any hospital program involving the pharmacy department, such as projects relating to the quality use of medication.

There are three main applications for performance indicators in that they allow:

- intra-department monitoring, i.e monitoring our performance against our historical data to detect unexpected variations.
- monitoring the department service to clients, i.e. ensuring we meet the needs of patients, other departments, and other health professionals; and
- benchmarking in both quantitative and qualitative components.

Continuous Improvement Quality Cycle

When problems or deficiencies are found or when a complaint or incident report is received, the 'continuous improvement quality cycle' should be activated. This is a systematic approach to problem solving and involves:

- clearly defining the problem or deficiency (e.g. what, when, where);
- seeking information and evaluating all procedures in detail to try and establish the cause(s);
- seeking possible solutions. This may involve techniques such as Fishbone chart analysis or brainstorming;
- selecting the best solution(s);
- implementing the change; and
- monitoring the change to ensure the problem has been solved.

If the desired result has not been achieved the continuous improvement quality cycle should be recommenced since the aim is not only to 'fix' the problem but to ensure that it does not recur.

To be successful, this process must involve all relevant department staff or all members of a multidisciplinary team. It may also require further input from clients or customers. Feedback on progress should be provided to all stakeholders.

This process may be undertaken by quality teams in the organisation (e.g. ward pharmacist peer review committees or quality circle groups) or by a team set up for a specific project.

The process should be adequately documented for future reference.

STANDARDS

Standards come in many forms but they usually have both a qualitative and a quantitative component.

Criterion of the Standard

This describes the desired feature or goal for a procedure, service or product. This is the qualitative component.

Some standards are absolute where the result is either 'right' or 'wrong' e.g. dispensing accuracy.

Other standards are relative because the process under review has natural variation which occurs because of a number of confounding factors. In such cases a maximum acceptable variation (threshold value) is specified in the standard's criterion.

Performance Level of the Standard

The aim is to achieve compliance with the criterion of the standard 100% of the time, i.e. the philosophy of 'zero defects'. This is the quantitative component of a standard.

Selection and Review of Standards

All relevant staff must be involved in developing and

selecting a standard for it to be successful. For example, input should be sought from experts in the area of practice and users of the services or products, utilising the 'peer review' and 'quality circle' concepts. These standards should be actively promoted and communicated to all staff, especially new staff.

Standards can be set by State and Commonwealth legislation and professional bodies or by non-legislative requirements such as the Code of Good Manufacturing Practice or the accreditation requirements of the Australian Council on Healthcare Standards.

Standards should be constantly reviewed and evaluated. Changes may be required for a variety of reasons, e.g.

- the result of performance evaluation;
- changing work patterns;
- an increase in the sophistication of the department services; and
- reports on practice in other hospitals and/or in the literature.

Outcome

There is increasing emphasis on outcomes, sometimes described as meeting the needs of customers or clients. In some cases outcomes cannot be measured. When this is the case, the process to achieve the intended outcome should be specified. Compliance with this specified process can then be monitored.

STAFF INVOLVEMENT

Administrative control, support and direction are necessary for a quality assurance program. But to be successful all staff must be involved in all aspects that directly relate to them. This may be achieved via peer review and quality circles. Equally important is the feedback of information to staff to enhance the feeling of involvement.

A department can establish a quality improvement committee which overviews the department's quality improvement plan and ensures peer review and/or quality circle groups are working effectively.

Peer Review

Peer review may be defined as peers reviewing and commenting on each other's performance. The aim is to improve and enhance services by enabling individuals to reach their full potential. It requires open and frank communication, trust, a supportive environment, a willingness to learn and an openness to new ideas.

The peer review approach is particularly valuable when staff often work independently and outside the department, e.g. in wards. It has the following objectives:

1. motivation of staff;
2. promotion of open frank communication between peers;
3. detection and resolution of problems;
4. promotion and setting of standards;
5. review and guidance;
6. education; and
7. administration and organisation aspects.

Peer review requires the delegation of authority to staff members. In larger hospitals this may require the formation of a department peer review committee. In smaller hospitals it may involve all pharmacists on the staff. For very small departments (e.g. a sole pharmacist) it may require linking with the pharmacy departments of other hospitals of similar type or geographical convenience.

A peer review committee should be given an appropriate name (e.g. Ward Continuous Quality Improvement Group). In the case of a ward pharmacist group, meetings should be held regularly and responsibilities should include organising meetings, ward visits, ward service checklists and ward surveys. It also requires the specification of practice procedures and standards from which a checklist, for review at ward visits, can be developed. The checklist may be tailored according to the area covered and/or the level of the pharmacist's experience.

Peer review is distinct from administrative assessment, which may be used when peer review is not successful.

Quality Circles

This process differs from peer review in that it involves all staff in a particular section and not just peers. The emphasis is also more oriented to the quality of services in the relevant section, especially problem solving and the use of resources and facilities. However, the objectives are similar to those of the peer review process. This enables the timely resolution of a number of section-specific problems and may extend into other aspects, e.g. the promotion of efficiency and productivity.

These meetings of section staff should be held on a regular basis, depending on need. The aim is to identify, select and analyse problems and to seek a suitable solution.

QUALITY PLANS

In order to have an effective quality program it is necessary to have an overall quality plan for the department, together with a yearly plan of quality promotion activities. These plans should be developed,

documented and distributed to all pharmacy department staff. The plan should cover:

Departmental Goals (long-term and the current year)

Routine/Standard Components (of your department's quality program)
Each aspect should be listed, e.g.
- current routine process monitoring (e.g. routine checking procedures and performance indicators, such as patient waiting times or budget performance);
- department meetings;
- standing review groups;
- department staff education programs.

Special Plans (for the current year)
This should list specific audits on service reviews or drug usage evaluations (DUEs) planned for the current year. A timetable should be included.

Management Aspects
This should specify:
- to whom the department's quality program activities are reported;
- a commitment to investigate complaints or incident reports promptly and to respond appropriately, including the resolution of problems when relevant;
- a statement of commitment to the pursuit of quality services and continuous improvement; and
- integration of department goals, services and evaluation processes with those of the hospital.

HOSPITAL QUALITY PROGRAM ACTIVITIES

It is essential that pharmacy departments be involved in all relevant aspects of a hospital's quality improvement activities. This can occur in a variety of ways:

Involvement in Hospital Committees
This includes active participation in committees such as:
- drug and therapeutics committee;
- research advisory and ethics committee;
- infection control committee;
- hospital quality improvement committee; and
- medication incident review working party.

Involvement in Treatment Teams
This includes the attendance and active participation in ward rounds and meetings by pharmacists, as well as participation in specialist teams such as the parenteral nutrition team, the pain management team, and the infectious diseases management team.

The pharmacist's role in the team includes providing communication links with the pharmacy department and the provision of expert advice.

Feedback to other healthcare staff about the interventions made by pharmacists should be a part of this involvement.

Pharmacists should also be involved in the development of hospital disease treatment plans and other protocols or guidelines.

Drug Usage Evaluation Studies
Such studies usually involve the pharmacy department and the drug and therapeutics committee. The pharmacy department should play a leading role in the coordination and administration of the process.

Adverse Drug Reactions
The pharmacy department should play a key role in promoting awareness of the need to report adverse drug reactions (ADRs). This includes active participation in the preparation of ADR reports. It is also important for the ADR reports to be reviewed and evaluated for opportunities to avoid future problems. This is normally done in conjunction with the hospital's drug and therapeutics committee.

Hospital admissions or unplanned readmissions due to an ADR should be considered as areas for review.

Clinical Indicators
The Australian Council on Healthcare Standards Clinical Indicators include some that relate to drug therapy. Pharmacy departments should play a leading role in collecting the data and in the feedback of the information to the relevant parties. This includes involvement in the assessment of the data collected.

CONCLUSION

Hospital pharmacy departments provide a diverse range of complex services and therefore we need to have quality programs of equal sophistication. To be effective, resources and time are needed. One of the most common complaints from hospital pharmacists is that they 'don't have enough time' and administrators complain that they do not have sufficient funds. However, we must consider the cost and lost time that occurs with 'quality failure' (more commonly known as the 'cost of quality'). If possible these implications should be converted into an estimated dollar value. This may help to justify the resources needed to conduct sound quality activities and gives a more potent meaning to 'quality failure'.

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Appendix 1. Examples of quality activities

1. Planning and Organising for Quality

Examples of the types of issues involved include:
(a) detailed documentation of duty statements and procedures for each position, including the qualifications, responsibilities, training and accreditation of personnel;
(b) 'checking' procedures in all areas of the department, i.e. methods, documentation and the responsibilities of personnel;
(c) documentation of manufacturing procedures and records including the use of master formulary worksheets;
(d) documentation required for all procedures and the design of forms and records, including accountability of documents and labels;
(e) material specifications and methods of verification;
(f) equipment to be used in procedures, including in-process checking of equipment, together with the maintenance and monitoring of procedures and records plus the calibration and validation of equipment. This may also include disposables and clothing;
(g) documentation of microbiological monitoring procedures including methods, materials, sample size and selection, equipment, procedures, including quarantine procedures and action to be taken when a product failure is encountered;
(h) documentation of labelling requirements and the use of warning or supplementary labels;
(i) documentation of patient medication counselling, education and interview procedures, including patient pamphlets or medication compliance aids or charts;
(j) documentation of storage requirements of materials and products and receipt and issue procedures;
(k) documentation of packaging procedures and records, including container and label specifications;
(l) documentation of analytical procedures, including sample size and selection, procedures, methods, materials, equipment, quarantine procedures and the action to be taken when a product failure is encountered;
(m) documentation of cleaning procedures; and
(n) documentation of drug recall procedures originating both from within and outside the department.

2. Monitoring for Quality

Areas which could be considered are:

Periodic monitoring

(a) Product or service review and audits

This involves a regular periodic review of a particular service provided by the pharmacy department to evaluate performance in terms of outcome. This includes the detection of 'common cause' problems and the seeking of a permanent solution, e.g.
- procedure evaluation;
- evaluation of service outcome; and
- benchmarking.

(b) Audits of documentation

Performance should be evaluated against a set criterion for each audit type, for example the completeness of the document. Examples include:
- manufacturing work sheets;
- endorsements on patient drug charts and prescriptions;
- written drug information answers;
- adverse drug reaction reports; and
- pharmacist intervention records.

(c) Client or customer surveys

There are a variety of groups to target including:
- patients;
- ward unit nurse managers; and
- medical staff.

(d) Ward service peer review

Ward visits where performance is reviewed against previously agreed criteria.

Continuous Monitoring

(a) In-process control (e.g. prescription checking procedures)

(b) Complaints management

(c) Monitoring incident reports

(d) Monitoring of performance indicators

This is the routine monitoring of selected 'performance indicators' (or statistics) in order to detect unexpected variation which should act as an 'alert' to initiate a review or investigation, since such variations may illuminate an undetected problem. When a problem is detected a Quality Problem Solving Cycle should be initiated.

Performance indicators may relate specifically to the pharmacy department or to other aspects of the hospital service, especially in regard to projects relating to the quality use of medication. Generally, performance indicators are monitored against data collected over a period. On occasions, however, it is useful to benchmark some of these performance indicators against data collected by other hospitals.

The performance indicators chosen should be:
- specific to the service being monitored;
- measurable and reliable;
- achievable with available resources;
- relevant and useful to our clients and ourselves; and
- interpretable.

In the case of pharmacy department performance indicators, it is important to concentrate on key pharmacy services, which include:
- dispensing and supply of medication;
- clinical services, which include the promotion of safe and effective drug therapy;
- education of patients, students and others;
- provision of drug information and advice to patients and other health professionals;
- product preparation, including extemporaneous products, and sterile products;
- research, including involvement in clinical drug trials.

Factors to consider when documenting these performance indicators are:
- purpose of the performance indicator;
- method of data collection;
- frequency of data collection; and
- designation of who is responsible for collecting and compiling the data.

Examples of pharmacy department performance indicators are:
- the number of interventions collected by ward pharmacists per bed-day or per 100 bed-days, excluding day patients;
- the percentage of attempted interventions that are successful;
- the incidence of 'stock outs' of pharmaceutical items which are normally kept in stock as part of the hospital's inventory and where the cause of the 'stock out' is due to a failure of pharmacy department systems;
- outpatient prescription waiting times, for example, a sample collected each month;
- the stock turnover ratio;
- the number of dispensing errors detected, for example, regu-

lar sample surveys or data collected as part of a double or triple check process;
• the number of patient complaints;
• the number of pharmacy incident reports, the number of drug of addiction incident reports or the number of medication incident reports;
• workload statistics;
• the number of drug usage evaluation studies conducted annually;
• the turnaround time of discharge prescriptions;
• the number of drug of addiction balance check problems within the pharmacy department;
• the number of patient or client surveys conducted per year, in total or by specific area of practice;
• the number of training courses and/or conferences attended by staff or hours of staff education each year;
• the percentage of patients counselled about their medication on discharge from the hospital;
• intravenous admixture or TPN solutions returned unused;
• the average drug cost and/or labour cost per patient separation or Weighted Inlier Equivalent Separation; or
• the percentage of patients counselled about their medication by a pharmacist on discharge from hospital and/or when attending the pharmacy department outpatients dispensing area.

When problems are detected the principles of the Continuous Improvement Quality Cycle or Quality Problem Solving Cycle are employed.

Examples of **hospital performance indicators** which may involve the pharmacy department, particularly in regard to promotion of quality use of medication:
• collecting data for the ACHS Clinical Indicators 6.1 & 6.2;
• monitoring adverse drug reactions and conducting an analysis of common cause problems;
• monitoring hospital admissions or unplanned readmissions due to adverse drug reactions;
• various drug usage evaluation projects;
• pharmacy department involvement in care mapping/managed care/critical pathway care project and systems.

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13. George L, Senturk-Raif R, Hodgkinson M, Emmerton M, Larmour I (2011) “Impact of a surgical preadmission clinic pharmacist on the quality of medication management from preadmission to discharge: A randomised controlled trial”. Journal of Pharmacy Practice and Research 41(3), 212- 216. Citations 9

Impact of a Surgical Preadmission Clinic Pharmacist on the Quality of Medication Management from Preadmission to Discharge: a Randomised Controlled Study

Lewis JW George, Reyhan Senturk-Raif, Marisa R Hodgkinson, Maggie Emmerton, Ian Larmour

ABSTRACT

Background: Studies evaluating the impact of surgical preadmission clinic (PAC) pharmacists have reported significant improvements in medication management. However, despite the increased uptake of pharmacy services in this area, randomised controlled studies are limited.

Aim: To investigate the impact of a surgical PAC pharmacist on the quality of medication management from preadmission to discharge.

Method: A prospective, randomised, controlled design was used to assign patients to either the intervention or control groups. The intervention group received standard PAC care plus assessment by a PAC pharmacist. The control group received standard PAC care only. Both groups also received standard inpatient care, and were followed from PAC to discharge, and data collected on pharmacist interventions, medication reconciliation and medication history documentation.

Results: 171 patients were randomised to the intervention group and 184 to the control group. The intervention group had significantly more regular and as required prescription medicines, and complementary and alternative medicines documented per patient than the control group; and significantly more pharmacist interventions (31%) than the control group. The PAC pharmacist made 27% of interventions in the intervention group. Medication reconciliation at admission was 81% for the intervention group and 75% for the control group. Medication reconciliation for both groups was 90% at discharge.

Conclusion: A surgical PAC pharmacist had a positive impact on medication management through improved quality of medication histories and documentation, interventions and medication reconciliation.

J Pharm Pract Res 2011; 41: 212-16.

INTRODUCTION

Surgical preadmission clinics (PACs) are an established service in many hospitals.[1-7] The main objective of PACs is to provide surgical and anaesthetic assessments of patients prior to elective surgery, in order to avoid surgery cancellations and enable patient admission on the day of surgery. Surgical PACs also provide an opportunity for patient education, allied health access, discharge planning and obtaining patient information.[8] Although some hospitals include pharmacists in the PAC team, it is not an established pharmacy service in most institutions.

Lewis JW George, BPharm, GradDipHospPharm, BA (Hons), AUA, FSHP, Pharmacist, **Reyhan Senturk-Raif,** BPharm, Pharmacist, Dandenong Hospital, **Marisa R Hodgkinson,** BPharm, MSc, Pharmacist, Monash Medical Centre, **Maggie Emmerton,** MPharm, GradDipBus, Deputy Director of Pharmacy, Dandenong Hospital, **Ian Larmour,** BPharm, MSc, FSHP, Director of Pharmacy, Southern Health, Clayton, Victoria

Address for correspondence: Lewis George, Pharmacy Department, Dandenong Hospital, Dandenong Vic. 3175, Australia.
E-mail: Lewis.George@southernhealth.org.au

The question of whether experienced clinical pharmacists can add value to PACs has stimulated research in recent years.[1-7,9] Surgical PAC pharmacists have been involved in medication history documentation, medication reconciliation, pre- and post-operative medication management, writing prescriptions, providing medicines information, patient education, discharge planning and general practitioner liaison.[1-7] However, randomised controlled studies investigating the value of pharmacy services to PACs are limited.[4]

A non-randomised controlled study in the UK that compared interventions made by the PAC pharmacist with those made by the clinical pharmacists reported that the clinical significance of PAC pharmacist interventions was rated higher than clinical pharmacist interventions, and the number of medication prescribing errors, including omissions, was reduced in the PAC pharmacist group.[3] In a randomised controlled Canadian study, a PAC pharmacist undertook medication reconciliation prior to surgery for 227 patients.[4] The number of patients with at least one postoperative medication discrepancy associated with their usual medications was halved, and the number of potentially harmful discrepancies reduced by 17%.[4] In a prospective Australian study of 150 patients, patient-completed medication histories in a PAC were inaccurate in 80% of cases, and the authors concluded that PAC pharmacists can ensure the availability of an accurate medication history.[5]

These studies suggest that experienced clinical pharmacists in PACs add value in three key areas: provision of an accurate and complete medication history; resolve discrepancies identified when obtaining medication histories and optimising medication management prior to elective surgery; and provision of documentation which facilitates reconciliation of the patient's pre-operative medications with medicines prescribed at admission and discharge.

This study aimed to investigate the impact of a surgical PAC pharmacist on the quality of medication management from preadmission to discharge.

METHOD

Patients were eligible if they attended the PAC at a large metropolitan teaching hospital in Melbourne prior to orthopaedic, colorectal and vascular surgery. Patients from these surgery types were selected as they would benefit from a PAC pharmacist's input, due to their age, length of inpatient stay, potential for comorbidities and complex medication regimens. Patients completed the Health Status Questionnaire prior to attending the PAC, which was reviewed along with pharmacy dispensing records, to determine age, comorbidities and medication use. Patients were eligible if they were either aged 60

years or over, with or without comorbidities or current medication use, or under 60 years of age, with at least one pre-existing comorbidity and taking regular prescribed medication. Patients for non-elective, day and other surgical procedures and those unable to give written informed consent were excluded.

The study hospital has a well established PAC, where patients are assessed by nurses, surgeons and anaesthetists, approximately 2 weeks prior to surgery. The study commenced around one month after the new pharmacy service began at the PAC, utilising two pharmacists on rotation on the 3 days each week that patients from the selected surgery types were in attendance. These pharmacists had 2 and 8 years clinical pharmacy experience respectively, although no previous experience in PAC.

The study protocol was approved by Southern Health's Human Research and Ethics Committee.

Enrolment and Randomisation

Eligible patients attending clinic days when the PAC pharmacist was in attendance were invited to participate. Consenting patients were sequentially, but randomly, assigned to either the intervention or control groups by a pharmacy technician. Computer-generated randomisation numbers and group assignments were pre-sealed in sequentially numbered, opaque envelopes held by the pharmacy technician. The intervention group received standard PAC care plus assessment by a PAC pharmacist, while the control group received standard PAC care only. Both groups saw allied health staff when appropriate. The PAC, pharmacy and ward staff were aware a study was underway, but were not privy to the study protocol or patient allocation.

Participant numbers were based on the prediction that the control group would show a 15% improvement in medication reconciliation between medicines taken prior to hospital admission and prescribed during admission. Based on previous audits in the study hospital network, a reconciliation rate on admission of 90% was considered achievable for the intervention group, compared with 75% for the control group.[10] Thus, using *Stata 9,* $2n = 292$ ($p < 0.05$, power 90%) was the minimum number of participants required to detect this difference. A further 108 participants were included to provide a feasible participant target to ensure detection of a difference of at least this magnitude.

Medication History Interview and Assessment

The PAC pharmacist's conducted patient interviews in a dedicated consulting room and consisted of taking a history of patient's regular and as required medications, including self and doctor prescribed medication, on the hospital's Medication History and Reconciliation Form (MHRF). Details of the medication history provided by the patient were corroborated with at least one other source, e.g. patient's own medications, carer, general practitioner, community pharmacist, residential care facility, or hospital pharmacy dispensing record. Patient's medication supply requirements on discharge were also noted on the MHRF for attention following hospital admission. The intervention group was given a medication management plan detailing medications to cease and medications to continue or start up to and including the day of admission. The completed MHRF was filed in the medical record for reference by hospital staff when prescribing admission medications.

The PAC pharmacist contacted the intervention group patients during the pre-operative period (from PAC attendance to hospital admission) to confirm they understood their pre-operative medication management plan, and to document and advise on any medication changes since their PAC appointment. Patients were also asked to contact the PAC pharmacist if there were any changes to their medication regimen during the pre-operative period.

Both groups also received standard inpatient care on admission, including clinical pharmacy services from the rostered clinical pharmacist.

Medication histories documented by the PAC pharmacist on the MHRF for the intervention group were compared with the medication histories documented by the PAC doctor in the patient's medical record for the control group. The medicines documented for both groups were classified as regular or as required prescription or non-prescription or over-the-counter medicines. Medicines were further grouped according to their therapeutic classification as specified in the *Australian Medicines Handbook*.[11]

Interventions, Severity Assessment and Classification

Pharmacist interventions were any actions that resulted in a change in medication management or therapy.[12] Interventions were documented by the PAC and ward pharmacists on the hospital's standard pharmacist intervention form. Additionally, participants' medical records were reviewed after hospital discharge for evidence of interventions that were not recorded by the PAC or ward pharmacists. Patients' hospital identification numbers, the medicines involved, and a brief description of the interventions were recorded. Interventions were classified by the researchers as: incorrect medicines, unintentional omissions, clinical issues (unnecessary or inappropriate medicine, incorrect duration, inadequate or inappropriate monitoring, new medicine indicated, duplication of medicine, class or type), dosage (incorrect or omitted dose, strength or frequency including dose modification for renal impairment and incorrect dosage formulation), contraindications and/or adverse drug reaction requiring medicine cessation.

Interventions were assessed for clinical severity by two doctors, one nurse and one pharmacist using a validated tool.[13] Scores were entered by each rater on a visual analogue scale (0 = no potential adverse effect to 10 = potential for causing death or lasting impairment). The visual analogue scale score was assigned a corresponding severity assessment of minor (score 0 to 3.3, very unlikely to have any adverse effects), moderate (score 3.4 to 6.7, likely to cause some adverse effects interfering with therapeutic goals, but unlikely to result in death or lasting impairment) or severe (score 6.8 to 10, likely to cause death or lasting impairment).

Medication Reconciliation

Medication reconciliation was the process of checking that the medicines the patient was taking prior to hospital admission correlated with medicines prescribed during the admission and on discharge, and any discrepancies were intentional.[14] Patient's usual preadmission medicines were documented by either the PAC or ward pharmacist on the MHRF or medication chart. These details were compared with medications prescribed by the doctor on the first inpatient medication chart

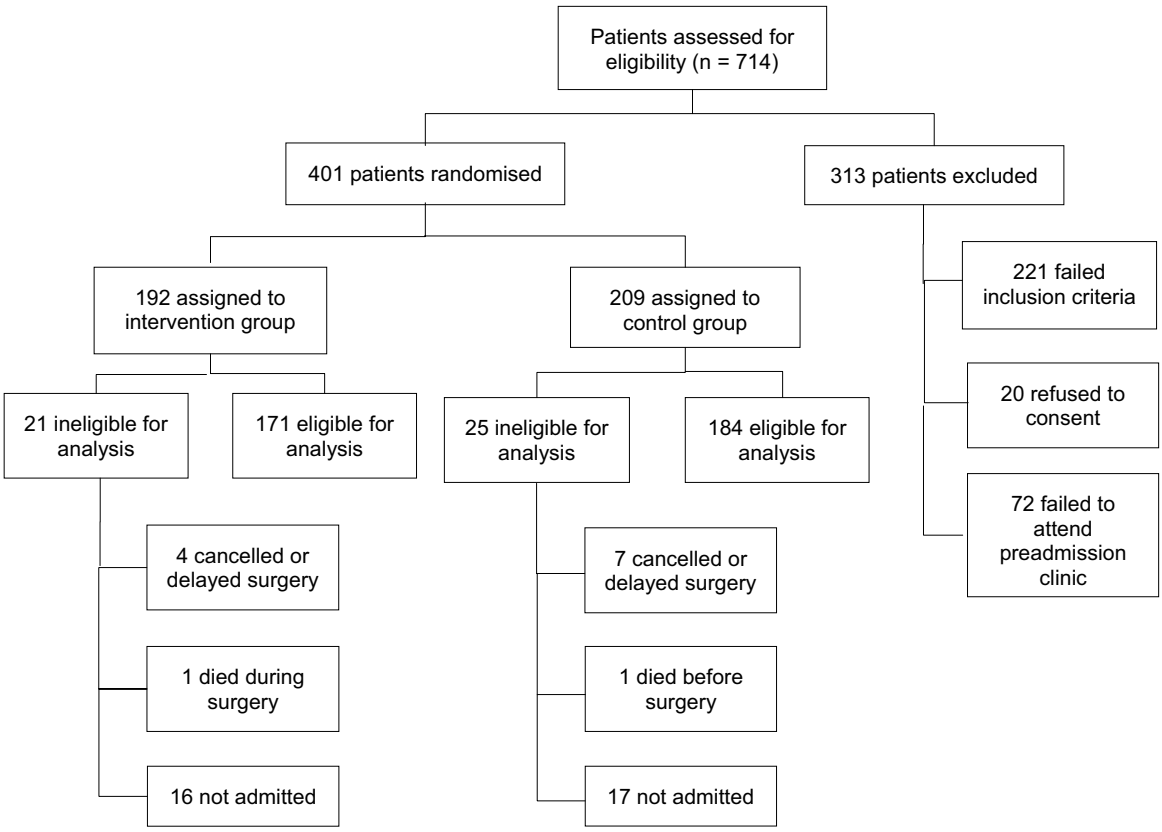

Figure 1. Flow diagram of patient participation through the study.

immediately after hospital admission. Patients' usual preadmission medicines and those prescribed on the medication chart were compared with medications prescribed on the discharge prescription. Unintentional discrepancies identified on admission or discharge were considered a failure in medication being reconciled at that transition point. Logistic regression was used to analyse medication reconciliation.

RESULTS

The study took place over 13 months from September 2007 to October 2008. The PAC pharmacist attended 66% (95/144) of PAC clinic days over this period. Patient participation through the study is described in Figure 1. An overview of the intervention group's journey and a summary of medication management provided in addition to standard care from PAC to discharge are described in Figure 2. Patient characteristics and medication documentation are presented in Table 1.

Prescribed Medicines

There were more (13%; 128/949) regular prescribed medicines documented for the intervention group than the control group. The intervention group also recorded (52%; 69/132) more 'as required' prescribed medicines than the control group. The most commonly recorded regular prescribed drug classes for both groups were cardiovascular (38%; 768/2026 of total regular prescribed medicines), endocrine and metabolic (14%; 275/2026), and blood and electrolytes (13%; 259/2026). The most commonly recorded 'as required' prescribed drug classes for both groups were analgesics (39%; 131/333 of total 'as required' prescribed medicines) followed by respiratory (20%; 65/333) and cardiovascular (11%; 37/333).

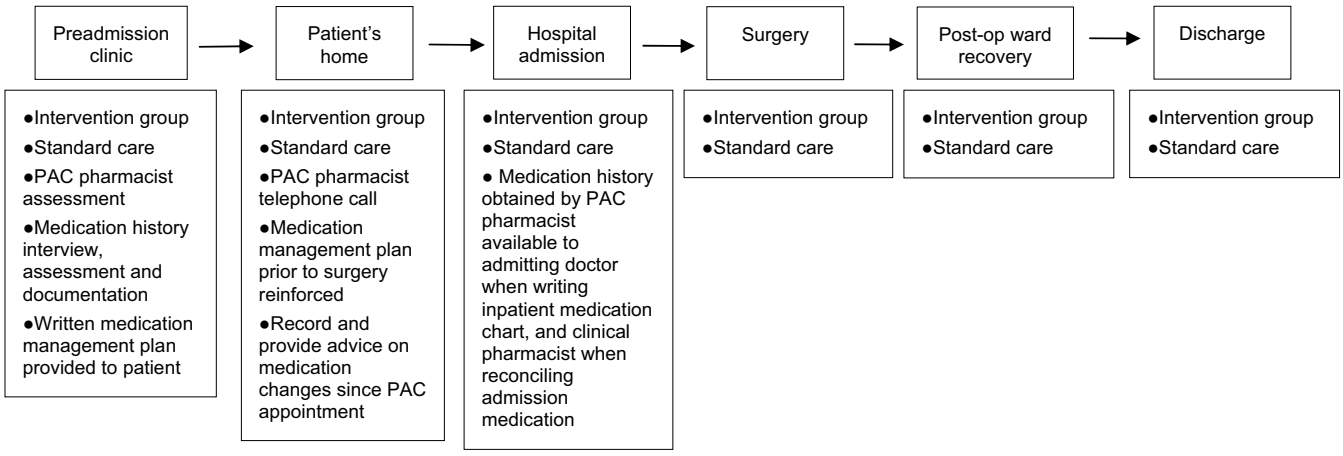

Figure 2. Intervention group's journey from surgical preadmission clinic to hospital discharge as well as summary of medication management provided by the PAC pharmacist.

Table 1. Patient characteristics and medication documentation for the intervention and control groups

Patient characteristics		Intervention group (n = 171)	Control group (n = 184)	P-value
Male gender		78 (46%)	90 (49%)	0.98*
Age (years)†		68 (61-75)	67 (60-76)	0.54‡
Current smoker§		29 (17%)	28 (16%)	0.99*
English preferred language		140 (82%)	155 (84%)	0.99*
Non-English speaking§		29 (17%)	19 (10%)	0.5*
No. of comorbidities per patient§†		3 (2-4)	3 (2-4)	0.2‡
Surgical type	Orthopaedic	94 (55%)	89 (49%)	0.8*
	Vascular	35 (21%)	37 (20%)	1.0*
	Colorectal	38 (22%)	55 (30%)	0.6*
	Other	3 (1.8%)	2 (1.1%)	0.99*
Time between PAC appointment and hospital admission (days)†		19 (7-28)	19 (9-29)	0.58‡
Length of stay (days)†		5 (3-9)	6 (2-9)	0.75‡
Medication documentation‖				
No. of prescribed regular medicines per patient		5.6 (SD 3.7)	4.6 (SD 3.7)	0.003¶
No. of prescribed prn medicines per patient		1.1 (SD 1.2)	0.7 (SD 1.03)	0.0¶
No. of CAMs per patient		0.5 (SD 0.86)	0.3 (SD 0.7)	0.03¶
No. of over-the-counter medicines per patient		0.3 (SD 0.56)	0.3 (SD 0.6)	0.25¶
No. of all medicines per patient		7.5 (SD 4.3)	5.9 (SD 4.3)	0.0¶

*Chi-squared. †Data presented as median (first and third interquartile range). ‡Pooled medians test. §Data obtained from the Health Status Questionnaire completed by the patient prior to the PAC appointment. ‖Intervention group medication documented by PAC pharmacist and control group medication documented by PAC doctor. Data presented as mean (SD). ¶Mann-Whitney U test.

Non-Prescribed Medicines

There were more (38%; 25/66) complementary and alternative medicines (CAMs) documented for the intervention group than the control group. The most common CAMs (n = 157) recorded for both groups were vitamin and mineral supplements (78%), glucosamine/chondroitin (6.4%) and fish oil/omega 3 (3%). The most common over-the-counter medicines (n = 120) used by both groups were musculoskeletal (53%), analgesics (27%) and gastrointestinal (5.8%).

Interventions, Severity Assessment and Classification

A total of 155 interventions were made for both groups. The intervention severity assessment, type and stage are described in Table 2. There was a significant difference in the total number of interventions made between the two groups. Although there were no significant differences in the severity assessments and type of interventions, the intervention group had 57% more interventions related to clinical issues. The highest scoring intervention (average visual analogue score = 8.5) was a lethal insulin dose where a control group patient was prescribed 300 units instead of 30 units.

Medication Reconciliation

Medication reconciliation at admission occurred in 81% (139/171) of patients in the intervention group compared with 75% (138/184) in the control group. Both groups achieved medication reconciliation of 90% for patients on discharge. Reconciliation percentages for both groups were not statistically significant for admission (OR 1.5, 95%CI 0.9–2.5) or discharge (OR 1.1, 95%CI 0.5–2.2).

Table 2. Pharmacist interventions classified by severity, type and stage of patient journey for both groups*

Pharmacist intervention		Intervention group	Control group	P-value†
Severity	Minor	34 (39%)	25 (37%)	1.0
	Moderate	52 (59%)	41 (61%)	1.0
	Severe	2 (2%)	1 (1%)	1.0
Type	Incorrect medicine	2 (2%)	4 (6%)	0.9
	Unintentional omission	26 (30%)	27 (40%)	0.7
	Clinical issue	26 (30%)	11 (16%)	0.5
	Dosage	23 (26%)	18 (27%)	1.0
	Contraindication	8 (9%)	5 (7%)	1.0
	Administration error	3 (3%)	2 (3%)	1.0
Stage	Preadmission clinic	24 (27%)	NA	NA
	Admission	20 (23%)	18 (27%)	0.99
	Inpatient stay and discharge	44 (50%)	49 (73%)	0.2

*Interrater reliability: ANOVA between assessors p = 0.0001. †Chi-squared.

DISCUSSION

PAC pharmacists documented significantly more prescribed regular and as required medicines, and CAMs per patient than the PAC doctors. The number of all medicines per patient documented was higher in the intervention group, which was consistent with other studies, although the number of medicines per intervention group patient recorded in our study was higher (7.5) than other studies (4).[3,4,9] This demonstrates the value of a PAC pharmacist in obtaining an accurate

medication history, which has important clinical significance in optimising medication management prior to anaesthesia and surgery and minimising medicines related risks on admission.[15] The PAC pharmacist recorded significantly more prescribed 'as required' medicines and CAMs per patient than the PAC doctor, suggesting that specific questioning of patients on the use of these medicines should be emphasised by clinicians when taking a medication history.

There were 31% more pharmacist interventions in the intervention group than the control group. The difference was primarily due to those made by the PAC pharmacist and were interventions that otherwise may not have been made. The intervention group had 136% more interventions involving clinical issues, i.e. the PAC pharmacist was proactively contributing to optimising medication management and quality use of medicines in addition to resolving medication discrepancies.

Our study did not demonstrate a difference in interventions associated with discrepancies in medication history taking, such as medication omission and incorrect drug prescribed, compared with other studies.[3,4,6] We attribute this to the different surgery types and populations, and also a key difference in study design. In our study, the inpatient medication chart was written by the admitting doctor, whereas in other studies, it was written by the PAC pharmacist (with doctor countersignature) at the PAC.[3,4,6] Although there may be some benefit in writing the inpatient medication chart at the PAC, the median peri-operative period was 19 days in our study compared to a median of 6 days in the Canadian study, providing more opportunity for pre-admission medication changes to occur, which could introduce other risks.[4,9] The availability of a completed MHRF to the admitting doctor when prescribing the first inpatient medication chart did not impact on the number of interventions made on admission. However, as the MHRF was introduced 5 months prior to the study, the admitting doctor may not have always referred to this document.

Our study did not demonstrate a significant difference between the two groups in medication reconciliation on admission or discharge. However, in studies that demonstrated improved medication reconciliation on admission, transcribing of the inpatient prescription was undertaken by the PAC pharmacist.[4,6] The availability of the MRHF on admission in our study to facilitate inpatient prescribing and medication reconciliation did not involve transcription of inpatient medications by the PAC pharmacist. Improvements could be made to ensure more complete reconciliation on admission, such as greater promotion of the MHRF to ensure that it is used when writing the first medication chart, and exploration of the PAC pharmacist transcribing the first inpatient medication chart, with countersignature by the admitting doctor. If medication transcribing is undertaken at the PAC, the inpatient medication chart would need to be re-checked on admission to ensure any medication changes are addressed. In our study, both groups were supported by ward-based clinical pharmacy services from admission to discharge, which explains the same reconciliation result of 90% at discharge.

Our study had several limitations. Pharmacy services to the PAC were new rather than established, meaning that the PAC pharmacists needed to build relationships, mode of working and expertise within the PAC during the study. Moreover, the other PAC staff were not fully aware of how best to access and utilise the PAC pharmacist. The part-time nature of the service meant its full potential could not be evaluated. Notwithstanding, the results demonstrated the added value that a PAC pharmacist can provide, and also confirmed that the patient selection criteria used were justified. However, patient outcomes were not measured in this study. Some of the services provided by PAC pharmacists in other countries are not currently applicable in Australia due to legal and funding constraints. Therefore, a wider scope of services could not be evaluated.

In conclusion, a surgical PAC pharmacist had a positive impact on medication management through improved quality of medication history taking and documentation, interventions and medication reconciliation. Our results are being used to guide the continuing development and evaluation of PAC services in the study hospital.

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Competing interests: None declared

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Chapter Two

Examining the Impact and Detection of Adverse Drug Reactions

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Citations 55

(N.B. This article was used as a significant reference in the National Health Strategy Issues Paper No. 4 (June 1992) “Issues in Pharmaceutical Drug Use in Australia”)

A Prospective Study of Hospital Admissions Due to Drug Reactions

Ian Larmour, Roger G. Dolphin, Heather Baxter, Scott Morrison, David H. Hooke, Barry P. McGrath

Abstract

A prospective study of drug-related hospital admissions over a 6-month period was carried out in a major Melbourne teaching hospital. There were 5623 patients admitted to the hospital over the survey period. A total of 136 admissions (2.4%) was considered to be drug-related. There were 90 admissions (1.6%) as a result of adverse drug reactions (ADRs) and 40 (0.7%) due to drug overdose or accidental poisonings. Drug interactions accounted for 27 (30%) of the admissions due to ADRs.

The most frequent types of ADR were gastrointestinal bleeding, cardiac arrhythmias, blood dyscrasias and postural hypotension. Drugs most frequently implicated were non-steroidal anti-inflammatory drugs, digoxin, warfarin and theophylline. Compared to the reference population, patients with ADRs were older, more likely to be female and taking significantly more drugs (mean±SD, 4.9±2.6 v. 3.0±2.8, $p<0.01$).

The results of this study highlight the need for continuing education at all levels (prescriber, pharmacist, patient) to minimise the risks of ADRs in patients, exposed as they are to an increasing number of available therapeutic agents.

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Introduction

The problem of significant illness and resulting hospital admission due to complications of drug therapy was first highlighted by Hurwitz.[1] This early work has been followed by reports from other groups, including the Boston Collaborative Drug Surveillance Program.[2-6]

The frequency of such hospital admissions has been reported in these studies to range from 1.8 to 6.2%. The reports include admissions due to factors such as adverse drug reactions (ADRs), erroneous or inappropriate drug use, drug overdoses, poor compliance and problems detected by therapeutic drug montoring. Most studies have involved admissions to selected medical units. However the problem has been largely unstudied in Australian hospitals. In one retrospective study from Perth by Black and Somers, 6.2% of admissions to a single general medical unit were attributable to a drug-related illness.[5]

We conducted a prospective study of all patients admitted to a Melbourne general teaching hospital over a 6-month period. The relationship between each patient's current drug therapy and the reason for admission was assessed.

Methods

The study was conducted at the Prince Henry's Hospital campus of the Monash Medical Centre. Prince Henry's Hospital is a 407-bed adult general teaching hospital affiliated with Monash University. All wards were serviced by ward pharmacists, who routinely reviewed all patients' drug charts twice a day, and examined patients' clinical histories and laboratory reports. They also attended unit ward rounds and meetings.

A prospective study of all admissions, excluding day patients, to the hospital was conducted over a 6-month period (June to November 1987). Each patient's drug therapy and clinical history were reviewed by a ward pharmacist at an admission interview, with reference to the admission notes, and discussed with the attending medical staff. Details of those patients in whom drug therapy was thought to have contributed to their admission in any way were documented, including drug overdoses, suspected ADRs, poor patient medication compliance, toxic drug levels, events suspected of being related to drug therapy (e.g. bone fractures in the elderly as a result of a fall) or any other unexplained admissions.

A preliminary review of the medical history of each of these cases was conducted by the senior ward pharmacist (one of the authors, RD) in conjunction with both the ward pharmacist and ward medical staff. Each case was then further reviewed by one or more of the other authors. This review found no documented evidence to support a causal relationship in 35 cases and these were therefore excluded from the study.

Ian Larmour, BPharm, FSHP, MSc
Manager of Pharmaceutical Services
Roger G. Dolphin, BPharm, Grad Dip Hosp Pharm
Senior Pharmacist
Heather Baxter, BApplSci
Medical Records Administrator Student
Scott Morrison, BPharm
Pharmacist
David H. Hooke, MBBS, FRACP
Renal Physician
Barry P. McGrath, MBBS, MD, FRACP
Associate Professor of Medicine
Monash Medical Centre, Prince Henry's Hospital
St Kilda Road, Melbourne Vic. 3004

Address for correspondence:
Mr Ian Larmour
Manager of Pharmaceutical Services
Monash Medical Centre, Prince Henry's Hospital
St Kilda Road, Melbourne Vic. 3004

Admissions due to drug overdose, i.e. attempted suicides or narcotic overdose, were documented but not subjected to further analysis.

Where a drug-related admission was suspected, all case histories were reviewed by a team of 3 of the authors (IL, BMcG, HB). The following information was recorded on a check list: patient demographic data, details of all drugs being taken by the patient, symptoms, type of problem, physiological system affected, severity, the probability of the admission being drug-related, the suspected drugs, potentially predisposing factors (e.g. renal impairment, liver disease), previous drug hypersensitivity or ADRs, action taken and outcome. In the case of ADRs, an assessment was made of the probability of the reaction being drug-related.

The definition used for an ADR was that of the World Health Organization: 'a noxious and unintended reaction that occurs at drug doses used in man for prophylaxis, diagnosis or therapy'.[7] The following criteria were used:

1. Confirmation by laboratory data, e.g. excessive drug serum concentration, eosinophilia or confirmation of reaction type.
2. Known toxic effects of suspected drugs.
3. A temporal or spatial relationship between the ADR and drug therapy.
4. Recovery on cessation of the suspected drug therapy.
5. Consideration of alternative explanations, e.g. symptoms due to a worsening of the disease state.

Each ADR was noted as being definite, probable or possible, according to the strength of the relationship with these criteria. The ADR was graded as severe if the reaction was potentially life-threatening or necessitated surgery or blood transfusion, moderate if specific treatment or hospitalisation for greater than 2–3 days was required for recovery or monitoring, or minor.

Reference Population – Those Without Drug-Related Problems

To examine potential risk factors for ADRs, a separate study was conducted over a two-week period, during which detailed information was obtained from all 364 patients admitted to the hospital. Day care patients were excluded. Age, drug intake and previous ADRs or drug hypersensitivity were documented. The same screening methodology, as outlined above, was employed in this study to detect patients with potential drug-related problems. In this group, 12 such patients were identified (5 drug overdose, 7 ADRs). However, data were also obtained from the 352 patients considered not to have had a drug-related problem, and these were used as a control population.

Statistics

All data were coded and entered onto a microcomputer spreadsheet for subsequent analysis. Comparison between group means was made by the non-paired Student's t-test. The chi-squared test was employed to examine differences between the ADR group and the reference population. All results are expressed as mean ±SD.

Results

There were 5623 hospital admissions during the 6-month study period. One hundred and thirty-six admissions (2.4%) were considered to be drug-related. These consisted of 40 (0.7%) cases of drug overdose, 90 (1.6%) cases in which an ADR contributed to the admission and 5 cases in which poor compliance with medication was suspected as the main cause of admission. However, patient medication non-compliance was suspected of being a significant factor in a number of other cases. There was also one admission classified as inappropriate use. In this case a 31-year-old heroin addict injected flunitrazepam tablets, crushed and dissolved in tap water, into his thigh, resulting in the need for extensive vascular surgery.

Adverse Drug Reactions

The 90 admissions which were thought to be due to an ADR involved 84 patients, including four patients who had two separate admissions and one who had three separate admissions.

The age distribution of patients admitted with an ADR was compared to that of the total hospital population over the survey period (Figure 1). There was a distinct skewing towards the elderly in the ADR group, with 53% of patients being 70 years of age or older compared to 24% of the total hospital population falling into this age group ($\chi^2 = 18.8$, $p < 0.001$) indicating a greater frequency of ADR admissions in the elderly. In the ADR group, the mean age was similar in males (67 ± 18 years) and females (62 ± 21 years).

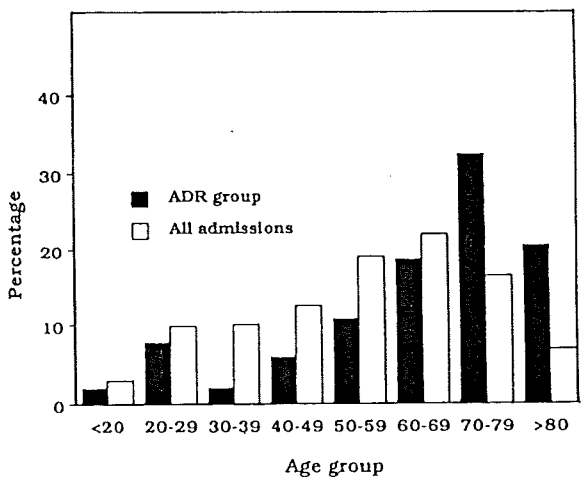

Figure 1. Comparison of age distributions (expressed as percentages) of patients with adverse drug reactions (n = 90) and total hospital population (n = 5623) over the 6-month study period

There were similar numbers of males (44) and females (40) in the ADR group. However, there was a significantly greater percentage of females in the ADR group compared to the total hospital admission population. Females composed 47.7% of the ADR group but only 42.3% of the total admission population ($\chi^2 = 5.7$, $p < 0.02$).

The length of stay in hospital tended to increase with age. The average length of stay was 5.5 days for patients 20–39 years, 5.7 days for patients 40–59 years, 8.5 days for patients 60–79 years and 11.0 days for those >80 years. No significant difference was found in the length of stay of patients admitted due to an ADR compared to the normal hospital population, when adjusted for age.

The ADRs were considered to be definite in 60% of cases, probable in 28% and possible in 12% of cases. Reactions were judged to be severe in 39%, moderate in 58% and minor in 3% of cases. There were 5 cases in which an ADR was suspected as a contributing factor to the patient's death. Three of these involved haemorrhage (Table 1).

The types of ADR encountered were classified as idiosyncratic in 19%, related to drug interaction in 30%, normal-dose side effect in 44%, and dose-related toxicity in 7% of cases.

Sixty-seven different drugs, alone or in combination, were implicated in causing an ADR, the most common drug groups being non-steroidal anti-inflammatory drugs (NSAIDs) and cardiovascular drugs (Table 2). Digoxin, warfarin and NSAIDs (especially aspirin, diclofenac and piroxicam) were commonly implicated, reflecting the widespread use of these drugs. Two-thirds of the ADR cases were thought to be caused by a single drug, while a combination of two or more drugs was implicated in the remainder of cases.

ADRs were grouped by the physiological system affected (Table 3). The most common reactions were bleeding from the gastrointestinal tract (26%), and cardiovascular complications (22%).

Table 2. Drugs most frequently involved in adverse drug reactions: number of cases

Drug	Single drug	Combination of drugs	Total
Digoxin	5	5	10
Aspirin	3	9	12
Warfarin	2	6	8
Piroxicam	4	3	7
Diclofenac	3	3	6
Theophylline	3	2	5
Methotrexate	4	–	4

Drug Interactions

Twenty-seven suspected drug interactions were encountered, 6 of which were classified as pharmacokinetic in nature and 21 as predominantly pharmacological (Table 4). In some cases both mechanisms may have been contributing when more than two drugs were involved.

Risk Factors for Adverse Drug Reactions

As shown in Figure 1, patients who suffered an ADR were predominantly elderly, with 53% of ADRs occurring in patients aged >70 years, whereas only 24% of the total hospital admissions over the same period were in this age group.

Female sex also appeared to be a potential risk factor, with more females in the ADR group (47.7%) compared to the total hospital population (42.3%). This may, however, be an age-related phenomenon.

The mean number of drugs being taken by patients in the ADR group was 4.9 ± 2.6. This was significantly greater ($p < 0.01$) than the 3.0 ± 2.8 drugs taken by the control population of 352 patients admitted to hospital without ADRs. The average number of drugs taken by all patients at the time of admission to hospital was noted to increase with age. However, for each age group, the mean number of drugs taken by the ADR group was higher than that seen in the control population of patients without ADRs (Figure 2).

Table 1. Details of adverse drug reactions in patients who died

Age	Sex	Medical conditions	Suspected drugs	ADR effects	Probability rating for ADR
27	F	Systemic lupus erythematosus; venous thromboembolism and pulmonary hypertension	Cyclophosphamide, warfarin, aspirin	Pancytopenia, haemoptysis, haemorrhagic cystitis	Definite
58	M	Cerebrovascular disease; chronic obstructive airways disease	Warfarin, co-trimoxazole, cimetidine	Haematemesis, anaemia, cerebrovascular accident	Definite
96	M	Osteoarthritis; chronic obstructive airways disease; congestive heart failure; past duodenal ulcer	Diclofenac	Haematemesis and melaena, anaemia	Definite
61	M	Non-Hodgkin's lymphoma	Bleomycin (3 courses, total dose 225 mg)	Pulmonary fibrosis, neutropenia, thrombocytopenia	Definite
82	F	Osteoarthritis; chronic obstructive airways disease	Naproxen	Haematemesis and melaena	Probable

Of the patients admitted due to an ADR, 24% had a previously recorded ADR. However, in only 6% of cases was the current ADR related to the previous episode. Only one case was related to drug hypersensitivity. In the reference population, where admission was not drug-related, a similar proportion (28%) of patients had a history of previous drug hypersensitivity or ADR.

Table 3. Physiological systems involved in adverse drug reactions

System	% of ADRs	
Gastrointestinal tract		39
– haemorrhage	26	
– other	13	
Cardiovascular system		22
– cardiac arrhythmias	13	
– hypotension	8	
– other	1	
Nervous system		10
Haematological system		8
Liver		2
Urinary tract		9
Respiratory tract		3
Skin		1
Unclassified		6

Renal disease (22%) and liver disease (13%) were the most common concurrent diseases present in the ADR group of patients. The frequency with which these occurred in the reference population was not examined.

Discussion

This study confirms that drug-related hospital admissions are a significant problem in our community. One in forty admissions to the Monash Medical Centre (Prince Henry's Hospital campus) over a six-month period could be attributed to a drug-related admission. In our hospital, ADRs were a more common cause of admission than drug overdoses. The present survey included all hospital admissions rather than those to selected medical units. This is thought to be the likely explanation for the incidence found in our study being towards the lower end of the reported range. We would suggest that the figure of 2.4% more closely reflects the true incidence in an Australian general adult teaching hospital than could be inferred from previous studies.

The drugs most frequently implicated in ADRs, the most common types of ADR and the risk factors found in this study are similar to other reports,[1-6,8-13] except perhaps for the higher incidence of gastrointestinal bleeding associated with NSAIDs. Of the 20

Table 4. Drug interactions

Suspected drugs	Effects
1. Cardiovascular drugs	
Digoxin + amiodarone	Bradycardia, digoxin toxicity* (6.3 nmol/L)
Digoxin + amiodarone + verapamil	Arrhythmias, anorexia, digoxin toxicity* (8.4 nmol/L)
Digoxin + atenolol	Heart block, digoxin toxicity* (7.0 nmol/L)
Digoxin + atenolol + nifedipine	Bradycardia, digoxin toxicity* (2.8 nmol/L)
Methyldopa + chlorothiazide + verapamil + chlorpromazine	Postural hypotension, fall and ankle injury
Methyldopa + hydralazine + verapamil + chlorpromazine	Postural hypotension, Colles' fracture
Cyclopenthiazide + metoprolol + hydralazine	Postural hypotension, collapse
2. Anti-inflammatory drugs	
Diclofenac + aspirin	Haemoptysis
Diclofenac + aspirin	Haematemesis and melaena
Diflunisal + piroxicam	Haematemesis and melaena, anaemia
Dipyridamole + aspirin	Melaena, anaemia
Indomethacin + aspirin	Melaena
Ketoprofen + aspirin	Melaena, anaemia
Naproxen + aspirin	Haematemesis and melaena, anaemia
Piroxicam + aspirin	Haematemesis and melaena, anaemia
Piroxicam + diclofenac	Hyponatraemia, cardiac failure
3. Anticoagulant drugs	
Warfarin + co-trimoxazole + cimetidine	Haematemesis and melaena
Warfarin + co-trimoxazole + doxycycline	Haematemesis and melaena, vomiting, dehydration
Warfarin + aspirin + prednisolone	Haematemesis and melaena, anaemia
Warfarin + aspirin + cyclophosphamide	Pancytopenia, haemoptysis, haemorrhagic cystitis
4. Other drugs	
Theophylline + allopurinol	Nausea, vomiting, dehydration, collapse
Theophylline + ranitidine	Anorexia, nausea, vomiting
Methotrexate + co-trimoxazole	Severe mucositis
Glibenclamide + metformin	Hypoglycaemia, confusion, collapse
Promethazine + prochlorperazine	Dystonia, extrapyramidal effects
Morphine + oxycodone	Confusion, drowsiness
Bromocriptine + thioridazine	Confusion, sedation

*Therapeutic range 1.0–2.6 nmol/L

patients in this category, 10 had been taking NSAIDs for less than 3 weeks. In 6 patients, 2 or more NSAIDs were being taken.

It appears from the results of our study, and those of others,[4,8,13] that the patient at particular risk of experiencing an ADR is the elderly patient with multiple medical problems, including renal or hepatic dysfunction, who is taking a large number of different medications. We did not find a higher incidence of previous adverse reactions or hypersensitivity to drugs in our ADR group compared to the reference population. Elderly patients with multiple medical problems often require a variety of different medications. However, in view of the associated increased risk of an ADR occurring in such patients, there is need for frequent review of the indications for currently prescribed drugs and for regular reappraisal of the risk–benefit ratio of all medications.

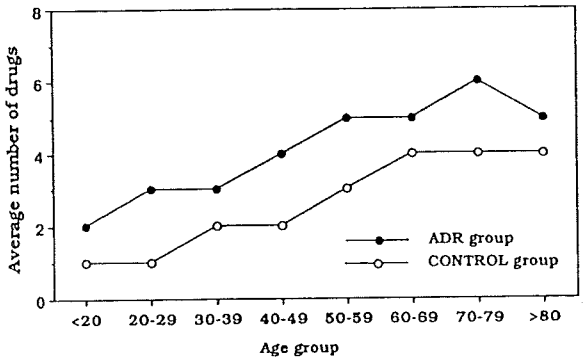

Figure 2. Average numbers of drugs taken in each age group of patients with adverse drug reactions compared to reference population

It is salutary to consider the costs of this form of iatrogenic disease to our community. Such costs to patients and their families in terms of illness and even death are, of course, immeasurable. The financial costs associated with a hospital stay and treatment are also considerable. Take, by way of example, the 156 bed-days of treatment required for 20 patients because of gastrointestinal bleeding associated with NSAIDs in the present study. A conservative estimate of the hospital-related costs in these patients is $110 000. Included among these patients was a previously well 52-year-old male who was prescribed piroxicam for the treatment of 'tennis elbow'. Three weeks later he presented with a perforated ulcer requiring emergency surgery and extended hospitalisation (32 days) and treatment.

In the 5 fatal cases (Table 1), it is a difficult task to ascertain to what extent the suspected drugs contributed to the patients' deaths. In 2 patients cytotoxic drug therapy was being used. In one this was for the treatment of malignancy and the second patient had systemic lupus erythematosus. The adverse effects and unfortunate consequences of the use of potent and toxic drugs in such disorders are well known. However, gastrointestinal haemorrhage in the other 3 patients was likely to have been a major factor in their demise.

The study highlights the need for a wider appreciation of the risks of drug interaction as a cause of ADRs. One-third of all ADRs were due to drug interactions.

The problems associated with ADRs highlight the potential benefits of having in place some system for regular monitoring of patients for ADRs and the importance of patient education in relation to their medication. Patients alerted to potential adverse effects are more likely to seek early attention for their problems, which may reduce the extent of any ADRs. The use of computers to assist in a problem detection system at the time of drug dispensing could be valuable.[14] This could theoretically be linked to the use of computer-generated prescriptions.

The importance of avoiding unnecessary medications, keeping dosage regimens simple and being aware of potential drug interactions, particularly in the elderly, cannot be over-emphasised. It is also important to maintain accurate records of the drugs a patient receives from other sources. This is often a difficult task when a patient is seeing different doctors, attending different clinics, buying over-the-counter products and attending centres where alternative medicines are prescribed. Continuing education of all parties (prescriber, pharmacist and patient) is necessary if difficulties, such as those outlined above, are to be minimised.

Conclusion

Drug-related hospital admissions are important contributors to health care expenditure. The approach used in this study could be used more widely in ascertaining the incidence and nature of these admissions.

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In the Journal . . . . . 25 Years Ago

'Hospital Pharmacists should increase their knowledge of pharmacology and allied subjects, so that they may retain the role of pharmacological "know-how" and remain the person with a thorough knowledge of drugs and drug therapy . . .

With increased knowledge gained from this study, the Hospital Pharmacist should be able to converse more freely with the medical staff and thus become part of the hospital team. This greater involvement in patients' care will require visits to the wards and the patients' bedside. This will enable the Pharmacist to observe at first hand the effects of drugs on patients. Pharmacists must take part in medical seminars, lectures and hospital programmes.'

— P.L. Jeffs, Evans Medical Oration
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Identification of Adverse Drug Reactions Using the ICD-10 Australian Modification Clinical Coding Surveillance

Marisa R Hodgkinson, Nicole J Dirnbauer, Ian Larmour

ABSTRACT

Background: Adverse drug reactions (ADRs) pose a significant burden on patients and the health system. ADR reporting contributes to data that guide patient safety strategies. Despite numerous strategies aimed to improve ADR reporting rates, ADRs continue to be under-reported.

Aim: To compare the effectiveness and efficiency of identifying institutional ADRs using the International Classification of Diseases 10th Revision Australian Modification (ICD-10-AM) clinical coding surveillance and spontaneous reporting.

Method: Medical records of multi-day (staying overnight or longer) inpatient separations (single patient encounter resulting in discharge) assigned an ADR-related ICD-10-AM code were retrospectively reviewed to verify if an ADR had occurred and whether the codes assigned were appropriate. ADR reports received via the spontaneous reporting system were also reviewed. ADRs were assessed for causality, seriousness and type of reaction. The drugs, type of adverse reactions involved and the resource implications of this reporting method were also investigated.

Results: ICD-10-AM coding surveillance and spontaneous reporting resulted in an ADR reporting rate of 3.3% and 0.4% of inpatient separations, respectively. ICD-10-AM coding surveillance was more likely to identify type A ADRs than spontaneous reports although there were no significant differences in seriousness or causality. The ICD-10-AM codes assigned were appropriate in 94% of cases, with the omission of drugs being the most common discrepancy.

Conclusion: The ICD-10-AM coding surveillance is an effective and efficient method of improving ADR reporting by utilising data collected for administrative purposes.

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INTRODUCTION

Adverse drug reactions (ADRs) pose a significant burden on patients and the health system. Identifying and reporting ADRs is important as it ensures that ADRs and drug–drug interactions are identified in post-marketing surveillance of new drugs; risk factors are identified and preventive measures implemented; knowledge of the incidence and outcomes of ADRs are improved; and ADRs are documented in patients' medical records to reduce the risk of re-exposure and improve the information available for future medication management decisions.

Although Australia has one of the highest per capita ADR reporting rates in the world, ADRs are still under-reported.[1] A systematic review of 37 studies estimated a median under-reporting rate of ADRs of 94%.[2]

Marisa R Hodgkinson, BPharm, MSc, Quality Use of Medicines Pharmacist, **Nicole J Dirnbauer**, BPharm, Quality Use of Medicines Pharmacist, **Ian Larmour**, BPharm, MSc, FSHP, Director of Pharmacy, Southern Health, Clayton, Victoria
Address for correspondence: Marisa Hodgkinson, Pharmacy Department, Monash Medical Centre, Southern Health, Clayton Vic. 3168, Australia.
E-mail: marisa.hodgkinson@southernhealth.org.au

Most hospital inpatient settings rely on spontaneous reporting for identification of ADRs. Prospective identification of ADRs by trained health professionals visiting selected areas over a defined period to record all patients and all events is one of the most reliable ADR reporting methods because additional investigations and interviews can be performed to assess the causality of an ADR.[3] ADRs can also be identified by prospective and retrospective medical record review. However, these methods are resource intensive and have practical limitations for routine use outside of research settings. Information technology can be used to improve reporting and streamline case finding by identifying 'signals' for potential ADRs, which can then be directed to a trained health professional for further investigation.[4] Examples of signals include medication orders used to treat ADRs, such as antihistamines, and abnormal laboratory test results, such as doubling in serum creatinine concentrations or high serum drug concentrations.[4] However, ADRs identified by this method are limited to those that can be detected by electronically available information. This method is not viable in most Australian hospitals as computerised prescribing systems have not been widely implemented.

Australian clinical coding standards allow ADR codes to be applied to any diagnosis not just the principal diagnosis, therefore, retrospective ADR reporting is possible using coding surveillance.[5] Consequently, ADRs that occur at any time of the inpatient stay can be identified. Previous studies have used the International Classification of Diseases 9th Revision Clinical Modification (ICD-9-CM) for identifying drug-related hospital admissions, readmissions or adverse events including ADRs.[6-12] The introduction of the International Classification of Diseases 10th Revision Australian Modification (ICD-10-AM) resulted in significant changes to the classification of drugs that can cause ADRs.[5] The Y codes utilised in the ICD-10-AM to classify drugs have been expanded and new classes added when compared to the E codes used in the ICD-9-CM. This enables more comprehensive and specific coding of ADRs. The aim of this study was to compare the effectiveness and efficiency of identifying institutional ADRs using the ICD-10-AM clinical coding surveillance and spontaneous reporting. Since there is limited information on the accuracy of ADR-related ICD-10-AM coding, the study also sought to investigate whether the codes assigned accurately reflected the ADR.

METHOD

The study population included patients discharged from three public hospitals from the same hospital network from March to May 2004. The project was approved by the hospital network's Human Research and Ethics Committee. All inpatient separations (single patient encounter resulting in discharge) were coded using the

ICD-10-AM by clinical coders. The medical records of all multi-day (staying overnight or longer) inpatient separations assigned an ADR-related ICD-10-AM code between Y40 and Y59 (drugs, medicaments and biological substances causing adverse effects in therapeutic use excluding accidents in the technique of administration of drugs) were requested from the Medical Records Department. Patients were included in the study if their medical records were available and excluded if they were attending the emergency department without being admitted or if they were hospital-in-the-home patients.

The hospital network has a well established ADR reporting system comprising of spontaneous reporting using written, verbal or e-mail notification and a dedicated telephone hot-line. A monthly reminder letter is sent to registrars requesting them to identify patients that may have experienced an ADR. Surveillance of ADR-related ICD-10-AM codes is undertaken periodically, depending on staffing resources and the availability of reports.

Medical records were reviewed retrospectively to determine if an ADR had occurred and whether the ICD-10-AM code assigned accurately reflected the ADR as documented in the medical record. Medication charts, observational and laboratory data and pharmacy dispensing records were also reviewed, if required. Medical records assessed as having a questionable ICD-10-AM code assigned for an ADR were also reviewed by a clinical and coding services advisor and consensus reached. All ADRs were documented in the appropriate place in the medical record and reported to the Australian Adverse Drug Reactions Advisory Committee, if this had not already occurred. The time taken to review the medical record, assess whether an ADR had occurred and complete the ADR report was recorded to determine the staffing implication in using this ADR reporting method. ADR reports received via the spontaneous reporting system during the study period were also reviewed.

The World Health Organization's definition of an ADR, 'a response to a drug which is noxious and unintended and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function', was used in the study.[13] All ADRs identified were classified as either serious or not serious and assigned causality according to the World Health Organization criteria.[14] A serious ADR was defined as 'any untoward medical occurrence that at any dose results in death, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity, or is life-threatening'.[15] Each ADR was classified as type A (dose-related, augmented), type B (non-dose-related, bizarre), type C (dose-related and time-related, chronic), type D (time-related, delayed), type E (withdrawal, end of use) and type F (unexpected failure of therapy, failure).[16] Patient's sex and age, number of drugs taken, drugs suspected of causing the ADR and the reaction were recorded. Each drug implicated was assigned a World Health Organization's Anatomical Therapeutic Chemical classification.[17]

RESULTS

The ADR-related ICD-10-AM codes were assigned to 4.5% (552/12 414) of multi-day inpatient separations during the three month study period. ADR reports were completed for 75% (412/552) of these. The ICD-10-AM coding surveillance resulted in an ADR reporting rate of 3.3% (412/12 414). Table 1 displays the reasons why ADR reports were not completed for the remaining 140 inpatient separations assigned an ADR-related ICD-10-AM code.

Table 1. Reasons ADR reports were not completed for multi-day inpatient separations assigned an ICD-10-AM code

Reason ADR report not completed	No. of ADR reports (n = 140)
Medical record not available after one request.	79 (56%)
Case involved a subtherapeutic international normalisation ratio not resulting from a drug interaction.	16 (11%)
ADR attributed to deliberate overdose or disease progression due to under-dose.	13 (9.3%)
ADR involved a substance that was not a drug.	5 (4%)
Causality assessment of 'unlikely' when reviewed.	16 (11%)
Causality assessment of 'unassessable' when reviewed.	11 (7.9%)

ADR = adverse drug reaction. ICD-10-AM = International Classification of Diseases 10th Revision Australian Modification.

Of the 412 ADR reports identified by the ICD-10-AM coding surveillance, 377 patients experienced an ADR (31 patients experienced more than one ADR – 27 patients had two and four patients had three ADRs). The median age of patients was 65 years (1st and 3rd interquartile range 47 to 79; range 2 to 97) and the median number of drugs taken was eight (1st and 3rd interquartile range 5 to 10; range 1 to 21). Females accounted for 55% (228/412) of patients.

During the study period, 44 ADRs were reported spontaneously – 29 ADRs identified by spontaneous reporting alone and 15 ADRs were identified by spontaneous reporting and the ICD-10-AM codes. Spontaneous reporting resulted in an ADR reporting rate of 0.4% (44/12 414). Overall, 441 ADRs were identified during the study period (397 by ICD-10-AM, 15 by both ICD-10-AM and spontaneous reporting, 29 by spontaneous reporting) resulting in an overall ADR reporting rate of 3.6% (441/12 414).

Table 2. Most common therapeutic drug classes causing ADRs identified by the ICD-10-AM coding surveillance

WHO ATC classification system level 2 classes causing ADRs	No. of ADR reports (n = 524)*
Antibacterials for systemic use	72 (14%)
Opioids	68 (13%)
Diuretics	52 (10%)
Antineoplastic agents	44 (8.3%)
Antithrombotic agents	35 (6.7%)
Cardiac therapy	35 (6.7%)
Beta-blocking agents	24 (4.6%)
Agents acting on the renin-angiotensin system	19 (3.6%)
Corticosteroids for systemic use	19 (3.6%)
Anti-inflammatory and antirheumatic products	17 (3.2%)
Anaesthetics	17 (3.2%)

ADRs = adverse drug reactions. ATC = Anatomic Therapeutic Chemical. ICD-10-AM = International Classification of Diseases 10th Revision Australian Modification.
*Although 412 ADR reports were completed, n = 524 as more than one drug may have been implicated in the ADR.

Drugs and Adverse Reactions

There were 524 drugs implicated in the 412 ADRs identified using ICD-10-AM coding surveillance. Of the 178 different drugs implicated, the five most common drugs were digoxin, frusemide, glyceryl trinitrate, morphine and warfarin. The most common therapeutic drug classes associated with ADRs are listed in Table 2. There were 149 different ADRs experienced and the most common of these are described in Table 3.

Table 3. Most common ADRs identified by the ICD-10-AM coding surveillance

ICD-10-AM code	Adverse reactions	No. of ADR reports (n = 510)*
R11	Nausea and vomiting	28 (5.5%)
L27	Generalised skin eruption due to drugs and medicaments	25 (4.9%)
E87.6	Hypokalaemia	24 (4.7%)
I95.2	Hypotension due to drugs	24 (4.7%)
D68.3	Haemorrhagic disorder due to circulating anticoagulants	19 (3.7%)
E87.1	Hypo-osmolality and hyponatraemia	19 (3.7%)
D70	Agranulocytosis	16 (3.1%)
R55	Syncope and collapse	16 (3.1%)
K52.9	Noninfective gastroenteritis and colitis, unspecified	14 (2.7%)
R00.1	Bradycardia, unspecified	13 (2.5%)

ADRs = adverse drug reactions. ICD-10-AM = International Classification of Diseases 10th Revision Australian Modification. *Although 412 ADR reports were completed, n = 510 as an ADR may have resulted in more than one reaction.

Of the 441 ADR reports identified using ICD-10-AM coding surveillance and spontaneous reporting, 157 caused hospital admissions resulting in 1.3% (157/12 414) of multi-day inpatient separations being associated with an ADR as the cause of hospital admission. The seriousness, causality and type of reactions for the 441 ADRs are presented in Table 4.

Assignment of ADR-related ICD-10-AM codes

Of the 412 ADR reports identified using ICD-10-AM codes, 446 codes were assigned. The codes assigned were appropriate in 94% (420/446) of cases. Twenty-six codes were assessed as inappropriate – 15 were omitted despite being documented in the medical record, nine codes had the incorrect Y code for the drug implicated and two drugs were not implicated. There were no particular drugs more likely to be incorrectly coded, however, combination products such as Karvezide (irbesartan + hydrochlorothiazide) were more likely to result in one of the drugs being omitted.

Of the ICD-10-AM codes assigned, 7.6% (34/446) were correct according to the rules to which the clinical coders must assign codes, but were not considered the most appropriate code for the drug on a pharmacological basis. For example, tramadol was classified as a non-steroidal anti-inflammatory drug instead of an opioid and related analgesic. In a further 21% (92/446) of cases, the codes assigned were correct according to what was documented in the medical record but the researchers attributed the ADR to additional, different or more specific drugs.

Time Taken to Review Medical Records

The median time taken to review a medical record and complete an ADR report or assess that an ADR report

Table 4. Seriousness, causality and type of ADRs according to the method of ADR reporting

	ICD-10-AM coding (n = 397)	ICD-10-AM coding and spontaneous reporting (n = 15)	Spontaneous reporting (n = 29)
Seriousness			
Not serious	193 (47%)	6 (40%)	17 (57%)
Caused admission	140* (34%)	6 (40%)	11† (37%)
Death	3* (0.7%)	0 (0%)	0 (0%)
Disability	4 (1%)	0 (0%)	0 (0%)
Life threatening	50* (12%)	3 (20%)	2† (7%)
Prolonged hospitalisation	23 (5.6%)	0 (0%)	0 (0%)
Causality			
Certain	3 (0.8%)	0 (0%)	1 (3%)
Probable	227 (57%)	7 (47%)	16 (55%)
Possible	167 (42%)	8 (53%)	12 (41%)
Type of reaction			
A: Dose related (augmented)	343 (86%)	4 (27%)	13 (45%)
B: Non-dose related (bizarre)	49 (12%)	11 (73%)	16 (55%)
C: Dose-related and time-related (chronic)	5 (1%)	0 (0%)	0 (0%)
D: Time-related (delayed)	0 (0%)	0 (0%)	0 (0%)
E: Withdrawal (end of use)	0 (0%)	0 (0%)	0 (0%)
F: Unexpected failure of therapy (failure)	0 (0%)	0 (0%)	0 (0%)

ADRs = adverse drug reactions. ICD-10-AM = International Classification of Diseases 10th Revision Australian Modification. *Although there were 397 ADR reports, n = 413 because 16 reports were assigned two seriousness categories (15 reports caused admission and life-threatening, one report caused admission and death). †Although there were 29 ADR reports, n = 30 because one report was assigned two seriousness categories (caused admission and life-threatening).

could not be completed was 19 minutes (range 5 to 45) and 9 minutes (range 1 to 25), respectively. The median time taken to review a medical record regardless of whether an ADR report was completed was 18 minutes. Based on an average of 184 multi-day inpatient separations per month assigned an ADR-related ICD-10-AM code, 55 hours per month of pharmacists' time (0.34 full-time equivalent) would be required to fully utilise the hospital network's ICD-10-AM coding surveillance and improve ADR reporting.

DISCUSSION

The ICD-10-AM coding surveillance is an effective way of identifying ADRs, as it resulted in the reporting of an additional 397 ADRs that would otherwise have not been identified. This equates to an 849% (2.97/0.35) increase in ADR reporting rates compared with spontaneous reporting alone.

The ADR rates reported in this study should be compared to other studies with caution. Some studies did not use the World Health Organization's definition of an ADR or also included adverse drug events, such as therapeutic failures, poisoning, drug administration errors or non compliance, hence potentially overestimating the ADR incidence.[17] Other studies vary in their inclusion of serious and non-serious ADRs, causalities and whether the ADR caused hospital admission or occurred during hospitalisation. The type of hospital, patient inclusion criteria or patient age may also differ between studies.

Although the total ADR rate found in this study was 3.6%, it cannot be assumed this is the true rate. Our ADR rate was lower than a 1998 meta-analysis of prospective studies, which found an ADR rate of 6.7% in US hospitals but higher than that found in previous Australian studies.[18] Adverse drug events that included ADRs were associated with 1.8% of 14 179 hospital stays in a study of 28 hospitals in New South Wales and South Australia.[18,19] A Victorian study found that around 1% of inpatient separations from 247 hospitals were associated with an ADR.[12] A Western Australian study of ADRs in Australians aged 70 years and over found that 0.8% of hospital stays were ADR related.[20] These studies were retrospective in design and only the latter two studies used a definition of ADR similar to that used in our study and ICD codes for case finding. These studies were undertaken in states with different hospital funding arrangements and clinical coding requirements, which may have contributed to the different results. The funding for Victorian hospitals is dependent on the Weighted Inlier Equivalent Separation data, where the allocated funding is related to the diagnosis-related group assigned for an episode of care. Therefore, clinical coders need to obtain the highest diagnosis-related group possible and identifying and coding ADRs contributes to the diagnosis-related group.

The higher ADR rate found in this study may also be due to more drugs being prescribed, particularly for older patients and improved documentation of ADRs in medical records compared to when the earlier studies were undertaken.

ADRs were the cause of hospital admission in 1.3% of non-same-day inpatient separations. This is consistent with a prospective study in our hospital network which found that 1.6% of hospital admissions were due to ADRs.[21] A review of 14 Australian studies found that 2.4 to 3.6% of hospital admissions were drug-related, although this review included a wider definition of ADRs.[22] This study found there was no significant difference between ADRs identified by the ICD-10-AM coding surveillance and spontaneous reporting in causing hospital admission.

The drugs most commonly associated with ADRs were similar to those found in previous studies.[11,12,20,23,24] The ADRs identified were wide ranging and the majority were well recognised drug reactions. However, over half of the ADRs were classified as serious. There were no significant differences between the ICD-10-AM coding surveillance and spontaneous reporting with respect to seriousness and causality of the ADRs. The ICD-10-AM coding surveillance was more likely to identify type A reactions whereas spontaneous reports were more likely to identify type B reactions. Reporting of type A reactions is valuable because although they often involve known drugs and reactions, they are more likely to be preventable than type B reactions. This information can be used to provide evidence for focusing on certain drugs or patient groups and help with education and prevention strategies.

The ICD-10-AM coding surveillance is an efficient method of identifying ADRs, as 86% (383/444) of medical records reviewed resulted in an ADR report being completed. However, reliance on coding alone to identify trends in drugs causing ADRs and ADR incidence, without reviewing medical records has limitations. Furthermore, documentation in the medical record may be incomplete, inaccurate or non-specific and in routine clinical practice not all ADRs will be detected or documented in the medical record. The 29 ADR reports that were identified through spontaneous reporting and not detected by the ICD-10-AM coding surveillance were missed due to inadequate documentation in the medical records. In the 21% of cases, where the researchers would have assigned additional, different or more specific drugs than those coded, more information was obtained by reviewing the patient's medication chart, laboratory and observational data or pharmacy dispensing records.

The retrospective review of medical records assigned an ADR code is resource intensive. However, the ICD-10-AM coding data can be used to identify trends without recalling medical records to complete ADR reports and can be scanned for new or high-risk therapeutic drug classes. Reviewing the data for reaction codes that are clinically significant may also help streamline the medical records reviewed.

The ICD-10-AM coding surveillance is an effective and efficient method of improving ADR identification and reporting as it streamlines case finding and utilises outcome data that are collected for administrative purposes and is readily available. However, it is resource intensive as medical record review is needed to complete a formal ADR report and to ensure accuracy in the assessment of drugs implicated in the ADRs. The way forward for organisations that do not have the available resources but have reliable coding systems, may involve using the ICD-10-AM coding data to identify trends for education and prevention strategies and to target the review of medical records with therapeutic drug classes or ADRs of interest.

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Chapter Three

Examining New Concepts in Hospital Pharmacy Management Strategies

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RESEARCH ARTICLE

The impact of an integrated electronic medication prescribing and dispensing system on prescribing and dispensing errors: a before and after study

Marisa R. Hodgkinson, BPharm, MSc (Clinical Pharmacy)[1], Ian Larmour, BPharm, MSc (Pharmacology)[1], Susan Lin, BPharm[1], Adam J. Stormont, BPharm, GradDipPharmMgt, MHSM[1], Eldho Paul, MSc[2]

1 Pharmacy Department, Monash Health, Melbourne, Australia
2 Monash Centre for Health Research and Implementation, School of Public Health and Preventive Medicine, Monash Medical Centre, Monash University, Melbourne, Australia

Abstract

Background: Medication errors are a significant problem in Australian hospitals. This is the first study of the impact of an integrated electronic medication prescribing (e-prescribing) and dispensing system on medication errors.
Aim: To evaluate the impact of an integrated e-prescribing and dispensing system implemented in outpatient clinics and the emergency department on prescribing and dispensing errors.
Method: Prescribing and dispensing errors were identified over 2 weeks before and after implementation of the integrated system. Errors were identified through original prescription, e-prescribing and dispensing systems review. Error rates, types, severity and patient waiting times for prescription dispensing were compared.
Results: The study included 379 patients prescribed 654 medicines in the before group and 375 patients prescribed 635 medicines in the after group. Prescribing and dispensing error rates per patient were reduced by 93% (from 2.98 to 0.2; $p < 0.0001$) and 98% (from 1.27 to 0.03; $p < 0.0001$), respectively. The proportions of patients with at least one procedural or clinical prescribing error showed significant reductions of 81% (95% CI 77–85%) and 3.4% (95% CI 0.1–6.7%). The proportions of patients with at least one procedural or clinical dispensing error showed signicant reductions of 61% (94% CI 56–66%) and 2% (95% CI 0.7–3.6%). Fifty system-related prescribing errors were identified. Mean error severity score was minor in both groups. Median patient waiting time for prescription dispensing was reduced by 52% (from 27 to 13 min; $p < 0.0001$).
Conclusion: Implementation of the integrated system significantly reduced prescribing and dispensing errors and patient waiting times for prescription dispensing. Clinicians need to manage new system-related errors to reduce associated risks.

Keywords: electronic prescribing, dispensing, prescribing errors, drug safety, E-health.

INTRODUCTION

Medication errors are a significant problem in Australian hospitals that may lead to inappropriate medication use or patient harm.[1–3] Medication errors can occur at any stage of the medication management pathway,[4] including during prescribing, administration and dispensing.[5] Australian studies have identified prescribing errors in 2.4[6] to 25%[7] of prescriptions, with incorrect dose, route or frequency and incomplete information accounting for the majority of errors.[2] Dispensing error studies have identified error rates of 0.01–5% of medicines dispensed, with the most common errors being incorrect medicine, strength, formulation, quantity and labelling of directions.[8–11] The evidence for electronic medication prescribing (e-prescribing) in reducing medication errors for inpatients is compelling, although these studies are predominately from the USA and UK, with limited Australian studies.[12–15] There have been few outpatient studies,[16,17] with no published Australian studies in this setting. The e-prescribing systems used and prescribing and dispensing processes are different in Australia compared with other countries, and it is not known if results are generalisable across the different healthcare settings. Furthermore, the outcome measures

Address for correspondence: Marisa Hodgkinson, Monash Health Pharmacy Department, 246 Clayton Road, Clayton, Victoria 3168 Australia
E-mail: marisa.hodgkinson@monashhealth.org

of these studies have been reduction of prescribing or administration errors; there are no published studies investigating the impact of an integrated e-prescribing and dispensing system on prescribing and dispensing errors.

The study aim was to evaluate the impact of an integrated e-prescribing and dispensing system implemented in outpatient clinics and the emergency department (ED) on prescribing and dispensing errors. Primary outcome measures were the rates of prescribing and dispensing errors. Secondary outcome measures were the category and severity of prescribing and dispensing errors, identification of system-related prescribing errors and patient waiting times for prescription dispensing.

METHOD

Setting and Study Design

The before and after intervention study was conducted at a 640-bed, metropolitan, teaching hospital over two 14-day periods between 15 and 28 October 2012 (before) and 11 and 24 August 2014 (6 months after full implementation of the system). All original outpatient clinic and ED prescriptions for adult and paediatric patients handwritten on the hospital prescription form (before) or prescribed electronically (after) and dispensed at the study hospital pharmacy were included. Monash Health Human and Research Ethics Committee approval was obtained for the study.

The hospital pharmacy provided dispensing services for all outpatient clinics and the ED, along with clinical pharmacy services in some outpatient clinics (infectious diseases, liver) and the ED; these were comparable for both study groups. The pharmacy dispensing system utilised barcode scanning to verify the patient and medicine entered matched the dispensing label and product barcode on the dispensed medicine.

Before- and after-study clinicians received comparable prescribing and dispensing training through competency-based assessment programs. After-study clinicians received additional training on e-prescribing provided by an e-prescribing pharmacist. This involved presentations and/or face-to-face tutorials, with completion of an online training module that required the first time clinicians to login to the e-prescribing system. Pharmacy staff also received training on processing e-prescriptions using the pharmacy dispensing system. If required, ad hoc training was provided by an e-prescribing pharmacist and/or the outpatient clinic/ED pharmacist to manage any system-related errors identified. Training to manage errors related to individual end-user practices was provided directly to the clinician involved.

Intervention

The Pharmhos MerlinMAP e-prescribing system interfaced with the patient management system. Medicines were selected by generic name, strength and formulation with further prescribing information entered free-text or via drop-down lists prepopulated with common doses, units, routes, frequencies and quantities for the medicine selected. Active decision-support included mandatory entry of patient allergy/adverse drug reaction (ADR) status with alerts for potential medicine–medicine or medicine–medication class reactions, and moderate and severe medicine interactions. Passive decision-support included mandatory entry of patient weight for paediatrics and prepopulated prescribing and Pharmaceutical Benefits Scheme (PBS) information. Two paper copies of the e-prescription (for patient/pharmacist and Medicare Australia) were printed and signed by the prescriber, then given to the patient to take to the pharmacy. The e-prescribing system was integrated with the Pharmhos Merlin dispensing system and the two systems shared a common medication data set. On presentation to the pharmacy, scanning of the printed e-prescription barcode resulted in autopopulation in the dispensing system of patient and prescriber information, prescription date, medicine, strength, formulation, directions, quantity, repeats and PBS authority number (when applicable) which could be amended if required.

Prescribing and Dispensing Errors

A prescribing error was defined as a prescribing decision or prescription-writing process that resulted in an unintentional, significant reduction in the probability of treatment being timely and effective, or an unintentional, significant increase in the risk of harm, when compared with generally accepted practice.[18] Failure to document allergy/ADR status, legislative non-compliance, use of error-prone terminology,[19] and non-adherence to hospital formulary and PBS requirements, were also considered prescribing errors. Prescribing errors were prospectively identified and annotated on prescription forms by dispensing pharmacists. Annotations made by dispensing pharmacists also included clarifications, amendments and documentation requirements. Completed prescription forms and the e-prescribing and dispensing system records were reviewed retrospectively by the principal investigator, using a standard prescribing error assessment checklist (Appendix S1) which included category definitions and examples, to determine prescribing errors identified by dispensing pharmacists and any additional prescribing errors.

A dispensing error was defined as a deviation from an interpretable written prescription or medicine order, including written modifications to the prescription made by a pharmacist following contact with the prescriber or in compliance with pharmacy procedures.[20] Deviations from professional standards including failure to document allergy/ADR status or legislative non-compliance were also considered dispensing errors. Medicines recorded in the dispensing system but not supplied were not considered dispensed for this study. Only dispensing errors identified after the final dispensing check were included. All dispensing errors were identified retrospectively by the principal investigator using a standard dispensing error assessment checklist (Appendix S2) which included category definitions and examples. Completed prescription forms were reviewed to identify prescribing errors not identified or required annotations not made by dispensing pharmacists. Dispensing system records were reviewed to determine any dispensing errors when compared with the prescription form, including: patient name, medicine, strength, formulation, directions, quantity, prescriber name, prescription date, dispensed date, repeats and PBS requirements.

Prescribing and dispensing errors identified were categorised as procedural or clinical, and then more specifically, based on accepted standards and definitions.[18–22] Prescribing errors were also analysed to determine those which may have been system-related, defined as errors where there was a high probability that the functionality or design of the e-prescribing system contributed to the error,[22] and their underlying mechanism.[22] The hospital's incident management system was reviewed to identify any additional prescribing or dispensing errors recorded for the study patients during and for 1 month after the study periods.

Error Severity Assessment

All clinical prescribing and dispensing errors were assessed for severity based on the assumed consequence or impact of the error if an intervention was not made.[23] Based on a validated method previously published,[24] each error was reviewed independently by five judges (the principal investigator, two clinical pharmacists, one ED consultant and one senior nurse), scored for severity from 1 = insignificant to 5 = catastrophic[23] (Figure 1) and a mean severity score calculated.

Patient Waiting Time for Prescription Dispensing

A dispensing system report with electronic time stamps was reviewed to determine patient waiting times for prescription dispensing. Only patients waiting for their prescription to be dispensed and who had all medication orders on the prescription dispensed were included in this analysis. The patient waiting time was calculated from the time the prescription was presented to the

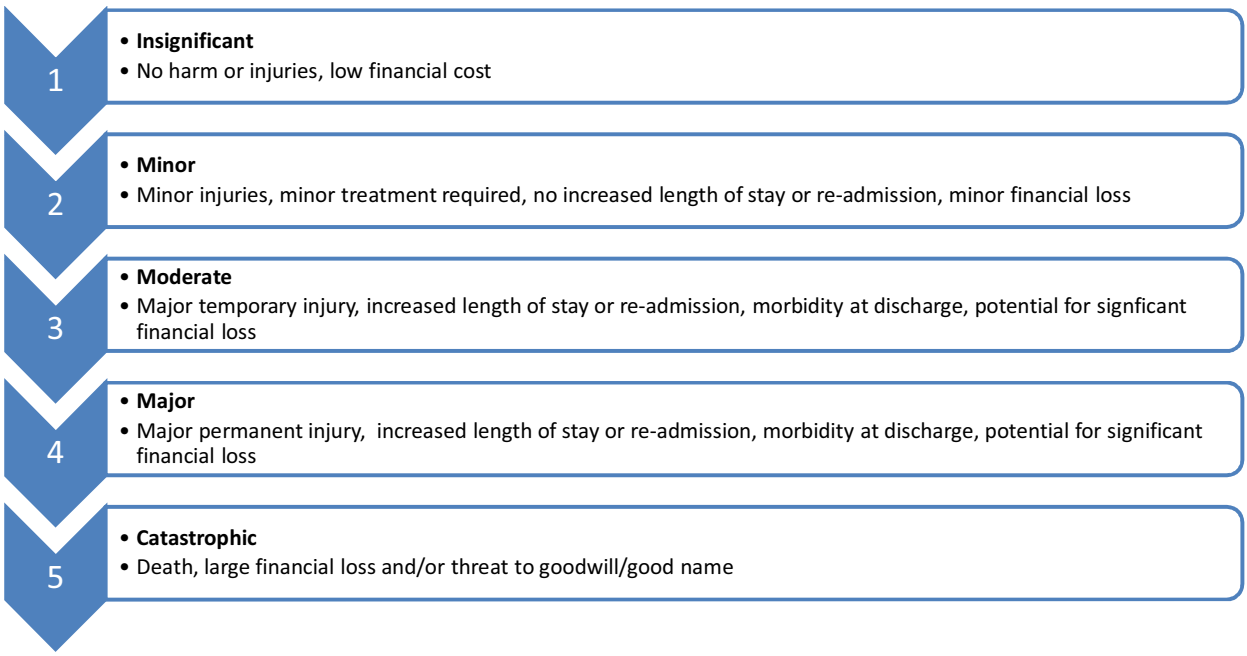

Figure 1 Error severity assessment scale from 1 (insignificant) to 5 (catastrophic). Score based on the assumed consequence or impact if an intervention was not made and probable (not worse case) scenario.[23]

pharmacy and the patient record first accessed in the dispensing system, until the check of the last medication order dispensed was electronically documented.

Sample Size Calculation and Statistical Analysis

The primary outcome measures were prescribing and dispensing error rates. To identify a reduction in prescribing errors from 85%[25] to 25% and dispensing errors from 5%[11] to 1%, based on previous studies undertaken in the study hospital, 429 medication orders were required in each study group. Both calculations were based on two-sided tests using continuity corrected χ^2 tests with $\alpha = 0.05$ and $\beta = 0.1$, with the larger sample size required for identifying dispensing error reduction used. Further participants were added to ensure all clinic types and weekdays were represented. Statistical analyses were performed using Stata software version 11 (StataCorp, College Station, TX, USA). Comparisons between groups (before *vs* after) were made using Student's *t*-tests or Wilcoxin rank-sum tests as appropriate for continuous and ordinal variables and χ^2 tests for categorical variables. Count data were analysed using Poisson regression and 95% confidence intervals (CI) were calculated for between group differences. A two-sided p-value <0.05 indicated statistical significance.

RESULTS

Patient and prescriber characteristics, and numbers of medication orders prescribed and medicines dispensed were well matched with no significant differences between the two groups (Table 1).

Prescribing and Dispensing Errors

Prescribing and dispensing errors are summarised in Tables 2 and 3, with error categories detailed in Table 4. Prescribing error rates decreased from 2.98 per patient

Table 1 Overview of medication orders prescribed and medicines dispensed, patient and prescriber characteristics and patient waiting times

	Before (handwritten)	After (electronic)	p-value
Patients, medication orders prescribed and medicines dispensed			
Total number of patients	379	375	–
Total number of medication orders prescribed	654	635	–
Median number of medication orders prescribed per patient (1st and 3rd IQR)	1 (1–2)	1 (1–2)	0.924[a]
Total number of medicines dispensed	636	600	–
Median number of medicines dispensed per patient (1st and 3rd IQR)	1 (1–2)	1 (1–2)	0.586[a]
Patient and prescriber characteristics			
Mean patient age (standard deviation)	42.7 (21.7)	41.5 (24.4)	0.48[b]
Patient female gender	188/379 (49.1%)	188/375 (50.1%)	0.884[c]
Clinic type			
Medicine	193/379 (50.9%)	178/375 (47.5%)	0.342[c]
Emergency	99/379 (26%)	104/375 (27.7%)	0.618[c]
Paediatrics	43/379 (11%)	46/375 (12%)	0.695[c]
Obstetrics and gynaecology	26/379 (6.8%)	22/375 (5.9%)	0.576[c]
Surgery	18/379 (4.7%)	25/375 (6.7%)	0.256[c]
Prescriber registration status			
Specialist	197/379 (52.0%)	180/375 (48.0%)	0.275[c]
General	165/379 (43.5%)	167/375 (44.5%)	0.783[c]
Provisional (intern)	13/379 (3.4%)	21/375 (5.6%)	0.151[c]
Limited	4/379 (1%)	7/375 (2%)	0.353[c]
Patient waiting time for prescription dispensing			
Number of patients waiting[d]	309/379 (81.5%)	308/375 (82.1%)	0.83[c]
Median waiting time for prescription dispensing (mins) (1st and 3rd IQR)	27 (16–43)	13 (7–23)	<0.0001[a]

IQR = interquartile range.
[a]Wilcoxon rank-sum.
[b]Student's t-test.
[c]χ^2 test.
[d]Patients waiting for their prescription to be dispensed and who had all medication orders on the prescription dispensed included only. Time taken for steps that occurred before the prescription was presented to pharmacy for dispensing and after the final check of the last medication order dispensed on the prescription was excluded.

Table 2 Prescribing error overview

	Before (handwritten)	After (electronic)	p-value
Prescribing errors			
Total number of prescribing errors	1128	74	–
Number of procedural prescribing errors	1096/1128 (97.16%)	57/74 (77%)	–
Number of clinical prescribing errors	32/1128 (2.8%)	17/74 (23%)	–
Median number of prescribing errors per patient (1st and 3rd IQR)	2 (2–4)	0 (0–0)	<0.0001[a]
Total prescribing error rate per patient	2.98	0.20	<0.0001[b]
Procedural prescribing error rate per patient	2.89	0.15	<0.0001[b]
Clinical prescribing error rate per patient	0.084	0.045	0.04[b]
Total prescribing error rate per medication order	1.72	0.12	<0.0001[b]
Procedural prescribing error rate per medication order	1.68	0.090	<0.0001[b]
Clinical prescribing error rate per medication order	0.049	0.027	0.04[b]
Patients with *at least 1* prescribing error (*excluding* patients with only error being allergy/ADR status incorrect/omitted/incomplete)	344/379 (90.8%)	43/375 (11.5%)	<0.0001[c]
Total patients with *at least 1* prescribing error (*including* patients with only error being allergy/ADR status incorrect/omitted/incomplete)	360/379 (95.0%)	51/375 (13.6%)	<0.0001[c]
Patients with *at least 1* procedural prescribing error	356/379 (93.9%)	49/375 (13.1%)	<0.0001[c]
Communication of patient or prescriber information	211/379 (55.7%)	11/375 (2.9%)	<0.0001[c]
Communication of prescribing decision or prescription writing	333/379 (87.9%)	36/375 (9.6%)	<0.0001[c]
Formulary or PBS adherence	29/379 (7.7%)	6/375 (1.6%)	<0.0001[c]
Patients with *at least 1* clinical prescribing error	28/379 (7.4%)	15/375 (4.0%)	0.045[c]
Mean severity score of clinical prescribing errors	2	2	–

ADR = adverse drug reaction; IQR = interquartile range; PBS = Pharmaceutical Benefits Scheme.
[a]Wilcoxon rank-sum.
[b]Poisson regression.
[c]χ^2 test.

and 1.72 per medication order in the before group compared with 0.2 per patient and 0.12 per medication order in the after group, representing falls of 93.2% per patient and 93% per medication order. Patients with at least one prescribing error decreased significantly from 95% to 13.6%, with an absolute reduction of 81.4% (95% CI 77.3–85.5%). Patients with at least one procedural or clinical prescribing error both decreased significantly with absolute reductions of 80.8% (95%CI 76.7–85%) and 3.4% (95%CI 0.1–6.7%) respectively.

Dispensing error rates decreased from 1.27 to 0.027 per patient and 0.76 to 0.017 per medicine dispensed in the before and after groups, representing falls of 97.9% and 97.8%, respectively. Patients with at least one dispensing error decreased significantly from 63.3% to 2.1%, with an absolute reduction of 61.2% (95%CI 56.1–66.3%). Patients with at least one procedural or clinical dispensing error both decreased significantly with absolute reductions of 61% (95% CI 55.9–66%) and 2% (95% CI 0.7–3.6%), respectively.

Overall, 50 system-related prescribing errors were identified in the after group; the underlying mechanism of the majority (60%) involved new tasks introduced by the e-prescribing system (Figure 2). No additional prescribing or dispensing errors for the study patients were recorded in the hospital's incident management system during and for 1 month after the study periods.

Error Severity Assessment

The mean severity score of the clinical prescribing and dispensing errors in each group was 2 = minor with no difference in clinical prescribing error severity; clinical dispensing error severity comparisons were not made as none were identified in the after group. Three moderate severity prescribing errors occurred in the before group: efavarinz prescribed 400 mg orally daily instead of 600 mg; omeprazole and simvastatin medicines interaction potentially leading to increased simvastatin levels and rhabdomyolysis risk; and zoledronic acid prescribed 4 mg intravenously (IV) monthly in a patient with renal impairment (creatinine clearance = 11 mL/min) and therefore dose modification to 3 mg IV monthly required (the dispensing pharmacist's failure to intervene on this error resulted in the one moderate severity dispensing error in the before group). There were two moderate severity prescribing errors in the after group: cyclosporin prescribed 50 mg orally twice daily instead of 75 mg orally twice daily and darunavir 400 mg × 2 prescribed orally daily as

Table 3 Dispensing error overview

	Before (handwritten)	After (electronic)	p-value
Dispensing errors			
Total number of dispensing errors	483	10	–
Number of procedural dispensing errors	476/483 (98.6%)	10/10 (100%)	–
Number of clinical dispensing errors	7/483 (1.4%)	0	–
Median number of dispensing errors per patient (1st and 3rd IQR)	1 (0–2)	0 (0–0)	<0.0001[a]
Total dispensing error rate per patient	1.27	0.027	<0.0001[b]
Procedural dispensing error rate per patient	1.26	0.027	<0.0001[b]
Clinical dispensing error rate per patient	0.018	0	<0.01[b]
Total dispensing error rate per medication dispensed	0.76	0.017	<0.0001[b]
Procedural dispensing error rate per medication dispensed	0.75	0.017	<0.0001[b]
Clinical dispensing error rate per medication dispensed	0.01	0	<0.01[b]
Patients with *at least 1* dispensing error (*excluding* patients with only error being allergy/ADR status incorrect/omitted/incomplete)	199/379 (52.5%)	2/375 (0.5%)	<0.0001[c]
Total patients with *at least 1* dispensing error (*including* patients with only error being allergy/ADR status incorrect/omitted/incomplete)	240/379 (63.3%)	8/375 (2.1%)	<0.0001[c]
Patients with *at least 1* procedural dispensing error	239/379 (63.1%)	8/375 (2.1%)	<0.0001[c]
Communication of patient or prescriber information	125/379 (33.0%)	7/375 (2%)	<0.0001[c]
Communication of prescribing decision/prescription writing error correction not annotated	169/379 (44.6%)	0	<0.0001[c]
Formulary or PBS adherence error correction not annotated	12/379 (3.2%)	0	0.0005[c]
Clinical prescribing error correction not annotated (dispensed correctly)	11/379 (2.9%)	0	0.0009[c]
Data entry on dispensing system	15/379 (4.0%)	1/375 (0.3%)	0.0004[c]
Patients with at least 1 clinical dispensing error	7/379 (2%)	0	0.008[c]
Mean severity score of clinical dispensing errors	2	-	-

ADR = adverse drug reaction; IQR = interquartile range; PBS = Pharmaceutical Benefits Scheme.
[a]Wilcoxon rank-sum.
[b]Poisson regression.
[c]χ^2 test.

required instead of regularly. The dispensing pharmacist intervened on both of these errors.

Patient Waiting Time for Prescription Dispensing

Patients in the after group had a significant reduction in the median waiting time for the prescription to be dispensed by pharmacy by 52% (14 min) (Table 1).

DISCUSSION

The implementation of e-prescribing significantly reduced the proportion of patients with at least one prescribing error by 86%, from 95% to 13.6%, compared with handwritten prescribing. This was higher than the 55% reduction in one US outpatient study.[17] Compared with studies in inpatient settings, the prescribing error rate falls of 93% for errors per patient and errors per medication order were higher than the 47% reduction in a UK study,[14] and 58% and 66% reductions in an Australian study,[15] although falls were consistent with the 84% reduction in Bate's landmark US study.[12] However, there are limitations in comparing these studies as the setting, error definitions, prescriber cohort, medicines prescribed and denominators (medication orders, patient admissions and 1000 patient days, respectively) vary.

Consistent with other studies,[13–15] the majority of prescribing errors were procedural (97.2% before and 77% after) with use of error-prone terminology (43.4%; 490/1128) and incomplete orders (28.9%; 326/1128) the most common in the before group. Although inconsistently included in other studies, procedural prescribing errors were considered an important patient safety risk, particularly those involving communication of patient information or prescribing decisions. Other procedural prescribing errors had financial implications or impacted dispensing efficiency. This study demonstrated a significant reduction in clinical prescribing errors, although this just reached significance. Of note is that not all clinical prescribing errors were prevented by decision-support and the e-prescribing system introduced new errors, some of which were clinical.

Table 4 Comparison of prescribing and dispensing errors by error category and type. Includes system-related prescribing errors (n = 50) which occurred in the after-study group

Error	Error category	Before (handwritten)	After (electronic)	p-value (χ^2 test)
Prescribing				
Procedural				
Communication of patient or prescriber information error	Patient name omitted from prescription/copies	7/379 (2%)	0	0.008
n = number of patients (before = 379; after = 375)	Additional patient identifiers omitted (unit record number/date of birth)	5/379 (1%)	0	0.025
	Allergy/ADR status incorrect/ omitted/incomplete	195/379 (51.5%)	9/375 (2%)[a]	<0.0001
	Weight incorrect/omitted when required	13/379 (3.4%)	1/375 (0.3%)	0.0013
	Prescriber signature omitted	2/379 (0.5%)	1/375 (0.3%)	0.57
	Prescription date incorrect/omitted	3/379 (0.8%)	0	0.084
Communication of prescribing decision or prescription writing errors	Medicine name misspelt/abbreviated	5/654 (0.8%)	0	0.026
	Illegible writing	2/654 (0.3%)	0	0.16
n = number of medication orders (before = 654; after = 635)	Ambiguous order	2/654 (0.3%)	1/635 (0.2%)[a]	0.58
	At least 1 error-prone terminology, abbreviation or symbol on medication order[b]	240/654 (36.7%)	0	<0.0001
	Dose calculation of liquid form omitted when required	6/654 (0.9%)	16/635 (2.5%)[a]	0.026
	Non-compliance with legislation	1/654 (0.2%)	21/635 (3.3%)[a]	<0.0001
	Incomplete order (at least 1 of strength, dose, form, route, frequency or quantity omitted from medication order)[c]	186/654 (28.4%)	2/635 (0.3%)	<0.0001
Formulary or PBS adherence errors	Non-adherence to formulary	1/654 (0.2%)	4/635 (0.6%)	0.17
n = number of medication orders (before = 654; after = 635)	PBS documentation omitted/ incorrect/suboptimal	38/654 (5.8%)	2/635 (0.3%)	<0.0001
Clinical				
Clinical decision making	Unintended medicine interaction	1/654 (0.2%)	0	0.32
n = number of medication orders (before = 654; after = 635)	Dose incorrect	12/654 (1.8%)	2/635 (0.3%)	0.009
	Frequency incorrect	2/654 (0.3%)	4/635 (0.6%)	0.39
	Dose/frequency incorrect – clinical condition required dose modification	1/654 (0.2%)	0	0.32
	Strength incorrect	11/654 (1.7%)	2/635 (0.3%)[a]	0.014
	Dosage form incorrect	0	2/635 (0.3%)[a]	0.15
	Route incorrect	1/654 (0.2%)	0	0.32
	Quantity or duration incorrect	4/654 (0.6%)	7/635 (1%)[a]	0.34
Dispensing				
Procedural				
Communication of patient or prescriber information prescribing error not corrected	Allergy/ADR status incorrect/omitted/ incomplete	119/379 (31.4%)	6/375 (1.6%)	<0.0001
n = number of patients (before = 379; after = 375)	Weight incorrect/omitted when required	8/379 (2%)	0	0.005
	Prescriber signature omitted	2/379 (0.5%)	1/375 (0.3%)	0.569
	Prescription date incorrect/omitted	1/379 (0.3%)	0	0.32
Communication of prescribing decision prescribing error not corrected	Medicine name misspelt/abbreviated	4/636 (0.6%)	0	0.045
	Ambiguous order	2/636 (0.3%)	0	0.159
n = number of medicines dispensed (before = 636; after = 600)	Dose calculation of liquid form omitted when required	1/636 (0.2%)	0	0.32
	Incomplete order (at least 1 of strength, dose, form, route, frequency or quantity omitted from medication order)[d]	166/636 (26.1%)	0	<0.0001

Table 4 (*continued*)

Error	Error category	Before (handwritten)	After (electronic)	p-value (χ^2 test)
Formulary or PBS adherence prescribing error not corrected *n* = number of medicines dispensed (before = 636; after = 600)	Non-adherence to formulary PBS documentation omitted/ incorrect/suboptimal	1/636 (0.2%) 16/636 (2.5%)	0 0	0.32 0.001
Clinical prescribing error correction not annotated (dispensed correctly) *n* = number of medicines dispensed (before = 636; after = 600)	Dose incorrect Strength incorrect Route incorrect	5/636 (0.8%) 5/636 (0.8%) 1/636 (0.2%)	0 0 0	0.027 0.027 0.32
Data entry errors *n* = number of medicines dispensed (before = 636; after = 600)	Incorrect prescriber Incorrect prescription date	9/636 (1%) 12/636 (1.8%)	0 3/600 (0.5%)	0.026 0.004
Clinical				
Clinical decision making/label directions incorrect *n* = number of medicines dispensed (before = 636; after = 600)	Directions on dispensed medicine label incorrect Dose/frequency incorrect – clinical condition required dose modification	6/636 (0.9%) 1/636 (0.2%)	0 0	0.014 0.32

ADR = adverse drug reaction; PBS = Pharmaceutical Benefits Scheme.
[a]Prescribing error categories that included system-related prescribing errors. Refer to Figure 2 for further information.
[b]Total of 490 error-prone abbreviations, terminologies or symbols identified in 240 medication orders.
[c]Total of 326 strength, dose, form, route, frequency or quantity data fields omitted in 186 medication orders.
[d]Total of 290 strength, dose, form, route, frequency or quantity data fields omitted and correction not annotated on original prescription in 166 medication orders dispensed.

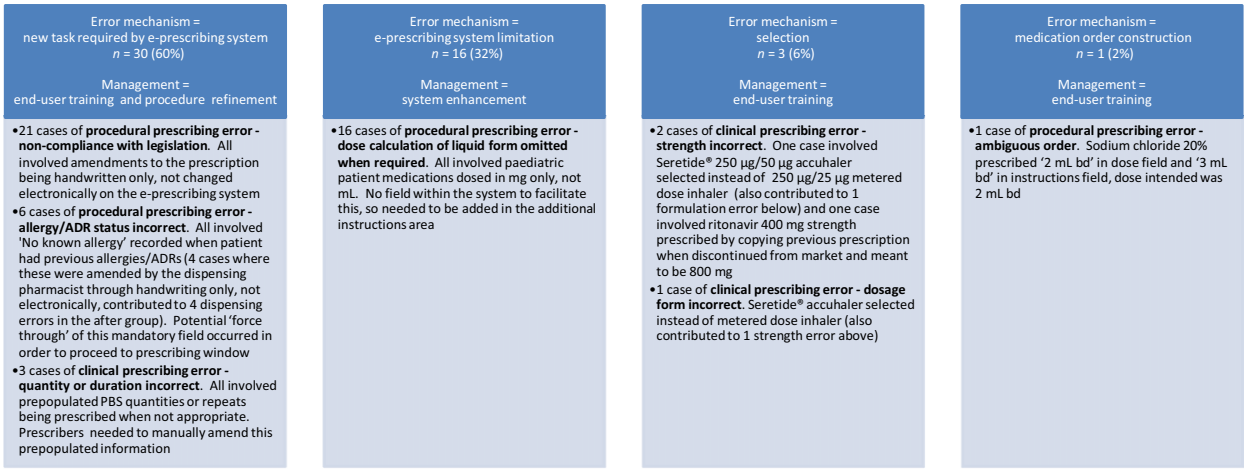

Figure 2 System-related prescribing errors associated with the e-prescribing system including error category, underlying error mechanism[22] and management.

The integration of the e-prescribing and dispensing system resulted in a significant reduction in patients with at least one dispensing error by 97%, from 63.3% to 2.1%. The before total dispensing error rate of 76% of medicines dispensed was higher than other published studies due to the inclusion of procedural dispensing errors; the before clinical dispensing error rate of 1.1% was consistent with other studies.[8–11] As this is the first published study of the impact of an integrated e-prescribing and dispensing system on dispensing errors, these results were unable to be compared.

The majority of dispensing errors were procedural (99% before and 100% after), with the failure of the dispensing pharmacist to annotate incomplete orders (60.0%; 290/483) and communicate allergy/ADR status (24.6%; 119/483) the most common in the before group.

Critically, all clinical dispensing errors were eliminated in the after group, predominantly by reducing incorrect labelling of directions. However, it cannot be generalised that all clinical dispensing errors will be eliminated through the integrated system. This study indicated dispensing errors resulting from incorrect data entry, including directions, prescriber and prescription date, may be reduced. Other errors including incorrect entry of patient or medicines were hypothesised to be reduced due to the functionality of the integrated system, but these benefits were unable to be demonstrated as these errors were not identified in this study.

This study identified 50 system-related prescribing errors, which accounted for 68% of prescribing errors in the after group. This was higher than the 42% demonstrated in an Australian inpatient study.[15,22] However, 42% of system-related errors in this study involved handwriting amendments on the printed e-prescription instead of amending the prescription electronically and reprinting, which is more applicable in the outpatient clinic/ED and discharge prescription setting. This is contrary to legislation and results in incorrect patient records, thereby increasing patient safety risks when prescribing repeats or making clinical decisions. New tasks introduced by the e-prescribing system accounted for 60% of system-related errors and were managed by end-user training and refining of amendment procedures. Other mechanisms for system-related errors including selection (6%) and medication order construction (2%), some of which have been described previously,[13,15,22] were also managed by end-user training. System enhancements should further reduce system-related errors, including a field to facilitate liquid formulation medicines being prescribed in mg and mL; failure to do so accounted for 32% of system-related errors. Other studies indicated additional system enhancements, including listing the most frequently used option first on drop-down menus or creating prestructured order sentences could also address some errors seen in the after group.[15,22]

The mean severity scores for the clinical prescribing and dispensing errors identified in each group were 2 = minor, with no difference in prescribing error severity scores. These results were consistent with one outpatient study, where the majority of prescribing errors were assessed as causing no harm and there was no difference in severity scores.[17] A mean severity score of moderate and no difference was demonstrated in one UK inpatient study,[13] and one Australian inpatient study demonstrated no significant reduction in serious clinical prescribing error rates.[15] As this study was in the outpatient clinic/ED setting, there may have been less severe prescribing errors due to the prescriber cohort and their expertise in the medicines prescribed. In addition, usually only medicines related to the outpatient clinic/ED attendance were prescribed instead of all medicines the patient was taking; hence errors of omission which may be considered severe were not a factor in this study.

Patient waiting time for prescription dispensing is a performance measure used by many organisations, with standard practice being to measure this waiting time from the time the prescription was first presented to pharmacy. Although other steps occurred before and after the time stamps for prescription dispensing used in this study, the time taken to complete these was considered comparable, as workflows involving these steps were similar in both groups. This is the first study investigating the impact of an integrated prescribing and dispensing system on patient waiting times for prescription dispensing, with a significant reduction in median waiting times by 52% demonstrated. Reasons for this outcome included: the e-prescription was more legible and complete; fewer prescribing errors needed to be resolved by the dispensing pharmacist; and improved prescription dispensing efficiency as accurate patient, prescriber, prescription and medication order information were autopopulated in the dispensing system, resulting in reduced data entry requirements and amendments.

A limitation of this study was the reliance on the principal investigator to retrospectively identify prescribing and dispensing errors through handwritten or printed prescription, e-prescribing system and dispensing system review. To ensure reliability of error detection, the principal investigator identified all errors using standard error assessment checklists and reviewed the hospital's incident management system. However, some dispensing errors can only be detected through direct observation, including the physical quantity dispensed and handing medicines to the wrong patient. These errors could have been missed; however, as errors were identified through the same method in both groups, any errors potentially missed should have been similar.

With the exception of changes to working practices directly introduced by the intervention and the availability of e-prescribing pharmacist support, there were no changes in staffing, workload, workflow or quality improvement processes between the before and after study that may have influenced the observed effects of this study. There were differences in prescribing and dispensing training programs; however, these differences were directly related to systems use, rather than competency-based or clinical training, therefore their impact as a confounding variable would be minimal.

This study was undertaken with one version of a homegrown e-prescribing system in one hospital;

generalisability to other settings and systems is unknown. There are limitations in evaluating a system that experienced a staged implementation over 16 months, as the time between the before and after-study periods was 22 months. This may have resulted in this study being subjected to the inherent limitation of before and after studies which cannot control for the effects of time, particularly as there was no control group. The time between full implementation and the after study was 6 months. This should have been an appropriate 'settling in' period. However, even after this period, software, integration and workflow issues were being identified. These resulted in software and integration enhancements and procedure refinements being required that could have led to the system appearing less effective than it was and subsequently is today.

The integration of the e-prescribing and dispensing system was achievable and workable, and resulted in significant reductions in prescribing and dispensing errors and improved efficiencies in the dispensing process. The majority of errors were procedural rather than clinical; hence the harm avoided may not be directly proportional to the errors reduced. However, both error types were reduced and this system has the potential to enable clinicians to focus on other aspects of medicines use. New errors were introduced, although strategies were available to minimise these and other risks, including ongoing system enhancements and end-user training. This study has provided compelling evidence to other organisations to introduce similar technology in their workplace and reproducible methods for evaluating these systems. However, it is important to emphasise these systems need to be continually monitored and enhanced to ensure their benefits are optimised and disbenefits minimised in order to optimise patient safety and medicines use.

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Supporting information

Additional supporting information may be found in the online version of this article:

Appendix S1. Prescribing error assessment checklist.
Appendix S2. Dispensing error assessment checklist.

Competing interests

None declared.

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Cultural Change and Drug Expenditure

Ian Larmour, Elizabeth Creber

ABSTRACT

Australian hospitals are increasingly being placed under financial constraint and as a result pharmacy department directors are increasingly being required to play a major role in the management of drug expenditure.

This paper describes the strategies and methods used at Monash Medical Centre to promote a culture of efficient utilisation of drug therapy. The strategy involved two main concepts, the development of a framework for change and secondly, the promotion of drug utilisation efficiency. This required the application of a mixture of traditional and innovative concepts. The strategies adopted enabled a satisfactory budget result to be achieved.
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INTRODUCTION

Monash Medical Centre (MMC) is a 747-bed general teaching hospital associated with Monash University. The hospital provides services to patients in all major specialties, including paediatrics and obstetrics.

The medical services are divided into seven Divisions: Medicine, Surgery, Anaesthetics, Obstetrics and Gynaecology, Paediatrics, Psychiatry and Family Medicine.

The Pharmacy Department has a well established clinical pharmacy service to all wards and a computer system to monitor drug expenditure in all wards and departments. An effective stock control system operates and the Department is involved in negotiating competitive contract prices directly with manufacturers and via a major wholesaler. Outpatient services are limited to patients who require complex or multidisciplinary care.

The MMC drug budget for 1992–93 and 1993–94 was set at $5.3 million for drugs not recouped under the Highly Specialised Drugs Program. However, the drug expenditure trend in the first 6 months of 1992–93 indicated that drug expenditure was likely to be $1 million over budget. This paper outlines the approach taken at MMC to deal with this type of situation. It involved the use of both old and new concepts in an attempt to promote drug utilisation efficiency and to influence the organisation's culture with respect to drug costs.

As a result of the initiatives discussed the drug expenditure in 1992–93 remained within the budget limit and was $116 000 below budget in 1993–94.

OVERALL STRATEGY

To deal with this problem the Pharmacy Department, in conjunction with the Therapeutics Committee, developed a multifaceted strategy designed to produce long-term cultural change in the use of medication at MMC.

The Therapeutics Committee was the vehicle used for development, coordination, implementation and management of this strategy, since it was able to cross all Department and Division boundaries.

The aims of the strategy were to:

1. promote rational, cost-effective drug use;
2. minimise wastage;
3. involve medical staff in decision making; and
4. promote joint accountability.

To achieve these aims, four steps were identified and adopted:

1. to create a general awareness of the need to contain drug costs;
2. to create a general awareness of the cost of medication and to educate prescribers on the drug costs they generate. This involved feedback and the use of activities to focus attention on cost efficiency;
3. to develop methods to promote efficient drug utilisation via specific projects and by encouraging autonomous activity by prescribers in the achievement of the hospital's corporate goal of containing drug costs by utilising education, feedback, involvement, accountability, expert opinion and/or review, negotiation and policy;
4. to negotiate the acceptance and successful implementation of the strategy.

The first major concept in the strategy was to introduce changes in the drug formulary processes to provide a framework for the promotion of cost awareness and the efficient use of drugs.

The objectives of the change were to develop a communication, advisory and authority matrix to facilitate the above goals.

Ian Larmour, BPharm, FSHP, MSc
Elizabeth Creber, BPharm, FSHP, Grad Dip Hosp Pharm, Grad Dip Ed Admin
Pharmacy Department
Monash Medical Centre
Clayton, Victoria

Address for correspondence:
Ian Larmour
Director of Pharmaceutical Services
Monash Medical Centre
246 Clayton Road
Clayton Vic. 3168

THERAPEUTICS COMMITTEE

The Therapeutics Committee had a strong formulary policy in place, with limits on the authority to prescribe a number of high-cost drugs. Requests for new drugs had to be made in writing by a senior member of the medical staff with the supporting signature of the relevant Unit Head.

A procedure also existed for dealing with urgent, one-off, non-formulary drug requests between meetings of the Therapeutics Committee. Such requests had to be made in writing and required the supporting signature of the Unit Head. The interim approval was granted by the Secretary (Director of Pharmacy) and Chairman of the Therapeutics Committee.

The following changes in policy and organisation were made:

1. Finance & Drug Utilisation Subcommittee

An expert advisory committee was formed to carry out a detailed review of specific projects. This was necessary because the normal business schedule of the Therapeutics Committee allowed insufficient time for such detailed planning. The membership of this subcommittee included key members of the Therapeutics Committee plus the Director of Financial Services and the Research Officer, Clinical Management Support. Other experts were coopted as required.

2. Applications for New Drugs

The supporting signature of the relevant Division Chairman was made compulsory, in addition to the existing requirements. This was to involve Division Chairmen in the process and to make them aware of cost implications. Divisions were also encouraged to undertake their own peer review of requests before submitting them to the Therapeutics Committee. The Division representatives on the Therapeutics Committee also played a key role in promoting this concept.

Details of cost offsets or cost benefits were requested for new drugs with the potential for a major impact on drug expenditure. This, in effect, was the introduction of a second level of selection criteria for new drugs (Table 1). The aim of this policy was to make applicants more aware of the problems faced by the hospital and, at the same time, opened the door for negotiations on how the new drug could be used in the hospital. Applicants were therefore encouraged to take part in finding a solution to the funding problem. This policy presented two options:

(a) The Therapeutics Committee recognised that the use of some new high cost drugs could achieve savings in other areas of hospital practice.

(b) Changes in other prescribing practices or drug choice could achieve sufficient savings to cover the cost of the new drug.

Table 1. Therapeutics Committee selection criteria for new drugs

Level 1 criteria

- Improved efficacy over drugs already on the hospital's formulary or where an efficacious drug treatment option was not previously available; OR
- Significant reduction in the risk of adverse drug effects or toxicity; OR
- If efficacy and toxicity are equivalent, the new drug should have a lower cost per patient.

Level 2 criteria
(for drugs which have major cost implications)

- Opportunities for cost offsets (changes in drug therapy already used either for this condition or other conditions); OR
- Cost benefits for the hospital in other areas of hospital expenditure.

In other words, the introduction of a new drug could improve the hospital's productivity, for example, by reducing length of stay, theatre costs or other treatment costs. The aim was to have the necessary portion of the global hospital savings (or increased productivity) achieved by the use of the new drug, added to the drug budget. This, in effect, meant the transfer of budget funds within the organisation. The implications of this policy are far reaching. The development of a mechanism to achieve this successfully is still being developed, although some success has been achieved (Table 2). This philosophy has become more relevant with the introduction of casemix funding by the Victorian Government in 1993–94.

Despite the difficulties, this requirement focused the attention of applicants on the need to develop a case based on real and achievable savings. A significant problem with this approach is that many benefits are beyond the hospital's field of operation. This is an important issue but is beyond the scope of this paper.

3. Urgent Drug Requests

In order to encourage peer review and to provide feedback to the Division Chairmen on the cost implications to their Division, it was decided that:

(a) applications for urgent, single-use drug requests must have the supporting signature of the Division Chairman if the cost of the drug treatment was equal to or greater than $100;

(b) every month each Division Chairman was provided with a summary of the costs associated with such requests;

(c) other expert advice could be requested, for example, from a clinical microbiologist, if thought appropriate by the therapeutics committee secretary and chairman.

Table 2. Drug savings due to cost offset agreements

Drug	Unit	Decision	Mechanism
Colfosceril palmitate (Exosurf Neonatal)	NICU*	Cost to be offset from savings in NICU bed days or other savings	Budget offset $48 000
Ondansetron	Medical Oncology	Reduced dosage of folinic acid in 5-fluorouracil protocol. Maximum of 40 patient treatments per month for ondansetron. Also decision to use ondansetron in the acute phase (1–2 days) instead of one week and twice daily dosage instead of three times a day dosage. Cost per treatment $100 instead of $460	Maximum $40 000 to be covered by reduced expenditure on folinic acid
Dinoprostone vaginal gel (Prostin E)	Obstetrics and Gynaecology Division	Routine use of lignocaine instead of prilocaine (saving $10 000 per annum) Saving of $7000 due to prostaglandin F2 alpha no longer being used. Use limited to consultants according to agreed protocol	Budget, maximum $17 000 per annum, offset by saving on the use of local anaesthetics and replacement of prostaglandin F2 alpha

* Neonatal Intensive Care Unit

4. Protocols with Drug Cost Implications

The Therapeutics Committee adopted the policy of requesting Divisions to advise the Therapeutics Committee of changes in drug use protocols where the change had major drug cost implications. The objective was to have these cost implications reviewed in the same manner as for new drug applications.

DUPLEX BUDGETING

Due to the need to manage, monitor and review drug expenditure on a hospital wide basis, it was felt that the overall drug budget should remain centralised under the control of the Pharmacy Department and the Therapeutics Committee. On the other hand, it was felt the various Divisions and Units needed to be aware of the costs they generated in comparison with their budget targets.

From these two needs grew the concept of duplex budgeting. This is basically a process of joint management of drug expenditure and utilises a central budget and a series of decentralised sub-budgets.

However, due to the limitations of the computer system available and because of the way in which beds were distributed to Units and Divisions, it was not possible to generate totally accurate data. Therefore methods had to be developed to produce indicative budget and expenditure data.

The duplex budgeting concept was adopted at two levels: Division sub-budgets and High Drug Cost sub-budgets.

1. Division Sub-Budgets

A cost model was developed which enabled indicative expenditure to be tracked on a Divisional basis. Some wards and clinics clearly belonged to one Division, whereas others did not. In the latter case, a proportion of the costs for the relevant Division was calculated from sample analysis of drug usage and bed/patient allocation. From this model it was possible to develop indicative Division budgets (a proportion or sub-budget of the total drug budget) against which expenditure could be monitored. This also enabled each Division to be allocated an expenditure savings target.

The Director of Pharmacy Services met with each Division Chairman on a routine basis to provide feedback on Division costs and to discuss specific projects aimed at containing drug costs or improving drug utilisation efficiency.

2. Sub-Budgets for High Cost Drugs

Independently of these Division sub-budgets, a separate series of more specific (targeted) sub-budgets were developed.

Due to the difficulties of producing indicative budgets and expenditure reports for all Units, it was decided to concentrate on specific areas of high drug cost. This sub-budget strategy was developed for eight areas and they were of two types:

- High cost wards i.e. those wards with high drug utilisation and cost. The data were generated via the pharmacy computer system and covered the Intensive Care Unit and the Neonatal Intensive Care Unit (NICU).
- Drug group based i.e. drug expenditure groups that could be clearly identified by pharmacological category or specific use and where a designated person could be identified as having a major influence on the use of these drugs.

The drug expenditure groups were:
— Anaesthetic drugs
— Antibiotics
— Cyclosporin for immunological diseases
— Gastroenterology drugs

— Medical Oncology drugs
  — cytotoxics
  — filgrastim
  — interferon
—Nephrology drugs
  — cyclosporin
  — erythropoietin
  — monoclonal antibodies
  — dialysis fluids.

For each of these sub-budgets a coordinator or 'facilitator' was chosen. Facilitators were chosen because of their expertise and knowledge of the relevant area. All were Unit Heads and their role in the hospital gave them at least partial control of the specified area of expenditure. They were thus able to influence others in the use of these drugs.

The facilitators were not held personally responsible for all the expenditure in the relevant sub-budget, but obviously a degree of joint accountability existed. Their help was enlisted to find and encourage ways of reducing drug expenditure by improving the efficient utilisation of drugs within available resources.

Each month the facilitator was provided with a report on current year-to-date expenditure and an estimate of the potential overrun in expenditure. This concept was initially discussed with each facilitator by the Chairman and Secretary of the Therapeutics Committee. Subsequent regular meetings were held between the facilitator and the Director or a Deputy Director of Pharmacy Services.

PROMOTION OF EFFICIENT DRUG UTILISATION

The second major concept in the strategy was a multifaceted program to promote efficient drug utilisation.

This involved:

1. target selection and the negotiation of agreement between key players; and
2. the development and implementation of policies to promote efficient drug utilisation.

1. Target Selection

(a) New Drug Applications

New drug applications were reviewed according to Level 1 and 2 criteria, (Table 1). In the case of the high cost drugs, the Finance and Drug Utilisation Subcommittee and the Pharmacy Department administration analysed the implications of using these drugs and negotiated with Unit Heads or established a working party of relevant experts.

The agreements reached were monitored by data analysis and drug utilisation surveys.

For some very high cost drugs, e.g. long-term use of octreotide, each patient request was reviewed and approved by the Therapeutics Committee.

(b) Drugs Already on the Formulary

Target areas for reduced drug expenditure were:

- high cost wards;
- specific high cost drugs;
- high cost drug groups; and
- high cost procedures.

In some cases additional information (e.g. indications and dosage regimens) on the use of these drugs was obtained via drug utilisation surveys conducted by the ward pharmacists and by more detailed data analysis.

Each of these targets was then presented to the Finance and Drug Utilisation Subcommittee for review. When necessary, information-seeking discussions were held with key personnel prior to the matter being passed on, but in most cases the Therapeutics Committee approved the policy in principle prior to these discussions (Table 3).

Table 3. Key personnel involved in expenditure reduction targets

Key personnel	Agent
Division Chairman	Therapeutics Committee Division representative Secretary, Therapeutics Committee (Director of Pharmacy)
Sub-budget facilitators	Director or Deputy Director of Pharmacy
Unit Heads	Secretary, Therapeutics Committee (Director of Pharmacy)
Working parties of key prescribers (normally consisting of Unit Heads)	Chairman, Therapeutics Committee Secretary, Therapeutics Committee Therapeutics Committee Division representative when appropriate

Depending on the issue, the key parties involved all or some of these personnel so as to develop an interactive group of stakeholders.

The types of decisions that were negotiated are outlined below. The agreement reached was monitored by a computer report analysis and drug utilisation surveys.

These drug utilisation surveys not only concentrated on high cost drugs but also inappropriate practices (e.g. inappropriate hypnotic use).

2. Policies Used to Promote Efficient Drug Utilisation

Once a target area was identified, a number of inter-related policies were developed and employed, with often more than one of these options being used for the one target area:

(a) Alternative Options

The development of practical alternative prescribing options, suggested by expert opinion and with the

negotiated acceptance of key personnel. This was applied to:

- Drug Choice

This included drugs that were cheaper but offered equivalent clinical efficacy and safety (Table 4).

Table 4. Examples of practical, alternative drug choice options

Target drug	Alternative drug(s)	Indication
Cefoxitin injection	Ticarcillin sodium & potassium clavulanate (Timentin) **or** Ampicillin, metronidazole and gentamicin	Antibiotic prophylaxis in gastrointestinal surgery
Cefoxitin injection	Cephazolin and metronidazole	Antibiotic prophylaxis in caesarean birth
Vancomycin capsules	Metronidazole (oral)	First line therapy in the treatment of *Clostridium difficile* infection
Omeprazole capsules	Cimetidine or ranitidine	Duodenal ulcer
Ranitidine injection	Sucralfate (tablet or suspension)	Prophylaxis for stress ulceration in ICU when oral medication is not contraindicated
Amoxycillin injection	Ampicillin injection	Normal indications
Cephalothin injection	Cephazolin injection	Normal indications
Lactulose mixture	Sorbitol mixture	Constipation

- Dosage Regimen

This covered drugs where the dose, frequency of dosage or the duration of therapy could be adjusted without compromising patient care. For example, metronidazole twice daily rather than three times a day and cephazolin three times a day rather than four times a day in appropriate patients.

- Procedures and Practices

This covered a range of practices, not all of which had major cost implications, but which were nevertheless thought to be inappropriate or wasteful and where practical alternatives could be employed without compromising patient care. For example, the practice of using polygeline (Haemaccel) solution to administer insulin was strongly discouraged. The policy was developed in conjunction with the Head of the Diabetic Unit.

(b) Practice Guidelines

At MMC several prescribing guidelines have been produced for drugs known to cause difficulties, e.g. phenytoin, warfarin and heparin.

The *Heparin Guidelines* included the concept of standard strength intravenous heparin infusions, where the dosage was adjusted by changes in the infusion rate. This avoided the wastage of partly used heparin infusion solutions when doses were changed.

(c) Patient Selection Criteria

In order to encourage the most efficient use of high cost drugs, considerable effort was spent in negotiating patient selection criteria. Drugs included in this approach were high cost antibiotics, omeprazole and muromonab-CD3.

(d) Delegation of Authority

Greater emphasis was placed on patient selection criteria, dosage regimens and the setting of budgets for specific drugs.

The following methods were used.

- Authorised Expert and Patient Selection Criteria

This involved the negotiation of patient selection criteria with authorisation being delegated to a specific expert, for example:

sumatriptan — Head of Neurology

omeprazole — inpatient prescriptions had to be reviewed by a senior gastroenterologist or the gastroenterology registrar within 24 hours.

- Authorised Expert, Patient Selection Criteria and Set Budget for the drug

The patient criteria in these cases were generally negotiated with a group of experts and members of the Therapeutics Committee, with one member of the group being delegated the task of reviewing and approving individual patient requests.

This process was used for filgrastim and interferon, where the application had to be countersigned by the Director of Medical Oncology on the condition that expenditure would be within the set budget.

- Authorised Expert Teams

On occasions, specific expert groups were set up and encouraged to take a leading role in the management of particular areas of therapy. These teams also had a major educational role. The following expert teams were involved:

— Adult Total Parenteral & Enteral Nutrition Team

This group (consisting of medical staff, dietitians, and pharmacists) had the role of reviewing and monitoring all patients receiving parenteral nutrition and enteral nutrition. This included a limited number of home patients, where a separate sub-budget was used.

— Infectious Diseases Team

Following negotiation with the Division representatives on the Therapeutics Committee, an

additional review role was developed for a small list of high cost antibiotics.

The process required the prescribers to fill out an authorisation form and to record that they had obtained the approval (including an approval number) from one of the hospital's clinical microbiologists. The authorisation form listed the normal indications, as per hospital policy, for these antibiotics.

— Pain Control Team

This team operated along similar lines to that of the Infectious Diseases Team.

Apart from difficult cases, the team also monitored the use of epidural infusions and ketorolac. In the case of ketorolac, patients were converted from injectable ketorolac to oral naproxen as soon as the patient was able to take food (usually 1–2 days).

(e) Sub-Budget Facilitator

Negotiations and regular reviews took place between the facilitator, the Therapeutics Committee and administrative pharmacy staff.

Drug expenditure in 1992–93 was significantly decreased in all but one (Nephrology) of the designated sub-budgets, with an average decrease of 26% (range: 8–40%). A decrease was not achieved in the Nephrology sub-budget due to a higher than expected number of renal transplants being carried out by the Unit. However, further expenditure growth in this particular sub-budget was contained.

(f) Cost Offsets/Cost Benefit Negotiations

A number of agreements were made via this process (Table 2). However, these negotiations were often difficult due to the lack of reliable data. Furthermore, in some cases the benefits of using a new expensive drug were often accrued by the general community rather than the hospital.

Nevertheless, decisions were often reached and, if nothing else, the process enabled the parties to focus on actual rather than hypothetical benefits. On some occasions, negotiations resulted in pilot studies to clarify or evaluate the benefits of a new drug, e.g. urokinase in the treatment of peripheral vascular occlusion. The study found that only one-third of patients had a satisfactory result. This led to a further study using a revised dosage protocol.

(g) Education

A key element in the strategy was to raise awareness of the cost of drug therapy and to encourage the efficient utilisation of drugs. The education process involved the following methods:

- Printed material such as the pharmacy bulletin, technical memorandums and pharmacy newsheets. The use of published and local prescribing guidelines was also encouraged.
- A campaign which encouraged the early transfer of patients from intravenous to oral antibiotic therapy was also used.
- The role and involvement of key personnel in the strategy has been outlined above.
- The clinical pharmacists working in the wards were fundamental to the implementation of policy and assisted in the education of prescribers on efficient drug utilisation issues.

DISCUSSION

Cultural change is always a difficult task and it involves a number of key elements.[1] It is a continuing process where the outcome of various strategies are difficult to measure due to the complex, multifaceted nature of therapeutics.

The establishment of a framework to promote the awareness of drug cost, to enable the involvement of key prescribers and to develop the concept of joint accountability were thought to be key elements to developing cultural change. In particular the use of duplex budgeting proved to be very successful and this concept may well have application for other hospital clinical service departments.

Education remains a cornerstone to any strategy aimed at promoting efficient drug utilisation. The key elements are the role played by key medical experts, specialist multidisciplinary teams and clinical pharmacists.

The concept that is of most interest for all parties is that of global hospital benefit. This involves the transfer of a sufficient portion of the savings made in other areas into the drug budget. However, encouraging Divisions or Units to give up hard won budgets is not an easy process. Therefore, it may well be that a separate drug budget reserve pool of funds should be set aside so that these funds can then be allocated by the Therapeutics Committee as thought appropriate. This approach may well be practical given the likely impact of casemix budgeting, where, perhaps for the first time, there is a genuine economic incentive to increase patient throughput.

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Introduction of Pharmaceutical Benefits Scheme Reforms at Three Victorian Public Health Services

Ian Larmour, William (Bill) A Thomson, Michael K Tsui, Greg R Weeks

INTRODUCTION

The introduction of Pharmaceutical Benefits Scheme (PBS) reforms in public hospitals has two major objectives:

- To improve the continuum of care for patients moving from hospital to the community; and
- To provide equity of access for public hospital patients to the range of Commonwealth subsidised chemotherapy drugs available in private hospitals.

Victoria expressed an early interest in these reforms and the Geelong Hospital and the Royal Children's Hospital implemented outpatient PBS pilots during 1994/5. However, finalising the agreement between the Commonwealth and Victoria through a variation to the Australian Health Care Agreement was a long and tedious process, that concluded at the end of 2001.

Under the reforms, Pharmaceutical and Repatriation Benefit Scheme items as listed in the Schedule, can be accessed for outpatient/discharge drugs. Chemotherapy drugs are accessed for daypatients from an agreed list under the Highly Specialised Drugs Program (Section 100). The reforms also require hospitals to implement the Australian Pharmaceutical Advisory Council (APAC) 'National guidelines to achieve the continuum of quality use of medicines between hospital and community'.[1] Various APAC milestones are to be achieved over a 36-month period from the date a hospital commences the PBS reforms.

In the first year of the reform (2001/2) the Commonwealth made available $41.5 million for outpatient and discharge drugs provided under the PBS and $17.25 million for chemotherapy drugs. Each hospital is allocated a budget, with growth based on usage and the three-year moving average of PBS growth. Chemotherapy growth this year is limited to fifteen per cent. There is an automatic Commonwealth/State review if expenditure exceeds twenty-five per cent of the allocated budget. Under a risk-sharing provision in the agreement, the Commonwealth and State will share the cost 50:50 above the agreed threshold. The State would then recoup the amount from the hospital exceeding its budget. Refinement and reallocation of budgets is an ongoing process and to date Victoria has not exceeded its threshold.

To assist hospitals implement the reforms, the Victorian Department of Human Services (DHS) provided a one-off grant based on hospital activity levels. The grant was provided to improve the pharmacy department's information technology infrastructure and cover other PBS-related implementation costs.

In late 2000, the Pharmaceutical Reform Implementation Working Group (PRIWG) was established by the DHS. This group included representatives from the Pharmaceutical Benefits Branch of the Commonwealth Department of Health, the Health Insurance Commission (HIC), Veterans Affairs, the DHS, and hospitals with an interest in undertaking the reforms. Many issues were considered and debated, including processes for chemotherapy prescribing and claiming, formatting of the new hospital prescription, electronic prescribing, evaluation of the reform, prescriber numbers, training, implementation support, and standard approaches to charging PBS/non-PBS items.

Planning proceeded throughout 2001, and in the first quarter of 2002 three metropolitan health services in Victoria (Barwon Health, Bayside Health, Southern Health) commenced implementation of the reforms. A number of other hospitals followed later in 2002. It is anticipated that during 2003 most of the remaining Victorian public hospitals will follow.

This article is based on the experience gained by the authors during introduction of PBS reforms at Barwon Health, Bayside Health and Southern Health in Victoria. It describes the key issues that need to be considered by hospitals planning the introduction of these reforms.

PLANNING

Implementation of the PBS reforms is one of the most significant workplace changes for public hospital pharmacy and careful and detailed planning is critical for its successful introduction.

Stakeholder Groups

Some of the key groups that need to be involved at an early stage in discussions are the hospital executive; senior medical, pharmacy, nursing and finance personnel; the Drug and Therapeutics Committee; and the Medical Advisory Committee. In particular, enlisting support from the hospital executive is critical. Other groups to consider are those involved with patient admission and discharge planning. The early involvement of pharmacy staff is essential—some staff will have experience with the PBS and this is a valuable resource to utilise.

Business Case

The hospital executive may require the development of a business case to analyse the risks and benefits of introducing the PBS reforms. When developing the business case, it is critical to undertake a complete evaluation of additional resources required. In particular, special note should be made of the approaches for introduction of the seven principles contained in the APAC Guidelines.

Ian Larmour, BPharm, MSc, FSHP, Director of Pharmacy, Southern Health, Clayton, Victoria, **William (Bill) A Thomson**, BPharm, MSc, Director of Pharmacy, Austin and Repatriation Medical Centre (currently Executive Officer, Victorian Drug Usage Advisory Committee, Parkville, Victoria), **Michael K Tsui**, BPharm, BBus, Grad Dip Comp, FSHP, Acting Director of Pharmacy, Bayside Health, Prahran, Victoria, **Greg R Weeks**, MPharm, MHA, FSHP, Director of Pharmacy, Barwon Health, Geelong, Victoria
Address for correspondence: Greg Weeks, Director of Pharmacy, Barwon Health, Geelong Vic. 3220, Australia
E-mail: greg@barwonhealth.org.au

State Implementation Committee

As more hospitals undertook the reforms, the wider PRIWG was replaced by the Pharmaceutical Reform Users Group (PRUG). The PRUG is a forum for pharmacists to share information and progress issues through the DHS.

Hospital Implementation Committees

It is recommended that a hospital implementation committee be established, with representatives from public relations, finance (including patient accounts), patient admissions, medical staff (including junior medical staff), nursing, pharmacy and special interest groups such as social work. All campuses in the health service should have at least one representative.

A pharmacy implementation committee should also be established, with subcommittees to deal with specific tasks and issues. This group should include pharmacists from each grade, and pharmacy technicians.

IMPLEMENTATION

Pharmacy Coordinator

In most hospitals, a pharmacist has been appointed to coordinate the implementation of the PBS reforms. Alternatively, a team may be involved, with each member having a specific role and tasks. In general, the pharmacy coordinator position has been funded from implementation money provided by the DHS.

Additional Staffing

Our experience has been that additional pharmacy staff are required, including extra staff for meeting the APAC Guidelines. In general, extra staff have been funded by surplus created through introduction of the reforms. Consideration should also be given to the impact on medical and finance staff.

PBS Approval Number

Each hospital campus requires a separate PBS approval number under Section 94 of the *National Health Act 1953*. Application forms are available from the HIC.

Stationery

Dispensing Labels

Once the PBS approval number has been granted, five-part dispensing labels which list the approval number will need to be ordered from the HIC. A preexisting approval number will be revoked and a limited time is allowed by the HIC for the use of existing labels.

Prescription/Repeat Forms

A standard PBS prescription developed by the Implementation Working Group was chosen to replace existing outpatient and discharge prescription forms.

Prescription forms can be ordered from the HIC printers, allowing some weeks for these to be printed with the hospital-specific approval number. If electronic prescribing is to occur, the blank prescription forms with header should be ordered. Repeat stationery should be ordered at the same time.

The medication record used for inpatient prescribing should be modified, with an extra column for the recording of 'Supply? Yes/No'. During the counselling process ward pharmacists determine whether patients have an adequate supply of their own medication or require an item to be dispensed on discharge.

Security of Prescriptions

Prescription forms should be issued from the pharmacy department and stock kept in a secure location on the ward. Designated ward staff should be nominated to order the prescription forms and maintain ward security. It is too difficult to track the exact numbers of individual prescriptions issued, although the advent of prescriptions in books will assist the process.

Prescriber Numbers

The doctors' individual prescriber number must be recorded on all PBS prescriptions. Privacy restrictions prevent the HIC giving out information on prescriber numbers. Start early to collect prescriber numbers for all medical staff who will be prescribing drugs at the hospital, and enter these numbers into the pharmacy software system. A questionnaire can be used to collect this information.

Medicare and Concession/Safety Net Card Details

All patient admission points at the hospital need to be identified and staff in those areas trained to collect Medicare card numbers (including the 11th digit) and Concession/Safety Net Card numbers, including expiry dates. There are several types of Veteran Affairs cards and it is important to distinguish between them since the level of cover varies. Admission forms used in the peri-operative setting or sent to private rooms may have to be reprinted to allow for the collection of Medicare and Concession/Safety Net Card numbers. Hospitals will also need to consider how to collect data from Emergency admissions. Good systems for collection of these details at all admission points are vital for successful implementation of the reforms.

Computing

Hardware

A review of hardware requirements should be carried out. Additional dispensing terminals and thermal printers for labels will probably be required. Laser printers will be required for printing invoices and medication profiles, with separate laser printers required for repeat forms.

Software

Victorian hospitals have experience with implementing the PBS reforms using both Merlin and STOCCA pharmacy software systems. It is recommended that local software is adequately tested for it's suitability to manage PBS requirements. Points to consider are:

- The use of a test account for the PBS dispensing module for staff training and familiarisation purposes;
- The use of financial software for managing PBS debtors and how this will link with the pharmacy and finance software. There are many options depending on the hospitals financial system and the pharmacy department's requirements. One option is Merlin's debtors module linked to a point of sale system. Debt can be managed within this system from patient accounts or pharmacy, with periodic data extraction to the finance department for debt management; and
- Is there provision on the patient admission software to record Medicare and Concession/Safety Net Card details (with expiry dates)? Does the pharmacy system interface with the admission system so that this information can be sent to the pharmacy system? It is vital that the system has this capability.

Computerised Prescribing

Access to a computerised prescribing module as part of electronic discharge summaries will greatly facilitate PBS prescribing for doctors.

Staff Training

Forums and programs need to be provided for nursing and medical staff, staff working in patient accounts and patient admissions, pharmacists, and pharmacy technicians. A strategy that has worked successfully to train nurses and doctors is for ward pharmacists to develop educational packages for their specialist area; for example, the use of PBS in paediatrics. Ward pharmacists can also play a key educational role by assisting medical staff in the writing of PBS discharge prescriptions.

Training of medical staff can be organised through the HIC—on-site training is provided at the hospital for groups of 20 or more medical staff. For smaller groups, staff must attend a training session in the city before their prescriber number will be issued. At the hospital training session a pharmacist should be present to provide practical examples and orientate the session to hospital experience. Overseas doctors must take visa information and temporary registration details from the Medical Board to these training sessions. In Victoria, interns now receive their HIC training at the time of medical registration and prior to commencing their intern year at the hospital. This has avoided delays in obtaining prescriber numbers.

Public Relations

A range of public relations strategies have been used in Victoria; for example, hospital brochures advising of the reforms, local media articles or advertisements, contacting regularly readmitted patients by letter, and letters and brochures to general practitioners and community pharmacists. Community pharmacists need to be familiar with the hospital prescriptions and know that they can dispense them. The local branch of the Pharmacy Guild is another avenue for communication. The DHS have a number of useful poster resources specifically developed for hospitals.

An important strategy is for the Director of Pharmacy or PBS Pharmacy Coordinator to speak briefly to each medical specialty group in the outpatient clinic to outline the changes under the PBS reforms, show the new prescription form and answer questions. Problems that may not have been anticipated can be identified using this approach.

PBS Claim

Data Collection

Ensure there is a robust system for accurate data collection at the point of patient admission to meet the requirements of the HIC claim. Ensure that medical staff understand which prescription details need to be provided to ensure compliance with the PBS. Hospital pharmacists may clarify quantities if these are incorrect or not specified on the discharge or outpatient prescription; that is, specify quantity, endorse 'PBS pack size', initial and write 'BPharm'.

Processing the Claim

To facilitate the processing of PBS claims in pharmacy it is necessary to set up a system for sorting prescriptions and verifying prescription fields. This should be done each day. It is best to allocate an office area with computer and printer for claims processing.

Reporting

PBS claim and financial activity reports were developed with software vendors during the implementation phase. Any profit on the claim is the difference between the Commonwealth's reimbursed amount (11.1% mark-up on the ex-manufacturer's price less the patient contribution) less the drug cost, plus patient contribution. Items for general patients are charged at the same rate as community pharmacy, up to $23.10 (safety net items). An example of a useful summary report for printing with each claim is shown in Table 1.

Table 1. PBS claim and financial activity summary report

	No. scripts	Pt contribution	PBS rebate	Total	Base price	Gross profit
General PBS						
Entitlement						
Repatriation						
Safety Net						
PBS Totals						
Non PBS, Non S100, Outpatient			Nil			
Non PBS, Non S100, Discharge			Nil			
S100						
Grand Total						

PBS = Pharmaecutical Benefits Scheme
S100 = Section 100 of the Pharmaecutical Benefits Scheme

Commencement Date

A realistic commencement date should be set. Implementation can either be phased or there can be simultaneous introduction in all areas. Hospitals in Victoria have a cross-section of experience and can be contacted for their opinion.

POLICY DECISIONS

Review of Discharge Prescriptions

It is recommended that hospitals develop a firm policy to ensure that ward pharmacists review and sign off all discharge prescriptions (in-hours) prior to dispensing and discharge of the patient from hospital. Nursing and medical staff must be aware that medication safety issues can arise if prescriptions leave the hospital without pharmacy review. There is also a financial penalty as the higher reimbursement the HIC pays to community pharmacists is charged back against the hospital's budget. Community dispensing is an option for periods where pharmacy departments are suffering severe staff shortages.

After-Hours Policy

For after-hours discharges or daypatients undergoing evening procedures, the hospital may opt for these prescriptions to be taken by the patient to a community pharmacy. Emergency departments may also write after-hours prescriptions to be dispensed in the community rather than using after-hours stock. Alternatively, hospitals may wish to continue their existing after-hours cupboard arrangements.

Issuing Repeats

Hospitals will need to make a decision whether to issue repeats for discharge and outpatient prescriptions. Repeats may be required for patients returning to the hospital, such as mental health and oncology daypatients. Other special situations may also arise; for example, if a specialist has obtained an authority and the patient lives in a distant location, it may be considered reasonable to issue repeats. It may also be considered reasonable to issue repeats on antibiotic courses. To date, the allocation of costs of prescriptions dispensed in the community has not adversely affected hospital budget allocations. Some hospitals provide a repeat prescription service for outpatients.

Brands

Victorian hospitals that have implemented the reforms have continued with their generic prescribing policy and usually only stock one brand of a particular drug. To assist this process, the hospital prescription does not include the tick box option for 'Brand substitution not permitted'. Within Victoria, the brands of high-use items are determined through the collective buy tender and drugs without brand price premiums are favoured where possible.

Hospitals may choose to remove items from their formulary which demand a brand price premium to minimise the cost impact to patients. Hospitals may also choose not to impose the brand price premium; however, the patient will be disadvantaged if the prescription is continued in the community.

Non-Formulary PBS Items

Hospitals will need to have a policy for the availability of items which are listed on the PBS but are not on the hospital's formulary. These decisions should continue to be made by the Drug and Therapeutics Committee.

Patient Co-Payment

A carefully considered policy should be developed in relation to patients who are unable to pay the co-payment, including procedures for handling exemptions, such as for mental health patients. This will need to be decided between pharmacy, finance and the hospital executive. It should be clear that nonpayment of the patient co-payment would not prevent supply of drugs. Simple information sheets can greatly assist the patient's understanding of these charges.

Invoicing for Discharge Prescriptions

Pharmacy needs to work with the finance department to establish policies and systems for invoicing patients for discharge medications. Invoices can be printed automatically and given to the patient when a discharge prescription is dispensed. Issues to consider are:

- Where will discharge patients pay their invoice?
- Will collection sites be open for late discharges?
- How are account enquiries managed? One option is to establish an Account Hotline.
- What is the process for sending invoice reminders? These may be sent at 14 days or at other appropriate time intervals. You may decide not to follow-up amounts below $3.70.
- Will you charge account-keeping fees for overdue accounts?
- When a discharge patient does not provide their concession card prior to the PBS claim being finalised, the pharmacy is required to collect the general fee from the patient and issue a receipt for the patient to claim from Medicare. However, Medicare will not refund the dispensing fee or the Pharmacy Guild surcharges that hospitals apply to items between $3.70 and $23.10. This 'refund deficiency' has been the source of several complaints. Hospitals will need to consider a strategy for managing these situations—on occasions the pharmacy department has decided to refund the difference.

CONCLUSION

While there are many considerations and day-to-day issues in the early phases of implementing the PBS reforms in public hospitals, these can be managed with careful planning and resource allocation. The critical issue of effective systems to capture patient data remains a priority. Fears of hospitals exceeding their budget and entering a cost sharing arrangement have not arisen in the first two years. The Commonwealth budget allocation, Section 100 arrangements and the PBS growth formula will protect hospitals for the foreseeable future.

Our experiences to date have been positive for the following reasons:

1. Patients receive an adequate supply of medication on leaving hospital. There is more careful planning of their discharge needs, more judicious use of patients own medication, and improved consultation with community providers.

2. There is greater access to chemotherapy drugs for daypatients at public hospitals. Hospitals who have not previously been cost-shifting chemotherapy drugs have received significant financial benefits.

3. The profile of the pharmacy department has been raised through implementation of the reforms and as a result of ongoing liaison with hospital staff and the significant revenue streams attached to the PBS reforms.

4. Implementation of the APAC guidelines over time in at-risk patients is a laudable pursuit.

We await more formal evaluations of the impact of the PBS reforms on stakeholders when the Commonwealth/Victorian Government Consultancy is completed later this year and individual hospitals present research data.

Competing interests: None declared

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A therapeutic equivalence program: evidence-based promotion of more efficient use of medicines

Ian Larmour, Silvana Pignataro, Kerryn L Barned, Stav Mantas and Melvyn G Korman

ABSTRACT

Objective: The development of an effective therapeutic equivalence program (TEP) through the collaborative support of medical staff, using the principles of disinvestment.

Design and setting: A TEP was introduced at Southern Health, a metropolitan health service in Melbourne, in the 2006–07 financial year. Therapeutic classes were selected for the TEP by stakeholder consensus, and a preferred medication for each class was selected on the basis of cost considerations and therapeutic equivalence. New patients were commenced on preferred medicines, but patients receiving another medicine from a therapeutic class included in the program were not automatically switched to the preferred medicine. For the first 4 years of the program, prescribing patterns were monitored, and savings achieved (due to lower prices for and increased use of preferred medicines) were calculated on a monthly basis.

Main outcome measures: Prescribing trends for preferred medicines, as a measure of acceptance of the TEP, and savings produced by the program.

Results: Over the 4-year study period, 11 therapeutic classes were targeted. The use of all preferred medicines increased once they become part of the TEP and a total of $3.16 million was saved. The annual savings increased each year, and the rate of increase was six times that of the increase in patient separations.

Conclusions: The TEP at Southern Health resulted in significant savings. It showed that, by using a collaborative and evidence-based approach, the principles of disinvestment can be applied to use of medicines.

MJA 2011; 194: 631–634

The growing cost of health care presents a major challenge to governments all over the world, with one of the most complex components being the management of medication costs. This issue is no easier to handle at the hospital or hospital network level.

Southern Health (SH) is a large metropolitan health service in Melbourne's south-east; it includes five public hospitals, one private hospital, one day surgery centre, a number of community health centres and an extensive network of ambulatory care services.

In 2006, SH implemented a financial enhancement plan, in which expenditure on medicines was an area of focus. A number of successful strategies to contain medication costs and reduce wastage were already in place (including projects to promote the quality use of medicines). In addition, the introduction of the Pharmaceutical Benefits Scheme (PBS) to Victorian public hospitals in 2002 had led to the resolution of many equity-of-access anomalies and enabled reimbursement of most prescription medicine costs for outpatients, discharged patients and day oncology patients. Furthermore, generic prescribing and dispensing had been in place for several decades, as had local and state-based negotiation of special prices for a range of medicines. Thus there were no areas of medication expenditure that could be targeted for easy savings. Moreover, there was desire to avoid arbitrary authoritarian controls on medication expenditure which lacked clinician "buy in".

The concept of therapeutic equivalence is not new and has been used to promote efficient drug use,[1-4] but formal and effective application of the concept is not as common as might be expected. When it has been used to reduce drug costs, it has sometimes been associated with mandatory drug substitution.[3] An alternative strategy to encourage the use of cheaper therapeutically equivalent medicines has been to reimburse patients for only the cost of the cheapest alternative.[2-4] Nevertheless, therapeutic equivalence offered a sound strategy for potentially saving significant medication costs at SH.

We aimed to develop an effective therapeutic equivalence program (TEP) at SH through voluntary collaboration and collective support of medical staff, especially senior medical staff. We also aimed to use the principles of disinvestment to ensure limited resources were put to their most effective use. Key elements of the program are outlined in Box 1.

METHODS

The TEP was introduced at SH in the 2006–07 financial year, and we report findings to the 2009–10 financial year. It was approved by the Southern Health Therapeutics Committee and the Southern Health Medical Executive Committee. Representatives from these committees formed the High Cost Drugs Working Party, to provide support and guidance for the TEP. In addition, a project pharmacist was appointed to facilitate constant promotion of the concept to key stakeholders, with the position being funded from the savings achieved.

Choosing therapeutic classes and preferred medicines

Potential therapeutic classes to target were selected by:

- identifying therapeutic classes of medicines that are associated with significant costs and that act via clearly defined pharmacological targets;
- engaging directly with key clinical stakeholders (the medical head of unit and key specialists) to evaluate the acceptability of each potential therapeutic class for the TEP;

1 Key elements of the therapeutic equivalence program

- Medicines in the program need to be clinically equivalent in terms of safety and efficacy
- There should be no compromise to patient care
- The recognised objective is to maximise potential savings
- The therapeutic equivalence concept is separate from any arbitrary cost containment measures
- Money saved can be used to pay for expensive medicines which might not otherwise be available, or to minimise the need to place tight restrictions on the use of expensive medications ◆

- investigating the suitability of potential therapeutic classes for the TEP, based on published evidence; and
- undertaking a preliminary financial impact assessment.

The key selection criteria for target therapeutic classes were: multiple therapeutically equivalent medicines in the class; key clinical stakeholder support; evidence to support therapeutic equivalence available and accepted by medical heads of unit who frequently prescribe the medicines and key specialists in that area of practice; and the potential to obtain a lower price, if this had not previously been negotiated.

When a therapeutic class was accepted into the program, the costs of medicines in the class were compared. Pharmaceutical companies were invited to submit an expression of interest in becoming the preferred medicine supplier for the therapeutic class at SH. This enabled price negotiations to be conducted. To ensure transparency in choosing the preferred medicine, the lowest therapeutic equivalent daily treatment cost was the dominant selection criterion. This process commenced with three therapeutic classes, and other classes were added every few months from 2006–07 onward. The preferred medicines that were chosen are not listed in this article due to commercial-in-confidence obligations.

The designated preferred medicine from a therapeutically equivalent group was then to be used when patients commenced therapy with a medicine from that group. Patients already taking another medicine from a therapeutically equivalent group were not automatically or mandatorily switched to the preferred medicine. However, if such a change was clinically appropriate, this could occur. It was also expected that prescribers would have a sound reason for any instances of not following the TEP guidelines.

The medicines in each therapeutic class could change as market dynamics changed. Changes in the status of individual medicines and the inclusion of new target therapeutic classes were subject to continued total agreement from the key stakeholders.

Promoting the TEP

The strategies used to promote the TEP to prescribers included: posters in clinical areas; presentations and distribution of leaflets at grand rounds, unit meetings and medical intern tutorials; one-to-one or group meetings with key stakeholders and "academic detailing";[5] letters and memoranda to medical staff; and free promotional pens, on which "Think Therapeutic Equivalence" was printed. In addition, clinical pharmacists played an educational support role to reinforce the therapeutic equivalence concept.

2 Therapeutic classes targeted

- Angiotensin-II receptor antagonists
- Angiotensin-converting enzyme inhibitors
- Oral proton-pump inhibitors
- Injectable lincosamides
- Penicillins
- 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors
- Immunosuppressants
- 5-HT_3 antagonist antiemetics
- Bisphosphonates
- Glycoprotein IIb/IIIa inhibitors
- Atypical antipsychotics ◆

Calculating the savings

A spreadsheet was developed to calculate savings generated by the TEP on a monthly and cumulative basis. When a lower price was negotiated because of the preferred medicine process, the cost difference between the preferred medicine and the appropriate comparative medicine was multiplied by the total number of preferred medicine units used at SH over the relevant period. Data entered in the spreadsheet were based on the purchasing and issuing data in the Pharmacy Department computer system.

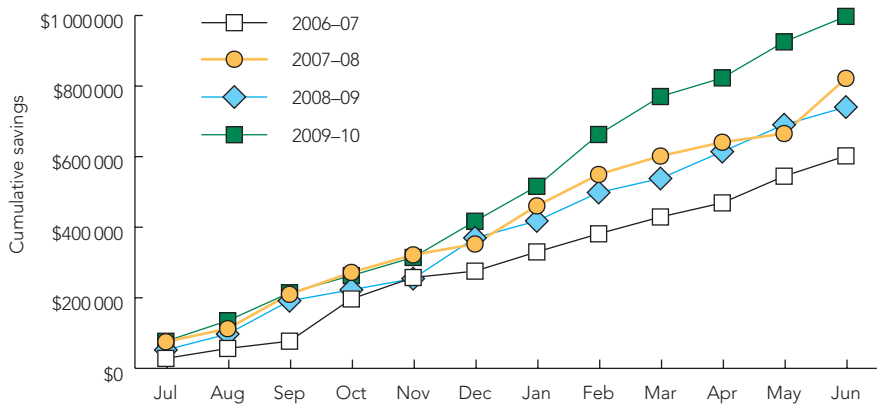
RESULTS

During the study period, 11 therapeutic classes were targeted (Box 2). A total of $3.16 million was saved as a result of the program, representing an average saving of $790 477 per annum (range, $602 207 to $997 418). The annual savings increased over the 4-year period (Box 3), as additional preferred medicines were included in the program. Between 2006–07 and 2009–10, TEP savings increased by 65.6%, whereas patient separations increased by 10.4% (162 720 separations in 2006–07, 179 633 separations in 2009–10).

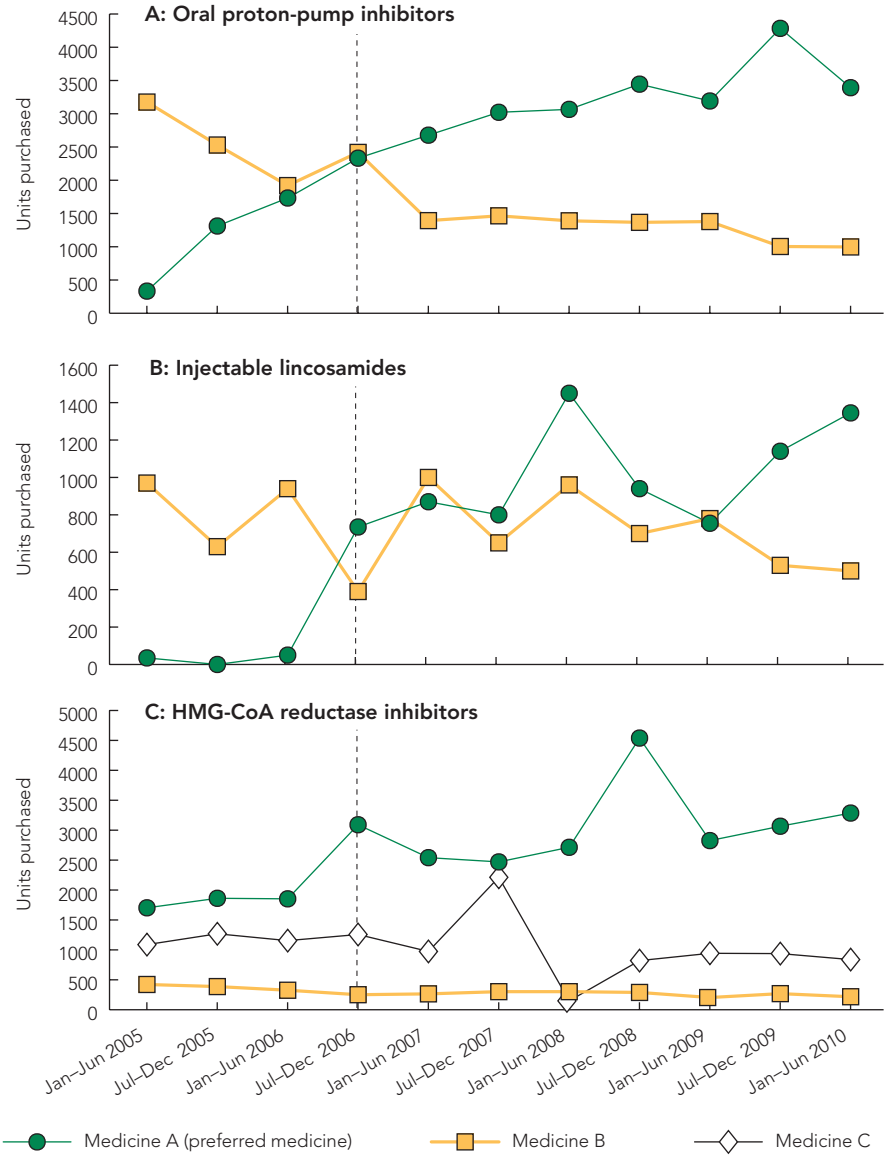
The costs incurred were the salary for the project pharmacist and expenditure on promotional materials. The net savings enabled the Southern Health Therapeutics Committee to support an increased number of single-patient requests for compassionate use of medicines. Over the study period, the High Cost Drug Working Party, the Southern Health Therapeutics Committee and the Adverse Drug Reactions Subcommittee received no complaints or adverse drug reaction reports relating to the effect of the TEP on patient care.

The use of all designated preferred medicines increased after their addition to the TEP, which indicated the support of medical staff for the program. However, the pattern of use varied according to how frequently the medicine was commenced in hospital and the extent of the background use of therapeutically equivalent medicines, especially for medicines that are widely used in the community. For oral proton-pump inhibitors, a clear growth in the use of the preferred medicine was seen because proton-pump inhibitors were frequently commenced in hospital (Box 4, A). However, significant background use of the alternative medicine continued because many patients were admitted to hospital on that medicine. For injectable lincosamides (which are largely used for inpatients), there

3 Cumulative savings produced by the therapeutic equivalence program, by financial year



4 Use of proton-pump inhibitors, lincosamides and HMG-CoA reductase inhibitors at Southern Health*



HMG-CoA = 3-hydroxy-3-methylglutaryl-coenzyme A. * Dashed lines denote introduction of preferred medicine to therapeutic equivalence program. ◆

was also a substantial rise in the use of the preferred medicine (Box 4, B). In this case, background use of the alternative medicine was largely due to use in paediatric patients, which was excluded from the TEP. For 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors, there was background use of two alternative medicines owing to their common use in the community. Nevertheless, there was a steady increase in the use of the preferred medicine (Box 4, C) because HMG-CoA reductase inhibitors were frequently commenced in hospital.

DISCUSSION

Between 2006–07 and 2009–10, preferred medicines from 11 therapeutic classes were introduced to the TEP at SH. Savings of $3.16 million were achieved during this period, and the annual savings increased each year. Increased prescribing of the preferred medicines indicated that the program was well accepted by medical staff. As the TEP did not dictate automatic switching to preferred medicines, a background of existing medicine use persisted, especially for patients who were admitted to hospital already on non-preferred medicines.

The funding of pharmaceuticals in Victorian public hospitals is a complex process. In 2009–10, SH spent $59.74 million on pharmaceuticals, of which 79.6% was recovered through the PBS, the Highly Specialised Drugs program and patient copayments. Inpatient and specialised medicine use are the major components of the remaining expenditure. The savings achieved by the TEP at SH in 2009–10 were equivalent to 1.7% of the total expenditure on pharmaceuticals and 8.2% of net expenditure on pharmaceuticals.

Although patient throughput (eg, patient separations) has a strong relationship with expenditure on medicines for inpatients, there was no such correlation between patient throughput and TEP savings in our study. While patient throughput would have had some influence on medicine expenditure, the savings achieved were largely dependent on the numbers and types of medicines included in the TEP.

Several factors are likely to affect the success of a TEP. First, the market dynamics for pharmaceuticals are constantly changing. Therefore ongoing vigilance is required to ensure that preferred medicines selected for a TEP remain the most economical options, and long-term price agreements should be closely monitored and maintained. Second, identification of new target therapeutic classes should be an ongoing process. Third, continuous marketing and promotion of the TEP concept, ideally through ongoing employment of a TEP project pharmacist, is essential, as is support from senior medical staff and clinical pharmacists.

At SH, it was important for medical staff to see the benefits of saving money in concrete terms, as reflected in the decisions made by the Southern Health Therapeutics Committee — for example, their support for compassionate use of rituximab for Wegener's granulomatosis, relapsing thrombotic thrombocytopenic purpura and antiphospholipid syndrome. However, the strongest motivation, irrespective of whether drug budgets are centralised or decentralised, may be the desire to maximise the benefits of limited resources. A key incentive for prescribers to support the TEP at SH was that it enabled savings to be achieved with no disadvantage to their patients. This enabled a less rigid system for the control of expenditure on expensive medicines and helped to facilitate easier access to medicines that might not otherwise be available.

An unexpected finding was the popularity of the TEP among junior medical staff. Promoting use of a narrow range of medicines enabled junior staff to gain a greater degree of expertise with the doses of the preferred medicines; hence this may have improved medication safety due to a lower risk of prescribing errors.

One issue that can be frustrating in a TEP is that there is often a lack of comparative data between the various medicines in a therapeutic class. Given the high expenditure on the PBS, it might be beneficial to invest in Phase 4 comparative clinical drug trials. The success of the TEP at SH indicates that such an investment could enable significant cost offsets to be achieved.

A TEP can be considered to be a genuine disinvestment process, in which resources are diverted to their most productive use. Disinvestment is a subject of increasing interest, and discussion on how this concept should be moved forward in the Australian health care setting has begun.[6] The achievements at SH indicate that therapeutic equivalence is one model of disinvestment that can succeed. However, the concept of therapeutic equivalence is a special subset of disinvestment, because it does not deal with obsolete medicine. Nevertheless it does illustrate that the process can be applied to drug therapy.

The TEP at SH has demonstrated that positive input and support from medical staff, in a collaborative environment, can lead to significant savings. These savings will continue as long as the strategy is maintained. It is hoped that the success of the TEP at SH will encourage others to pursue the same benefits.

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COMPETING INTERESTS

None identified.

AUTHOR DETAILS

Ian Larmour, BPharm, FSHP, MSc, Director, Pharmacy Department
Silvana Pignataro, BPharm(Hons), Clinical Pharmacist
Kerryn L Barned, BPharm(Hons), Clinical Pharmacist
Stav Mantas, BPharm(Hons), Clinical Pharmacist
Melvyn G Korman, MB BS, PhD, FRACP, Emeritus Director, Gastrointestinal and Liver Unit
Southern Health, Melbourne, VIC.
Correspondence:
ian.larmour@southernhealth.org.au

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Therapeutic equivalence program: continued economic benefits in the context of rising costs and increased demand

Tom Chynoweth[1,2] BPharm(Hons), GradCertPharmPrac, MBA, MSHP, Pharmacy Formulary and Business Development Manager

Ian Larmour[1] BPharm, FSHP, MSc, Emeritus Director of Pharmacy

[1]Monash Medical Centre, Monash Health, 246 Clayton Road, Clayton, Vic. 3168, Australia.
Email: ian.larmour@monash.edu

[2]Corresponding author. Email: tom.chynoweth@monashhealth.org

Abstract

Objective. The aim of this study was to describe the effect of a therapeutic equivalence program (TEP) in achieving financial sustainability from 2010–11 to 2014–15.

Methods. A TEP was introduced at Monash Health in 2006–07. Therapeutic medicine classes for inclusion were selected by stakeholder consensus and a preferred medicine for each class was chosen based upon therapeutic equivalence and cost considerations. New patients were commenced on a preferred medicine, but patients already prescribed another medicine from the same therapeutic class were not automatically switched to the preferred medicine. Data was obtained retrospectively from the pharmacy dispensing system, including the purchasing and issuing of all medicines from the preferred medicine classes. The prescribing patterns for preferred and comparator medicines were used as a measure of acceptance of the TEP, along with the savings produced by the program.

Results. Over the 5-year evaluation period, 18 therapeutic classes were targeted, including seven new classes. Six therapeutic classes from the 11 included in the TEP before 2010–11 were removed throughout the evaluation period when the comparative economic benefits were no longer present. The use of all preferred medicines increased following implementation and a total of AU$7.38 million was saved from 2010–11 to 2014–15 and AU$10.54 million across 2006–07 to 2014–15.

Conclusions. This paper provides an update on the progress of the TEP at Monash Health and outlines additional learnings gained. The market dynamics for pharmaceuticals means ongoing maintenance and review of the therapeutic medicine classes targeted is important to enable continued economic benefits.

What is known about the topic? There is continued and increasing focus on efficient, cost-effective and financially sustainable medication management. There is limited information available on strategies that can be implemented at a health service level.
What does this paper add? The TEP has resulted in sustained savings. The market dynamics for pharmaceuticals means ongoing maintenance and review of the therapeutic classes targeted is important to enable continued economic benefits.
What are the implications for practitioners? TEP is a process of genuine disinvestment. Identification and resolution of critical factors in the success of the program may assist implementation at other health services.

Additional keywords: health policy, health services management, hospitals, pharmaceuticals.

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Introduction

There is continued and increasing focus on efficient, cost-effective and financially sustainable medication management at an organisational, professional and government level. This focus has led the Monash Health (MH) Pharmacy Department to explore a diverse range of opportunities for improving efficient medication management.

MH is Victoria's largest metropolitan health service, located in Melbourne's south-east and including five public hospitals, one day surgery centre, one private hospital and an extensive network of ambulatory care services, community health centres and residential aged care facilities. MH was previously called Southern Health until 2012.

A therapeutic equivalence program (TEP) was introduced at MH in the 2006–07 financial year to improve the cost-effective use of medicines,[1] and this paper reports on the continuation of this work. Although the concept of therapeutic equivalence is not new in the promotion of the efficient use of medications,[1–5]

the implementation and application of the concept has not been common.[6] Generally, when the concept has been used to reduce drug costs, it has been associated with mandatory substitution.[4,7] An alternative strategy that has been used to encourage the use of less expensive therapeutically equivalent medicines, employed as part of the Pharmaceutical Benefits Scheme (PBS) Therapeutic Group Premium pricing structure, has been to only reimburse patients for the cost of the cheaper medicine alternative.[3–5] The approach at MH was to develop an effective TEP through the voluntary collaboration of prescribers and support through extensive stakeholder engagement, especially with senior medical staff.

In this paper we provide an update on the progress of the TEP introduced at MH and outline some of the additional learnings we have obtained from our experience in this area.

Methods

This paper covers the evaluation of the TEP at MH over the financial years from 2010–11 to 2014–15 and builds on the initial evaluation of the TEP from 2006–07 to 2009–10. Potential therapeutic classes were selected by: (1) identifying therapeutic classes of medicines associated with significant costs; (2) engaging with key clinical stakeholders, including head of unit or other key specialists, to evaluate the acceptability of the potential therapeutic class for inclusion in the TEP, based upon safety and efficacy; (3) investigating the suitability of the potential therapeutic class for inclusion in the TEP, based upon published evidence; and (4) undertaking preliminary financial impact assessment of the potential therapeutic class.

When a therapeutic medicine class was selected for inclusion in the program, pharmaceutical companies were invited to submit an expression of interest in becoming the preferred medication for that class at MH. The preferred medicine was selected on the basis of therapeutic equivalence and cost considerations. New patients were recommended to be commenced on a preferred medicine, but patients already prescribed another medicine from the same therapeutic class were not automatically switched to the preferred medicine and with the other medications in the class still being available for prescribing. The PBS Therapeutic Group Premium Policy differs to the TEP in that the TEP is driven by prescribers rather than by patient costs. The PBS does list medicines interchangeable by class, but does not specify a preferred medicine. The medicines in each therapeutic class could change as market dynamics changed. Changes in the preferred medicine status of a therapeutic class were subject to continued agreement from key stakeholders.

Data was obtained retrospectively from the pharmacy dispensing system progressively throughout the evaluation period, including the purchasing and issuing of all medicines from the preferred medicine classes. When a lower price was negotiated through the preferred medicine process, the cost difference between the preferred medicine and the appropriate comparative medicine was multiplied by the total number of preferred medicine units used at MH over the relevant period.

Results

Over the 5-year study period, 18 therapeutic medicine classes were targeted (Table 1), including the introduction of seven new classes. Six therapeutic classes from the 11 included in the TEP before 2010–11 were removed when the comparative economic benefits were no longer present. The key reason for this was due to changes in the market dynamics created by significant generic competition within the class.

Table 1. Therapeutic classes targeted at Monash Health from 2010–11 to 2014–15

Preferred medicine classes	
3-hydroxy-3-methylglutaryl coenzyme A (HMGCoA) reductase inhibitors	Glycoprotein IIb/IIIa inhibitors[A]
5-HT_3 receptor antagonist antiemetics[A]	Immunosuppresants
Angiotensin II receptor antagonists	Lincosamides[A]
Angiotensin-converting enzyme inhibitors[A]	Local anaesthetics[B]
Aperients[B]	Non-steroidal anti-inflammatory drugs[B]
Atypical antipsychotics[A]	Penicillins[A]
Bisphosphonates	Proton pump inhibitors
Dipeptidyl peptidase-4 inhibitors[B]	Topical local anaesthetics[B]
Echinocandins[B]	Volume expanders[B]

[A]Therapeutic classes removed throughout the evaluation period.
[B]Therapeutic classes commenced during the evaluation period.

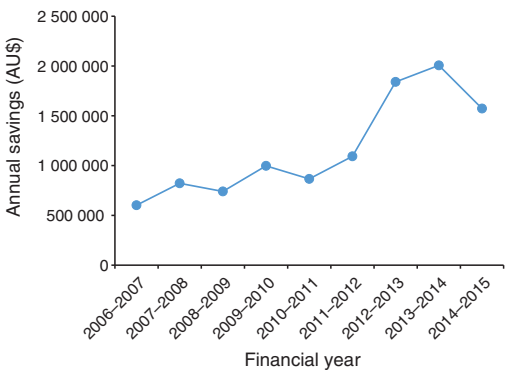

Fig. 1. Annual savings produced by the therapeutic equivalence program, by financial year.

The TEP over the 5-year period from 2010–11 to 2014–15 provided a total of AU$7.38 million in savings to the health service (Fig. 1). Annual savings from the program increased by 81.6% (from AU$865 965 in 2010–11 to AU$1 572 995 in 2014–15), whereas patient separations increased by 23.2% (ranging from 193 824 in 2010–11 to 238 798 in 2014–15) over the evaluation period. A reduction in the annual savings from AU$2 006 172.85 in 2013–14 to $1 572 994.61 in 2014–15 is seen. This reduction was attributed to the removal of several medications from the TEP throughout 2014–15 because comparative economic benefits were no longer present. However, many of the withdrawn medications had significant ongoing saving resulting from the introduction of generic competition within the class, with these savings occurring as a result of tenders conducted on behalf of Victorian public hospitals by Health Purchasing Victoria, but were not considered to be a result of the TEP. The savings achieved by the TEP in 2014–15 were

equivalent to 2.1% of the total expenditure on pharmaceuticals and 9.3% of net expenditure on pharmaceuticals.

The costs incurred were the salary for the TEP pharmacist and expenditure on promotional materials, which are not included in the calculations of annual savings above. With consideration of savings achieved between 2006–07 and 2009–10 of AU$3.16 million across 11 therapeutic medicine classes, the overall savings from the program have reached AU$10.54 million across 2006–07 to 2014–15 (Fig. 1).

Usage increased for nine of the 12 designated preferred medicines continuing throughout the study period, including the seven new preferred medicines added to the TEP. For the remaining three classes, although no increase occurred in the study period, the preferred medicine maintained its higher level of use compared with when the class was implemented and with the other medicines in the class. The patterns of use varied according to the proportion of medication prescribing that is exclusively commenced in a hospital setting, compared with

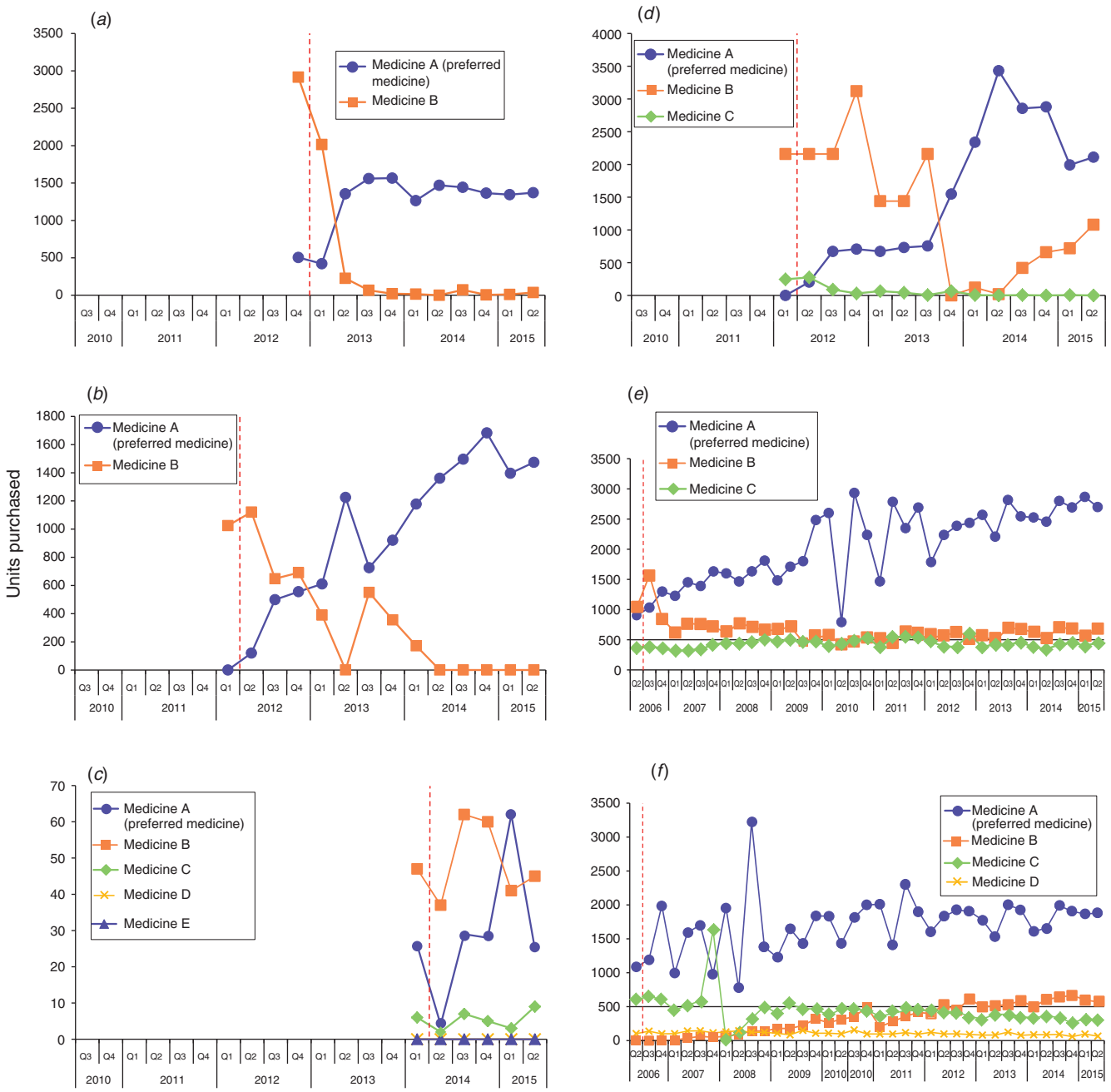

Fig. 2. Use of various medicines at Monash Health over time: (*a*) local anaesthetics, (*b*) aperients, (*c*) dipeptidyl peptidase-4 inhibitors, (*d*) topical local anaesthetics, (*e*) proton pump inhibitors, (*f*) 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors. The dashed line denotes the introduction of a preferred medicine to the therapeutic equivalence program. Q, calendar quarter.

those medicines that could be commenced in either the hospital or the ambulatory care setting. Several examples have been included in this paper to illustrate and discuss the reasons identified for some of the key variations found in use of the preferred medicines. For local anaesthetics, and similarly with echinocandins and volume expanders, where initiation is largely in the hospital in-patient setting, there was a substantial rise in the use of the preferred medicine following its inclusion in the TEP (Fig. 2*a*). In this setting, the use of the comparator local anaesthetic was reduced to inconsequential levels. For aperients implemented as part of the TEP, there was also a substantial rise in the use of the preferred medicine following implementation (Fig. 2*b*). In this case, the peak in use of the comparator medicine in July–September 2013 was associated with a shortage of the preferred medicine, with this continuing to have an effect on comparator medicine use in the following 6 months. For dipeptidyl peptidase (DPP)-4 inhibitors, there was ongoing background use of two alterative medicines owing to common use in the ambulatory care setting. Despite this, there was an increase in the cumulative use of the preferred medicine across the evaluation period (Fig. 2*c*). For topical local anaesthetics, and similarly with non-steroidal anti-inflammatory drugs, there was a rise in the use of the preferred medicine following implementation (Fig. 2*d*). The re-emergence of significant use of the comparator medicine, despite the majority of initiation occurring in the hospital setting, provides an example addressed in later discussion relating to diverse and unknown key stakeholders and influencers affecting preferred medicine use. For proton pump inhibitors, and similarly with angiotensin II receptor antagonists and bisphosphonates, which were implemented before the evaluation period, there was a decrease in the use of the preferred medicine across the evaluation period. Despite this decrease, the use of the preferred medicine was still greater than when the therapeutic class was included in the TEP, and there was still significantly greater use of the preferred medicine than the comparator medicine (Fig. 2*e*). For 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, and similarly with immunosuppressants, which were implemented before the evaluation period, there was an increase in the use of the preferred medicine across the evaluation period (Fig. 2*f*). This demonstrates the potential for ongoing benefit from the implementation of a preferred medicine.

Discussion

The TEP at MH commenced in the 2006–07 financial year and our experience over the subsequent 9 years has enabled a greater insight into the factors that have a significant effect on the effectiveness of the program.

Choice of therapeutic classes

A key component of the TEP is the choice of medications targeted. In our initial range of therapeutic groups, the following factors were considered: (1) the availability of significant evidence to support the concept of clinical equivalence in terms of safety and efficacy; (2) the opportunity for competition between medications in a therapeutic group; and (3) the potential extent of the cost savings to be gained.

Outstanding results were achieved with several of the therapeutic groups that were chosen, whereas in other cases only moderate financial benefit was achieved.

It is also critically important to recognise that market dynamics are in a constant state of change, hence the necessity to closely consider and monitor the effects of changes relating to the targeted therapeutic groups and to adjust the TEP targets and strategy as needed. Consequently, over the years, several of the original TEP-preferred medicines have been changed or removed from the program when the economic benefits were no longer present.

One of the key factors in such decisions is related to the stage in the life cycle of a medication. In particular, when the medication's patent protection expires there is a marked reduction in the price of the product. The effect on the TEP of a marked reduction in price may: (1) change the dynamics on which medication in the therapeutic group offers the greatest benefit, which may lead to a change in the designated preferred medicine; (2) the price reduction (e.g. due to generic competition) may be so marked for all medications in the therapeutic group that including the group in the TEP is no longer required, because the benefits are automatically obtained; or (3) the preferred medicine may continue to provide benefit, but this may be lower than before the expiry of a medicine's patent protection.

Conversely, these market dynamic changes may present new opportunities for the inclusion of new therapeutic groups in the TEP, including when new medications become available within a therapeutic class, such as the example of the DPP-4 inhibitors.

Factors affecting price

The greatest effect on price is the degree of competition, with the key factors limiting competition being patent protection and having only a single manufacturer for an off-patent medication.

It is also important to distinguish between benefits obtained from the availability of competition from generic products for a medication when it comes off patent and the benefits achieved by a TEP. In the case of generic medications, it is the availability of several brands of the same medication that produces reduced prices. However, in the case of a TEP, the aim is to promote competition between different, but similar, medications; this usually means different medications in the same pharmacological therapeutic class. It could also be related to different medication options for the same medical indication. That is, a TEP aims to promote and create competition between like products, regardless of the protection provided by patents or single supplier monopolies. However, to be effective, a TEP is dependent on the availability of comparative evidence and a belief of clinical equivalence by key stakeholders in terms of safety and efficacy. This is relatively straightforward when comparing different medications from a particular pharmacological class, especially for small molecule medications. However, in the case of biosimilars, a similar but more complex methodology is likely to be needed.

When the focus is on treating the same medical indication with medications from different medication classes, the process increases markedly in its complexity due to the availability of comparative data. Nevertheless, it is likely to become an

increasingly important subject, especially with the ongoing growth in the number of biosimilars and increasing diversity of modes of action with regard to pharmacological activity. This highlights the increasing need for Phase 4 clinical drug trials to fully evaluate the comparative effectiveness, safety and duration of benefit of different medications for specific medical indications. Given the high cost and extensive pipeline of biological medication treatments entering the market, such studies will be critical to ensure pharmacological treatment options will provide the best value for money for the PBS.[8] The potential benefits of using TEP to promote competition for these products is a matter that needs to be given high priority on an international basis in health policy.

Structural factors

The fundamental focus of the TEP run at MH is the voluntary collaboration and participation of prescribers, with a preferred medicine in a therapeutic group but other medications still being available. This depends on the leadership of the senior medical staff, and a preferred medicine only adopted once there is consensus within the relevant stakeholder groups, predominantly prescribers but possibly also clinical pharmacists and nursing staff as part of multidisciplinary care teams. This process has been a successful approach in most cases, but in some cases this approach has met issues unknown before implementation. Once these issues are identified, a modified strategy acceptable to stakeholders can be introduced to overcome these aspects.

We have identified several structural factors that may affect the effectiveness of the TEP in some areas and require additional education and engagement strategies. The factors identified are as follows: (1) when a diverse range of key multidisciplinary stakeholders are involved in medication prescribing and administration; (2) the presence of multiple unknown stakeholders or those who are not easily identified as key influencers when decision making occurs across medical, clinical pharmacy and nursing staff; (3) the degree of ownership of the strategy by stakeholders, for example different engagement of permanent and visiting staff across speciality units, which may lead to different viewpoints or understanding of the program; and (4) the opportunity and authority of a clear stakeholder leader or leadership group to influence policy and the practice of other prescribers and decision makers; this may include when there are differences in size, hierarchal structures and leadership styles used within stakeholder groups.

Therefore, it is important before commencement to identify all stakeholders and, in particular, every attempt should be made to draw out previously unknown or unidentified stakeholders. If the latter group is not addressed initially, the engagement of such stakeholders should occur immediately after identification.

In a small number of cases, it is more appropriate to only have one medication available within a therapeutic group. Such a strategy is most appropriate and has been most successful for medications used exclusively within the in-patient hospital setting, because patients are not commenced on an alternative to the preferred medicine before hospital admission.

Importantly, in addition to working closely with stakeholders, the TEP needs to work in conjunction with the hospital therapeutics committee or equivalent to provide the appropriate governance and support for prescribing and medication formulary procedures and guidelines.

The key components of a successful TEP are still closely linked with: (1) extensive and effective education that clearly and simply outlines the details of how the TEP functions, and the promotion of constructive awareness of the program and its objectives when attending medical staff unit meetings; (2) effective and collaborative negotiations with senior medical staff and all other key stakeholders, considering the diverse background of these stakeholders and their characteristics of practice; and (3) regular focused feedback on the results and benefits of the program, including a focus on reporting benefits, especially the benefits to patients, directly to the relevant unit.

Conclusion

The introduction of a collaborative TEP at MH has been extremely successful in producing significant and sustained savings over 9 years. The benefits found in the initial study[1] have been ongoing. The underlying concept of this success is in the premise of cost savings without compromising the safety and clinical effectiveness of patient care in order to enable expenditure on other important areas of medicine use where the opportunity for such savings does not exist. Critical to the success of the TEP has been the collaborative environment and positive support of the MH medical staff.

This can also be described as a form of genuine disinvestment, where limited resources are diverted to their most productive use, a concept that is being promoted in many areas of healthcare.[9,10]

This work has enabled many critical factors in the success of a TEP to be identified and resolved, hopefully creating an easier path for others to follow.

Competing interests

The authors declare no conflicts of interest.

Acknowledgements

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Mathematical Representation of Pharmacy Outpatient Workloads

by
IAN LARMOUR
Prince Henry Hospital, Melbourne

I am sure all of you are aware that long patient waiting times are a **constant** problem for the Outpatient Pharmacies, and today I would like to present a variation in the approach to this problem.

Firstly I would like to examine the aspects of patient waiting time. It has 2 components:

(1) The time required to dispense the Patients Book;
and,
(2) The time required to dispense the books that are already waiting when the Patient arrives.

This formula can be expressed in symbols viz.:

Patient Waiting Time	=	Time to Dispense Patients Book	+	Time to Dispense the books already waiting

$$T = ux + \frac{xu}{P} B \quad \text{Equation (1)}$$

where T is the patient waiting time
u is the number of units on the patient's book
x is the time required to dispense one unit
P is the number of Pharmacists dispensing
B is the number of books waiting to be dispensed when the patient arrives.

Now this first component, i.e. the time required to dispense a patient's book, has been discussed very thoroughly over the years, and thus I will only briefly mention some of the concepts employed to keep this dispensing time to a minimum.

These concepts include:

(1) The use of prepacked stock
(2) The specialisation of staff function, such as —
  (a) the employment of a typist in the Outpatients Pharmacy
  or
  (b) the designation of specific duties to each Pharmacist, e.g. labeling, dispensing and checking.
(3) The use of pre-printed labels.
(4) The design of Pharmacies to suit the workflow needs.
(5) Equipment, e.g. Microfilm Cameras.
(6) The checking of books on arrival so that extemporaneous preparations and dispensing problems (e.g. drug interactions or poor writing) can be dealt with as early as possible.

However dispensing time can only be reduced to a certain minimum, beyond which dispensing may become dangerous and certainly not in the patients interest.

Thus once this minimum is reached we must turn elsewhere to achieve a further improvement.

Now the second component of patient waiting time, is that amount of time required by the Outpatient Pharmacy section (as a whole) to dispense the number of books already waiting.

Naturally if there are *no* books waiting this component will not apply.

The number of books waiting at a particular time is related to the rate at which books accumulate. This is related to two factors —

(1) The rate at which books (i.e. patients) are arriving per unit time.
(2) The rate at which books are dispensed per unit time by the Outpatient Pharmacy as a whole.

viz.:

Rate of Accumulation of books	=	Books (patients) Arriving per — unit time	Books dispensed per unit time

$$= Y_{in} - Y_{out}$$

$$\frac{dB}{dt} = \frac{db}{dt} - \frac{P}{\ldots}$$

When the number of patients arriving per unit time exceeds the rate at which books are dispensed per unit time, an accumulation of books will occur, (i.e. $Y_{in} > Y_{out}$).

Let's look at these two factors more closely.

The first factor is the rate at which patients arrive at the Pharmacy. But before we can examine this we must know what the characteristics of the Outpatient Pharmacy workloads actually are.

These workloads will fluctuate from hour to hour, day to day, and from morning to afternoon; and it is related to the *number* of clinics, the number of patients attending the clinics, and the types of clinics on a particular afternoon or morning.

The first step is to collect data, and this may be done in a number of ways.

One such method is to record the total of actual units dispensed per hour. I used this method since units, rather than patients, represent the actual workloads, and the rate at which units are dispensed will roughly follow the inflow of patients, although naturally there is a time lag between when the patient actually arrives and when the units on his book are dispensed.

These statistics must be tabulated according to

the day of the week which they were recorded. This is in order to see the characteristics of each day. This data can be presented in a number of ways, but graphical representation is usually the easiest to follow.

The graph on Figure I shows the fluctuations in the daily Pharmacy Outpatient workload at Prince Henry's Hospital for different days. It represents units per hour versus time, expressed as a frequency diagram. The units per hour are expressed as a ratio to the smallest number for convenience in this graph.

It can be seen that the morning is usually busier than the afternoon, with the greatest influx of patients occuring from about 10 a.m. until 12 noon. It also shows a heavy bias towards Tuesday mornings, which illustrates the deficiency in the planning of Outpatient Clinic Schedules, and emphasizes the need for the Hospital Management to examine the impact that new and existing Outpatients clinics have on the supporting services, especially the Pharmacy Outpatients section.

Another method of representing this data, is to calculate the mean and standard deviation for the total number of units dispensed over each hourly interval on each day as in Figure II.

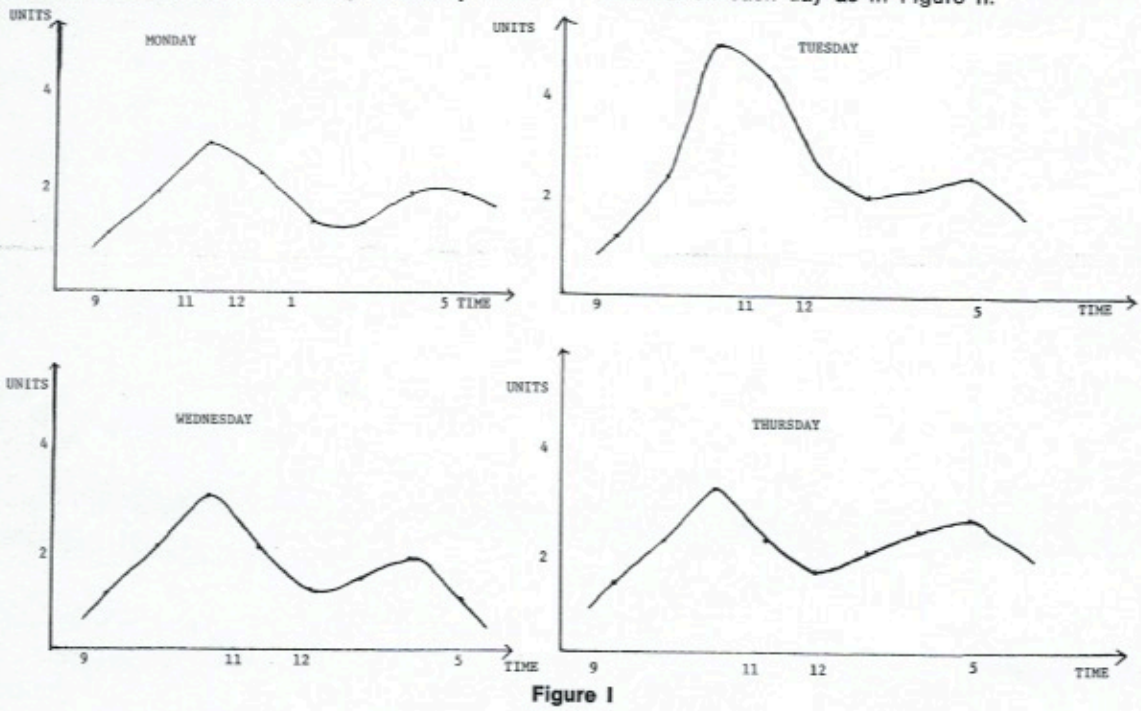

Figure I

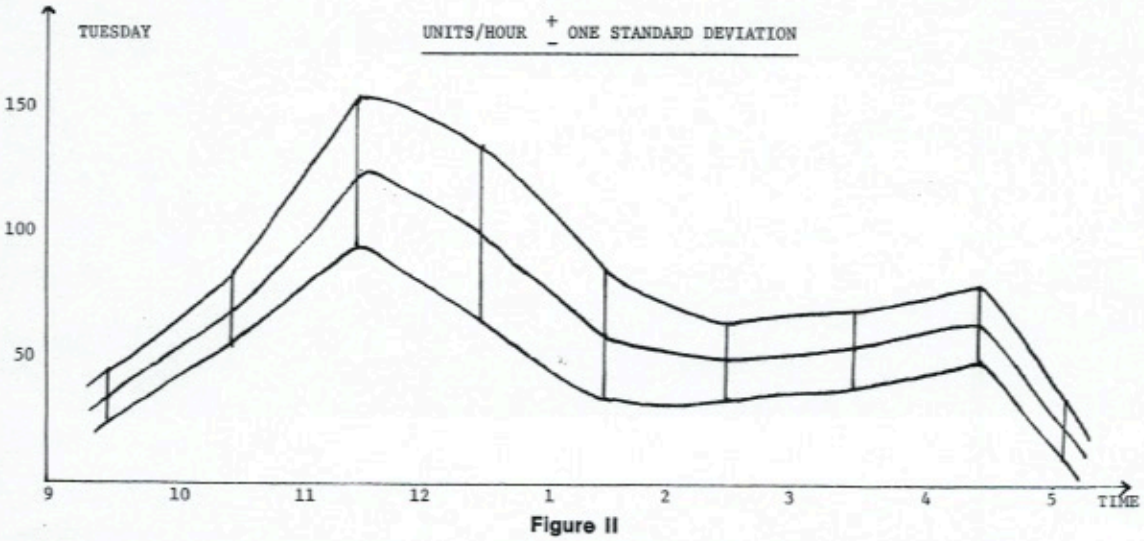

Figure II

This graph shows the mean ± one standard deviation for each hourly interval on Tuesdays. The Standard Deviation giving the spread of values around the mean, i.e. the middle line, and it illustrates the actual workloads that may reasonably be expected to occur. There are a number of other ways this type of data can be presented but I will not go into their details here.

A third alternative is to total the number of units dispensed on the different mornings as compared to the afternoons.

Taking morning as meaning from 9 a.m. until 1 p.m. and afternoon from 1 p.m. until 5.30 p.m.

If these totals are collected over the same number of days, it is possible to reduce these statistics to ratios of the smallest number for simplicity, for example:

Figure III

	Morning	Afternoon
Monday	1.6	1.4
Tuesday	2.3	1.6
Wednesday	1.6	1.1
Thursday	1.2	1.7
Friday	1.4	1.0

The statistics are broken up into the mornings and afternoons of each day, since this is usually how the clinics are scheduled.

From these figures one can quickly determine the mornings and afternoons where the heaviest workloads occur. Therefore it is possible to determine which days staff can be diverted to other projects or duties, e.g. staff meetings.

These ratios once again show a heavy bias towards Tuesday morning, but they also indicate that *Thursday* afternoon is the second busiest time. This was not apparent at first, from the frequency diagrams shown earlier. *But it must* be remembered that the total number of units in the afternoon is proportional to the area under the curve from 1 p.m. until 5.30 p.m.

Having established what the workload characteristics of the Outpatient Pharmacy are, we can now turn to the possible means by which they can be altered in order to even out the daily workloads, and to obtain a more even inflow of patients.

At Prince Henry's Hospital the patients attending the Outpatient Pharmacy section can be divided into four sub groups:—

(1) Staff
(2) Those with Repeat Prescriptions
(3) Discharge Patients
(4) Daily Outpatients and Casualty Patients.

The methods of regulating the inflow of these patients are as follows —

The most common method used for the first three types of patients is to *Redirect the non-urgent workload to the less busy times* — i.e. Concentrate on the prescriptions of waiting patients while the remainder are staggered throughout the day according to the time they are required.

The methods we use at Prince Henry's Hospital to achieve this are as follows —

(1) Staff Prescriptions which account for about 9.5% of our daily Outpatient workload. The staff members are instructed to call back and collect their medication at a later time, except when they are going home sick, or when they need *their* medication urgently.

(2) Repeat Prescriptions which account for about 10 - 14% of our daily Outpatient workload. The methods used here are —
   (i) Patients are encouraged to call in the less busy times
   or
   (ii) Patients are encouraged to post their book in advance, and to pick up their medication at a convenient date.
   We have attempted to do this by issuing a circular to patients with Repeat Prescriptions, and by erecting a sign in the Outpatient Pharmacy waiting area.

(3) Discharge Prescriptions which account for approximately 12% of the workload. These prescriptions are slotted in a special box according to the time of the day that they are required, thus the smallest possible number of discharge prescriptions are done in the busy periods.
   The Wards are also encouraged to send these prescriptions to the Pharmacy as early as possible in the day.

Now these first three types of patients mentioned only represent about 30 - 35% of the daily Outpatient Pharmacy workload. But due to circumstances not all these patients can be redistributed, and from experience we can only expect a limited success with those patients that can be redistributed.

Thus we can expect very little influence on the Outpatient Pharmacy workloads when using these methods.

I would now like to consider the methods of controlling the rate of patient inflow for the fourth group.

Now nothing can be done about the inflow of Casualty patients. However, the inflow of daily Outpatients is related to the *Arrangement of Clinic Schedules and also to the System of Appointments.*

(i) **Firstly Clinic Schedules.**

The inflow of daily outpatients to the Pharmacy is directly related to:—
   (a) The number of Clinics.
   (b) The average daily number of patients attending each clinic;
   and
   (c) The type of Clinics.

Thus if the characteristics of the clinics are known, it should be possible to allocate them to each morning, or afternoon, so that there is a more uniform distribution of the workload over the week.

(ii) **Secondly, Appointments.**

If the patient appointments were staggered throughout the morning or afternoon, instead of all the appointments being made for 9 a.m. or 2 p.m., a more orderly inflow of patients may be expected, and at least the waiting time at the clinics may be reduced.

Naturally there are many problems in implementing such a system, but none are insurmountable if all

those involved have a genuine concern for the patients welfare.

These aspects are beyond the control of the Pharmacy Department, but it should be brought to the notice of the Hospital Administration, since long waiting times do not only occur at the Outpatient Pharmacy, but in fact occurs with all the supporting services, as well as the clinics themselves, and long waiting times are bad public relations.

However, it is unlikely that these methods will be introduced in the near future, and even if they were implemented immediately, there is still likely to be a degree of fluctuation in the workloads.

I now wish to return to the second factor which regulates the accumulation of books and thus the patient waiting time, i.e. the rate at which the Pharmacy Outpatient section (as a whole) can dispense books, and this, naturally, is related to the number of Pharmacists working in Outpatients section.

Firstly let us consider the average dispensing time. It is the product of —

1. the average number of units per book (since it will vary from patient to patient (i.e. u) multiplied by —
2. the average time to dispense one unit (i.e. x).

This gives the average number of minutes it takes ONE Pharmacist to dispense one book (Fig. 6).

Average Dispensing Time = Average No. Units per Book × Average Time to dispense one unit

= xu minutes/book/Pharmacist

Total Average OP Dispensing Time = $\frac{xu}{P}$ minutes/book with P Pharmacists

Average OP Output Rate = $\frac{P}{xu}$ books/minutes with P Pharmacists

Therefore the *total* average Pharmacy Outpatient dispensing time for each waiting book, is the average dispensing time divided by the number of Pharmacists working on Outpatients at any one time.

While the average Outpatient Pharmacy OUTPUT RATE is the inverse of this, giving the average *number of books dispensed* per minute by the Outpatients section as a whole, for any given number of Pharmacists.

Thus it can be seen that as the number of Pharmacists dispensing on the Outpatients section increases, the rate of output of books will also increase.

Now as mentioned earlier, one can only expect a certain maximum rate at which Pharmacists can dispense safely. Thus there is a maximum to the output rate with any given number of Pharmacists, and once the rate at which books arrive exceeds this output rate, then books will accumulate and patient waiting time will increase.

Therefore, to increase the output of books above this maximum rate, we must increase the number of Pharmacists working on Outpatients; since we cannot control the inflow of patients.

To increase the number of Pharmacists we must either —

(a) *increase* the staff establishment; but this is really a long term project;

or

(b) *redirect* staff from the other Pharmacy sections to the Outpatients section.

i.e. Mobilisation of Staff Function.

It is this second part that I wish to deal with in more detail.

Now we all know that when the Outpatient Pharmacy is busy, the obvious thing to do is to put extra staff on Outpatients Section during these busy times.

However, the extra staff usually only start to arrive after long waiting times have already occurred. Thus the problem is really:—

(i) When to deploy extra staff.
(ii) How many extra staff should be deployed.
(iii) How long should they be deployed for.

This requires an examination of the aspects of waiting time and an estimation of dispensing time.

$$T = xu + \frac{xu}{P}.B \quad \text{Equation (1)}$$

where "T" is the patient waiting time;
and "u" is the average number of units on a patients book and this varies from morning to afternoon and from day to day;
and "x" is the average unit dispensing time by one Pharmacist, for each day or for each morning, and afternoon. This is found by collecting the number of units dispensed over a time period (e.g. ONE HOUR), with a set number of Pharmacists, when the Pharmacy Outpatient staff are very busy. This should approach the maximum output rate, if the data is collected over a number of days.

Now the number of books that have accumulated over a period of time (i.e. B) can be found at any time by counting the number of books waiting to be dispensed, *not* including those books already in the process of being dispensed.

Thus it is possible, using equation (1), to estimate the expected waiting time for a particular book.

However, what is more practical is to arbitrarily define what you consider to be an acceptable waiting time, e.g. 30 minutes (T = 30 minutes).

By transforming equation (1) to give equation (2) below, we can determine the average number of books which can be allowed to accumulate before this acceptable waiting time is exceeded — i.e.

$$B = (T - xu)\frac{P}{xu} \quad \text{Equation (2)}$$

This value of B will rise with an increase in the number of Pharmacists working on the Outpatients section. This can be calculated for each morning and afternoon of each day of the week and represented on a chart.

For example:—

Figure IV

No. Pharmacists	1	2	3	4	5	6	7	8	9
Maximum number Books allowed to Accumulate	3	6	9	12	15	18	21	24	27
	(to nearest whole number)								

This chart is for Tuesday mornings, and "B" is taken to the nearest whole number. Here we can observe how the value of "B" varies according to the number of Pharmacists.

Now from this chart (Figure 4) taking 5 Pharmacists, we get a value of B = 15.

i.e. One would normally expect the patient waiting time to be equal to, or less than, 30 minutes, if only 15, or less, books are waiting to be dispensed.

Another way of expressing this, is to say that it will be about 30 minutes before the 15th book is dispensed and issued to the patient.

Now if 17 books were waiting to be dispensed, from the chart we can see that the patient waiting ume is likely to be greater than 30 minutes for the 16th and 17th books, and also from the chart, we can see that we would need one extra Pharmacist (or 6 Pharmacists on the Outpatients section) to keep the patient waiting time less than 30 minutes, and if 20 books were waiting, we would need two or extra Pharmacists and so on.

The number of books waiting at *any time* may be counted at regular intervals, say hourly or half hourly in the less busy times, or every 10 minutes in the peak times.

Thus by counting the books, and using a chart similar to this one here, the Pharmacist in Charge of the Pharmacy Outpatients section can quickly estimate *when* extra staff will be needed, and also how many extra staff are required and *conversely* we can see when the extra staff can leave.

If the books are counted at short intervals, one can obtain an advance warning that long patient waiting times are likely to occur if the number of Pharmacists on the Outpatients section are not increased.

Also the effects of decreased staff over lunch and tea can be estimated from the chart, e.g. with 3 Pharmacists the maximum number of books allowed to accumulate is 9 and so on.

This is important since some staff are away at tea or lunch for about 30% of the working day.

At this point I would like to present an examination of the expected accuracy of this system.

The values of "x" and "u" are averages, and if they are calculated from a large number of observations, they will tend to compensate for the variations that can occur. However, it is necessary to examine the fluctuations around these mean values by calculating the standard deviations. If we find the standard deviation of "x" and "u", we can then estimate the standard deviation of "B" (i.e. the maximum number of books that can be allowed to accumulate).

But before we examine the extent of the expected variations we should consider their implications.

If the dispensing rate is quicker than the expected average, then by using the chart, and by counting the number of waiting books at regular short intervals, it will simply mean that any extra staff deployed on the Outpatients section will be able to leave sooner than expected.

On the other hand, if the books are dispensed more slowly than the average, then books will accumulate more quickly than expected and the chart will indicate that further staff are required. Thus, if more staff are available, this accumulation of books will tend to be compensated. The acceptable patient waiting time may be exceeded for a short period, but the aim of the system is to minimise its occurrence by minimising the effectiveness of our available resources. But it must be remembered that the actual dispensing rate can swing the other way just as quickly.

Where $\frac{P}{xu}$ (i.e. the dispensing rate) at any time is actually $= \frac{1}{x_1u_1} + \frac{1}{x_2u_2} + \ldots\ldots\ldots\ldots + \frac{1}{x_p u_n}$

where the values of "u" and "x" can vary with each book and with each Pharmacist respectively. Thus the probability that all the Pharmacists working on the Outpatients section will dispense at the slowest rate continuously over a 30 minute time period is unlikely, and the probability of this occuring decreases as the number of Pharmacists increases.

I would now like to examine the extent of the expected variation.

Now equation (2) viz.:

$$B = (T - xu)\frac{P}{xu}$$

can be simplified to

$$B = \frac{TP}{xu} - P \qquad \text{Equation (3)}$$

where T & P have fixed values.

Now if "a" is the standard deviation of "x" and, "c" is the standard deviation of "u" then the standard deviation of

$$B = \frac{1}{a \times c}$$

The chart in figure 8 for Tuesday mornings was derived using —

x = 2.78 minutes with a standard deviation = 0.51 minutes

and

u = 2.61 units with a standard deviation = 1.7 units

and the standard deviation of

$$\text{"B"} = \frac{1}{1.7 \times 0.51} = 1.2 \text{ books}$$

This indicates that the chart is accurate to within one Pharmacist, of the actual requirements.

since ± one standard deviation = ± 1.2 books,

and

since ± two standard deviations = ± 2.4 books.

But if a conservative approach is required, it would

be wise to decrease the value of "B" in figure 8 by one unit (i.e. approximately one standard deviation).

This examination indicates that the system should be accurate enough to fulfil the requirements of the Pharmacy Department.

But in order to make this system work it is obviously necessary to have staff from the other Pharmacy sections available for deployment on the Outpatients section.

This involves the examination of Pharmacy Outpatient workload statistics with respect to time, as mentioned earlier. This is to ascertain the likely times that the extra staff will be required.

Once you know the likely busy periods, then the other Pharmacy sections can organise their workload so that some Pharmacists *from these* sections are available for deployment at these times.

Naturally there is always a limit to the number of staff available, and this is related to the Staff Establishment.

Another application of this system is that it enables the number of Pharmacists required to dispense in the less busy times to be roughly determined (i.e. the number of Pharmacists required for direct productivity) and thus the remaining outpatient staff can be deployed in other tasks (indirect productivity) or in other sections; especially in those sections which are behind in their work because some of their staff were required on the Outpatient section during the busy periods.

This is very important with respect to staff morale. However, it must be remembered that this system can only give estimates, and the values of "B" above (i.e. the Max. number of Books that can be allowed to accumulate) may need to be varied from experience as mentioned above. In addition the values of both "x" and "u" can be expected to vary from hospital to hospital and from Pharmacy to Pharmacy.

But it is more systematic than the Ad Hoc approach used at present, and the extra staff may be deployed before the excessively long waiting times actually occur.

There is, however, a limit to the number of Pharmacists that can work efficiently in a particular Outpatient Pharmacy, since overcrowding produces inefficiency.

This is an important factor that must be considered in the design of Outpatient Pharmacies.

If an efficient Pharmacy cannot achieve its average maximum acceptable patient waiting time, e.g. 30 minutes,

then either this value must be raised,
or alternatively,

the staff establishment must be increased, and the above system provides a useful means to present such a case to the Management.

However, no system can accommodate the exceptional prescription which requires considerably more time to dispense than normal.

That is those prescriptions that fall outside the normal population of prescriptions and this may occur because of any of the following reasons:—

1. Prescribing Problems, such as —
   - (a) Poor Writing
   - (b) No authority to prescribe
   - (c) No permit to prescribe, e.g. for Drugs of Addiction
   - (d) Incorrectly written prescriptions, e.g. the absence of details on dosage, strength, directions or dosage form or the absence of legal requirements
   - (e) Drug Interactions
   - (f) Incorrect doses
   - (g) Incorrect transcribing or spelling.
2. Dispensing Problems —
   - (a) Stock or supply problems or shortages
   - (b) Pricing of Private Prescriptions
   - (c) Recording and filing of Drug of Addiction prescriptions
   - (d) Unusual extemporaneous preparations.

Naturally not all the prescriptions with above problems will fall outside the normal dispensing time range. However some will, but this is likely to be the exception rather than the rule, and it reflects the general administration throughout the Hospital as well as the Pharmacy Department.

Now the Mathematical Representation of "B" (i.e. the accumulation of books) can be derived as follows —

$$\frac{dB}{dt} = \frac{db}{dt} - \frac{P}{xu} \qquad \text{Equation (4.)}$$

where $\frac{dB}{dt}$ is the rate of accumulation of books.

and $\frac{db}{dt}$ is the rate at which books arrive at the Pharmacy.

and $\frac{P}{xu}$ is the rate at which books are dispensed by the Outpatients Pharmacy as a whole with "P" Pharmacists.

This equation can be integrated in terms of "B", which gives the area under a curve derived by the above equation, and it gives the total number of books which have accumulated over a particular time period, giving equation 5.

$$\text{i.e. } B = \int_{I}^{+Co} \left(\frac{Ab}{At} - \frac{P}{xu}\right) t \qquad \text{Equation (5).}$$

Now if the working day is broken up into time intervals such that At = t i.e. the time interval the

books are collected over, then after "n" time intervals the number of accumulated books (B(n)) is given by

$$B(n) = \left(\sum_{i=1}^{t=n-1} \left[b(i) - \frac{t\,P(i)}{xu} \right] \text{too} + \left[b(n) - \frac{t\,P(n)}{xu} \right] \right)_{O}$$

where $\sum_{i=1}^{t=n-1} \left[b(i) - \frac{t\,P(i)}{xu} \right]$ is the sum of accumulated books over n–1 time intervals.

and if, $b(n) = \frac{t\,P(n)}{xu}$ no books will accumulate.

and if, $b(n) > \frac{t\,P(n)}{xu}$ books will accumulate

However, since the books can only be dispensed after they have arrived, at the Pharmacy,

when $b(n) < \frac{t\,P(n)}{xu}$ no books will accumulate, and in addition if there are books waiting to be dispensed, having accumulated over the time intervals from i=1 to i = n–1, then the number of accumulated books will decrease.

But if no books are waiting then

$$\left(b(n) - \frac{t\,P(n)}{xu} \right) = O$$

i.e. $\left(b(n) - \frac{t\,P(n)}{xu} \right)$ can only have a negative value if the sum

$\sum_{i=1}^{i=n-1} \left(b(i) - \frac{t\,P(i)}{xu} \right)$ has a value greater than zero.

But although the mathematical representation of "B" may appear complex, in actual practice, to find "B" all you need to do is to count the number of books waiting to be dispensed.

Figure 5. is a simplified theoretical graph to illustrate the interactions of the various factors involved —

i.e. Input
Output
Accumulation of Books
Waiting time
Acceptable waiting time

Line C — is the maximum dispensing rate for a set number of Pharmacists. It would rise with an increase in staff, and conversely the effect of decreased staff over lunch and tea can be seen.

Line B — represents the inflow of patients (i.e. rate at which patients arrive at the Pharmacy).

There are usually 2 peaks ONE in the morning and ONE in the afternoon.

Line A — represents the rate of accumulation. It can be seen that this occurs when the rate of inflow exceeds the output of books.

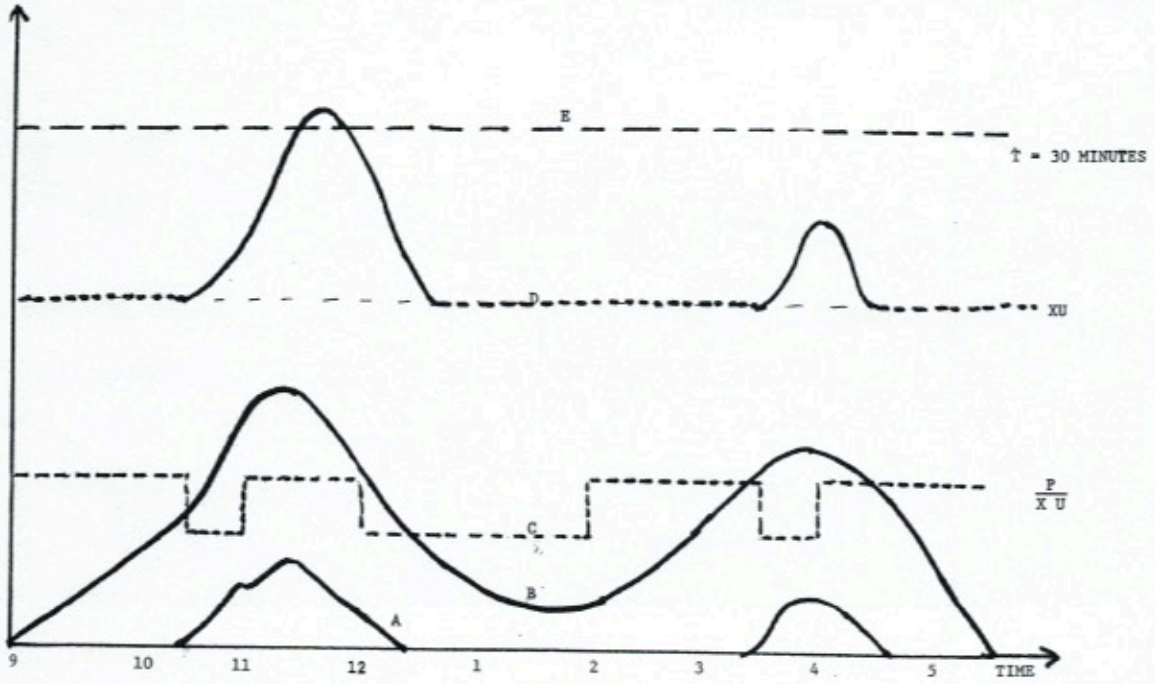

Figure V

The total of accumulated books at any one time is proportional to the area under line A over those times.

Line D — is the waiting time and the minimum waiting time is the average dispensing time (xu) and the waiting time increases with the rise in the number of accumulated books and it may exceed the maximum acceptable waiting time e.g. 30 minutes (i.e. Line E).

In conclusion I would like to thank Miss Shannon and the rest of the Pharmacy Staff for their help and co-operation in collecting the statistics (especially Mr. Long).
I would also like to thank the Staff of the Medical Illustrations Department at Prince Henry's Hospital for their help in producing the slides.

REVIEW OF A PUBLICATION OF VALUE TO ALL HOSPITAL PHARMACISTS

by **Miss P. D. THORNTON,** B.Pharm., M.S.H.P.,
Woden Valley Hospital, Canberra

"CONTROL OF MEDICINES IN HOSPITAL WARDS AND DEPARTMENTS"

a publication of the
Scottish Home and Health Department
and the
Scottish Health Services Council.

This is the report of a Joint Group appointed by the Standing Pharmaceutical, Medical and Nursing and Midwifery Advisory Committees on Control of Medicines in Hospital Wards and Departments.

This publication sets out proposals and recommendations for a standard system of prescribing, administration and recording of medicines throughout Scottish hospital practice. Many pertinent problems of physical control of drugs are discussed; for example, storage on wards, supply of medicines for emergency situations in the wards, supply of medicines to patients on discharge, supply of medicines when the pharmacy is closed, medicines brought into hospital by patients and supply of medicines to small hospitals.

Methods of prescribing and documentation of this are discussed in detail, and recommendations for a standard prescription sheet and supplementary sheets are presented.

Standard procedures for control of actual drug administration and recording of this are described. The authors also advocate a training programme, on an in-service basis if necessary, for medical and nursing staff, dealing with the prescribing, administration and recording of medication.

The concept of a ward pharmacy system aligned with the preceding control methods is applauded as an important factor in ensuring the safe supply and use of medicines.

This small booklet, published by Her Majesty's Stationery Office and which is available in Australia through the Australian Government Printing Office in each state, may provide an invaluable reference and **an excellent guide for any Australian pharmacist faced with the difficulty of obtaining administrative acceptance for a ward pharmacy scheme based on precedents derived solely from practice in the United States.**

One third of patients do not follow doctors' orders

HAMILTON, Ont., Canada (HF) — One of every three patients who goes to a doctor with complaints does not then follow the doctor's orders.

This startling revelation comes from a two-year long study of a newer kind of research dealing with "patient compliance". Not much has yet been done in this potentially very important field.

Dr. David Sackett, professor of clinical epidemiology and biostatistics at McMaster University, says the degree of patients' "compliance" or obedience seems to depend on the length, seriousness and type of disease, of course the patient's attitudes (what the patient **thinks** he knows) and many still mysterious factors.

The researchers are emphasizing the taking of medicine, that is, whether the patient really obtains the prescribed preparation and follows the instructions. But they also find that patients are often negligent in keeping appointments with doctors, in preventing further trouble and generally in promoting their own health through correct "life-styles".

Among patients without clear symptoms, up to half break their appointments, and even 20 per cent of those with obvious complaints do not appear in the doctors' offices, as promised.

If they are asked to do something for a rather short period to prevent further illness, about 20 per cent do not co-operate; and if long term prophylaxis is ordered, such as antibiotics for prevention of rheumatic fever, **half** fail to co-operate.

Patients with some mental disturbance, especially of the paranoid type, more often do not take their medicines than those with physical conditions, the researchers find.

Of course the more that a prescribed regimen interferes with a patient's unhealthy life style (smoking, drinking, poor diet and lack of exercise), the less likely that the patient will comply.

Socio-economic factors, even intelligence and educational level, do not seem to influence patient compliance, Dr. Sackett finds.

Doctors agreed in a workshop that until they know more about what causes patients not to comply, they cannot recommend a "strategy". Some do suggest that doctors might have to "negotiate contracts" with patients, after determining what each patient personally accepts.

Chapter Four

Examining the Potential Benefits of Hospital Pharmacy Outreach Services

22. Alvarez S, Larmour I, Tapley N, et al (2001) “Education Outreach to the Community: Does Hospital Pharmacy Have a Role” AJH.P, 31, 13-17. Citations 4

Education Outreach to the Community: Does Hospital Pharmacy Have a Role?

Stephanie J Alvarez, Ian Larmour, Nicole Tapley, Megan Buick, Louise Greene, Lisa Hines, Jan Davies

ABSTRACT

This paper describes the activities carried out by a hospital pharmacy department as part of a national co-ordinated care trial. The objective was to examine ways in which a hospital pharmacy could provide support to general practitioners (GPs) involved in the trial through the promotion of rational, safe, effective and economic use of medication. A Pharmacy Strategy Group was established and identified five service products: education outreach, drug information services, special medication review and counselling, medication check-up and computer database analysis. The scope of these services and the experience gained in the trial is outlined. The most successful service was the education outreach program. This was highly valued by the GPs and following the program there was a reduction in prescribing of non-steroidal anti-inflammatory drugs. The experience gained offers an insight into the potentially valuable contribution that hospital pharmacists can make to promote appropriate, safe and effective use of medication.
Aust J Hosp Pharm 2001; 31: 13-17.

INTRODUCTION

There has been increasing recognition of the need for effective links between hospital and community healthcare practitioners. The question facing many hospital pharmacists is how their department may be effectively involved in this process. At the Southern Health Care Network (SHCN) Pharmacy Department we had the opportunity to examine this question and develop the concept during our involvement in the SHCN Co-ordinated Care Trial (CCT)—Mark 1. This is one of many such trials across Australia.

The CCTs are a Commonwealth Department of Health and Aged Care initiative to test new models of healthcare funding and delivery. The SHCN trial had the support of the Victorian Department of Human Services. Funds were pooled from state and federal sources to give flexibility in service delivery and care co-ordination at the individual client level. The SHCN CCT involved clients and general practitioners (GPs) in the Dandenong, Sherbrooke and Pakenham Districts of outer Melbourne. The aims of the CCT were to:

- improve client outcomes;
- provide services which are individually and collectively more responsive to the assessed needs of clients; and
- find more efficient ways of funding and delivering services.

Stephanie J Alvarez, BPharm, DipPharmPrac (UK), **Ian Larmour,** BPharm, FSHP, MSc, **Nicole Tapley,** BPharm, **Megan Buick,** BAppSc (Nsg), **Louise Greene,** BAppSc (Nsg), **Lisa Hines,** BAppSc (Nsg), GradDipMarketing, **Jan Davies,** BSc (Hons), PhD, Southern Health Care Network Co-ordinated Care Trial, Victoria
Address for correspondence: Ian Larmour, Southern Health Pharmacy Department, Monash Medical Centre, 246 Clayton Road, Clayton Vic. 3168
E-mail: i.larmour@southernhealth.org.au

The trial commenced with 1750 clients in the intervention group and 657 clients in the control group. It also involved 423 medical GPs and was conducted in partnership with two local Divisions of General Practice and five Community Health Centres.

PHARMACY INVOLVEMENT

The SHCN Pharmacy Department was invited to participate in the trial and a multidisciplinary Pharmacy Strategy Group was established. Membership consisted of a general practitioner, a senior medical practitioner employed by SHCN, a community pharmacist, several CCT staff, the SHCN Pharmacy Department Network Director and the Drug Utilisation Evaluation pharmacist.

The goals of this group were to:

- promote effective and safe drug use;
- reduce unnecessary drug use;
- promote mutually beneficial relationships between various health providers and clients;
- identify clients thought to be at high risk of medication misadventure; and
- identify high-risk drug use.

The Pharmacy Strategy Group was fortunate to have a computer database that contained client details, including diagnostic categories, demographic details and the drugs prescribed for that client via the Pharmaceutical Benefits Scheme (PBS). This was only possible because the clients had given their consent for this information to be used when they joined the trial. A major limitation was that the database did not contain details on non-PBS drugs, nor did it cover drugs on the PBS which cost less than the client co-payment. Despite this, the database provided a very powerful research tool, especially in regard to the identification of 'at risk' clients.

The Pharmacy Strategy Group identified five service products that could be provided by the SHCN Pharmacy Department for GPs participating in the CCT:

1. education outreach, commonly referred to as 'academic detailing' in the literature;
2. drug information services;
3. specialist medication review and counselling referral —for clients considered to be at high risk by the GPs;
4. medication check-up referrals from the GP for clients with complex medication regimens. This role would be similar to the clinical review and monitoring of medication that is routinely provided in hospitals by ward clinical pharmacists in order to minimise the risk of avoidable drug toxicity; and
5. scanning of the database for clients at high risk due to drug interactions and contraindications.

Education Outreach Program

The aim of the program was to enhance the GP's knowledge and ability to make informed prescribing choices.[1]

All GPs who were linked to the CCT were sent an invitation to participate in this program in April 1999 and

40 immediately accepted. Due to limited resources, the target number of GPs in the project was set at this level and no further follow-up promotion was carried out.

The Drug Utilisation Evaluation Pharmacist (SA) undertook an academic detailers training course run by the University of New South Wales (Best Practice in Educational Visiting) in conjunction with the Drug and Therapeutic Information Service (DATIS) in South Australia.

The Drug Utilisation Evaluation Pharmacist carried out single visits to 27 GPs on a 'one-to-one' basis and undertook four group visits for 13 GPs in the CCT and five other GPs not involved in the trial. The 40 GPs involved with the trial managed a total of 224 CCT clients.

After consultation with senior SHCN medical staff the Pharmacy Strategy Group chose two topics for promotion at these visits. The topics were chosen after scanning the database for high-risk behaviour such as drug interactions or medication contraindications.

The first topic was *Helicobacter pylori* eradication therapy for peptic ulcer disease. This was chosen because it was a relatively new treatment and it was thought that the concept needed promotion. The objective was also to encourage a review of the treatment options for any clients on long-term therapy with a histamine$_2$-receptor antagonist or a proton pump inhibitor for prophylaxis against recurrent peptic ulcer disease.

The second topic was the use of non-steroidal anti-inflammatory drugs (NSAIDs). This was chosen because these drugs are frequently used and, although obviously of benefit in some indications, have a high risk of morbidity, especially in high risk groups such as the elderly. It has been estimated that 20% of ulcer haemorrhage is due to the use of a NSAID[2] and in one study 39% of drug-related hospital admissions were associated with a NSAID.[3] Therefore, the objective of this topic was to encourage rational use of NSAIDs and decrease unnecessary use. In addition, the introduction of the new cyclo-oxygenase type 2 (COX-2) inhibitors added further discussion points.

At the education outreach visit each GP was given several promotion documents that were developed by the SHCN Pharmacy Department in conjunction with CCT staff. The documents had been peer reviewed by senior hospital gastroenterologists, a senior rheumatologist and the CCT GP Advisory Panel. The documents included 'A Desktop Guide' and a double-sided summary sheet for each topic. Other information alerted GPs to the risk of drug-related hospital admission and the availability of the CCT medication 'Check-Up' service.

The GPs were also given an evaluation feedback sheet which they were asked to mail or fax to the SHCN CCT. Twenty-four (60%) GPs responded (Tables 1-4). The positive nature of these results was very pleasing, especially in regard to their intention to take action. Further visits were requested by 96% of the responding GPs. The most popular topics suggested for future visits were cardiac drugs and the rational prescribing of antibiotics.

Prescribing patterns were examined for trends following the program. We examined the data in two periods of three months, one before the visits (February to April 1999) and one after the visits (June to August 1999). The results obtained from the GP intervention group were compared to a control group of 40 GPs who were not visited. A random sample was chosen from the CCT database to form the control group.

There were too many confounding factors to enable comparison of the data regarding *H. pylori* eradication. There was, however, a slight decrease in the number of clients receiving long-term histamine$_2$-antagonists or proton pump inhibitors.

In the case of NSAIDs it was felt that changes in prescribing patterns could reflect effects of the education program. In June 1999, clients were required to con-

Table 1. Evaluation - documents and overall assessment
24 respondents

	Documents		Overall	
	Easy to understand	Clear and concise	Quality of information	Meets your needs
Excellent	15 (63%)	17 (71%)	16 (67%)	18 (75%)
Good	9 (38%)	7 (29%)	8 (33%)	6 (25%)
Average	-	-	-	-
Satisfactory	-	-	-	-
Not satisfactory	-	-	-	-

Table 2. Evaluation - further action or visits
24 respondents

	Do you intend to take any action following this education outreach visit?	Further visits requested?
Yes	18 (75%)	23 (96%)
No	4 (17%)	1 (4%)
	- already doing the practice recommended	
Maybe	2 (8%)	-

Table 3. Evaluation - value for client management
24 respondents

Useful for client management?	Number of respondents
Very useful	12 (50%)
Useful	12 (50%)
Somewhat useful	-
Not useful	-

Table 4. Evaluation - frequency of visits
24 respondents

Preferred frequency of visits	Number of respondents
3 months	9 (38%)
6 months	9 (38%)
12 months	4 (17%)
Other	2 (8%)

Table 5. Prescribing patterns for NSAIDs

	Number of prescriptions			Number of clients who had a prescription written		
	Feb-Apr 99	Jun-Aug 99	Change	Feb-Apr 99	Jun-Aug 99	Change
Education outreach group (n = 40)	35	16	-54%	18	13	-28%
Control group (n = 40)	11	14	+27%	6	7	+17%

sent to continue in the trial. Unfortunately, a small number withdrew from the CCT and these data were not included in the analysis (Table 5). In the intervention group there was a decrease of 19 prescriptions (-54%) in the post-intervention period compared to the pre-intervention period. In the control group there was an increase of 3 prescriptions (+27%) over the same period. This trend was also reflected in the number of clients prescribed a NSAID, with a decrease of 5 clients (-28%) in the intervention group and virtually no change in the control group.

Although relatively small numbers of clients were involved, given the sensitivity of the database and the size of the changes, it is possible that the program was responsible for an improvement in the prescribing of NSAIDs.

Drug Information Services

The SHCN Pharmacy Department Drug Information Centre located at Monash Medical Centre has been providing drug information services to community practitioners, the general public and SHCN staff for many years. Therefore, this was not a new service and the only change made was to provide a toll-free telephone number that was advertised to the CCT GPs. A focus group evaluation of this type of service showed that it was thought to be useful, but many thought that they had sufficient drug information on their 'Medical Director' computer software. This perhaps illustrates that many GPs do not understand the more specialised roles of information access, evaluation, interpretation and judgment that are provided by the drug information centre. Routine surveys of users of this service indicate a very high level of satisfaction with regard to the quality and timeliness of the service. However, it would seem that many GPs do not know that the service is available and, if they do, may have a poor understanding of the type of service provided by hospital drug information centres. Unfortunately, the CCT did not have the resources to undertake such an education program.

Special Medication Review and Counselling

The Pharmacy Strategy Group identified that the provision of specialist medication counselling for at-risk clients was a concept that needed consideration. This was not seen as a replacement for the routine medication counselling provided by a pharmacist when the client's medication is dispensed, rather it was a separate service that provided an in-depth review of all aspects of a client's medication. The Pharmacy Strategy Group developed guidelines for GPs to use in the selection of such clients. The risk factors were:

- history of medication non-compliance;
- complicated medication regimen;
- the use of inhalers (perhaps for the first time or where the GP suspected the client was having trouble with their inhaler technique);
- recently started or changed medication (e.g. after discharge from hospital); and
- physical incapacities.

The objective of this session was to evaluate the client's understanding of their medication, to identify potential problems and to provide practical assistance and ideas to help the client organise their medication. This service also aimed to give the GP a second opinion on whether there were problems and, if so, advise on strategies that could be used to minimise risks. GPs were sent a letter by the CCT staff to advise them of this service. Unfortunately this was only taken up by one GP but it was described as useful and helpful. The patient had multiple medical conditions including severe angina and it was found during the session that although a combination of nitrate tablets and patches was suitable there was no nitrate free period. The GP or community pharmacist had not noted this aspect. Most community clients would be unlikely to require such a service. However, there is little purpose in having it available unless it is effectively advertised and promoted, especially in regard to the purpose of the service. If there is no such understanding, it is not surprising that more GPs did not utilise it.

Medication 'Check-Up'

The aim of this service was to provide the GP with the opportunity to use experienced and specialist clinical pharmacists to review the medication of clients considered to be at risk. That is, the review of dosage regimens in relation to the client's clinical condition, potential drug interactions, contraindications and sub-optimal or inappropriate medication use. The objective was to minimise the risk of avoidable drug toxicity. This is a standard service that has been routinely available in hospitals for many years. Naturally not all community clients require such a detailed review, since the majority of clients are unlikely to be suffering from acute or complex disease and consequently are likely to have relatively simple medication requirements.

This service was promoted to GPs via a letter from CCT staff. To assist GPs in the selection of suitable clients, the following risk factors were proposed:

- age over 65 years;
- history of a previous adverse drug reaction or drug hypersensitivity;
- concurrent use of five or more medications;
- recent changes in medication regimen;
- recent discharge from hospital;
- concurrent renal, cardiac or hepatic disease;
- newly diagnosed illness or acute illness;
- use of high-risk medication, e.g. warfarin;
- unexplained symptoms.

The process involved the GP completing a referral form and faxing it to the SHCN Pharmacy Department. Two experienced pharmacists reviewed the details of the case, with additional information being obtained from the GP as needed. The pharmacists developed a series of recommendations that were discussed with the GP and a written report was faxed to the GP. In addition to the telephone contact, each GP was also asked to complete an evaluation form. Over a period of six months, these medication check-ups were provided for seven clients, some of which involved multiple ongoing consultations. An average of three to six recommendations were made on each intervention. Despite the disappointingly low response from GPs in general, those who used the service were very enthusiastic in regard to its benefits. All reported that they found the service excellent and indicated that they intended to implement the recommendations. All indicated that information was received in time to allow it to be of use.

The client report format was considered to be excellent by 75% of GPs and was rated as good by the remainder. Comments included 'details of interactions were a timely reminder', 'a very informative report and telephone call' and 'it gives a second opinion on medication as several specialists are prescribing medication and the GP has to monitor side effects'.

The GPs all indicated that they would like to receive ongoing reviews of their clients' medication usage, but there was some variation in the requested frequency of review (25% two-monthly, 25% quarterly, 50% six-monthly).

Database Analysis

The computer database offered a rare opportunity to evaluate the benefit of various search strategies. The review of prescriptions for potential drug interactions is a useful strategy to pick up potential problems. However, not all drugs used by the client were listed in the database and furthermore the extent of the problem often depends on how the drug interaction is managed, the drugs involved, pharmacogenetics and the client's clinical condition. Nevertheless, it offers the opportunity to scan for major drug interaction problems that can be followed up.

Another option was to link drugs and listed clinical contraindications. For instance, a search for clients taking beta-blockers and having a history of clinically diagnosed asthma, fortunately, found only one case.

Other strategies included linking the client's age to a drug or group of drugs, such as benzodiazepines in clients 65 years of age or older. The database also enabled searches based on the number of prescriptions for PBS medication. One survey of six months of data (July to December 1997) revealed that 20% of clients in the intervention group were routinely prescribed five or more medications. This group accounted for 87% of all prescriptions during the survey period. The data over the same period also indicated that 59% of prescriptions were for female clients and that clients over 45 years of age tended to have higher numbers of prescription items, with 40% of medication being prescribed to clients 63 years of age or older.

The survey revealed a group of 45 clients who were receiving 20 or more prescription items per month, some of whom were attending several GPs. However, for such strategies to be effective, it is essential that the GPs concerned be aware of this service and for them to be willing to receive advice on such matters. If this is not the case, it is likely that the GP will see such advice as gratuitous interference.

DISCUSSION

The effectiveness of 'academic detailing' was first demonstrated by Avorn and Soumerai[1] and others have confirmed these findings. The ongoing duration of this effectiveness remains uncertain, although May et al. demonstrated a benefit over five years in an ongoing education outreach program—DATIS.[4] This group found a 9% aggregate reduction in the dispensing of prescriptions for NSAIDs over a five-year period. The evaluation methods and the scope of the DATIS project differ significantly from our study. However, we have demonstrated a change in the prescribing of NSAIDs available on the PBS following an education outreach program and this provides further evidence of the effectiveness of this strategy. To be fully effective, such programs need to be ongoing and extensive. The labour intensiveness of this approach is likely to limit such services to the most critical areas of practice. A computer database offers significant advantages in this type of study but the privacy rights of clients cannot be compromised.

The uptake of the medication intervention, review and advisory services was disappointing. However, the feedback and response of the GPs who used these services was very positive and encouraging. This perhaps indicates a need for such services, but also illustrates that culture and practices change slowly.

It is unrealistic to expect GPs to suddenly use a new service if significant resources have not been used to raise levels of awareness and to explain the details and benefits of the services. The resources available to the CCT were not sufficient to enable an effective marketing campaign and available resources also limited the extent and duration of services. Nevertheless, the CCT has identified a number of services that can be of benefit to GPs. It has also helped to define more clearly the way in which the clinical expertise of hospital pharmacists can be utilised in a community setting.

It is to be hoped that these concepts can be more fully developed in future CCTs. Future funding of such projects could be more beneficial if it is targeted to specific service options. It may also be possible for bodies such as the National Prescribing Service to work more closely with hospital pharmacy departments on community education projects. This would enable a wider range of clinical expertise and resources to be developed and accessed by the National Prescribing Service. These links would also assist in the development of hospital-based education programs.

Projects of this type may also help to pave the introduction of the Continuum of Care Guidelines developed by the Australian Pharmaceutical Advisory Council.[5] The need for progress in these areas of research and development are well understood but this work needs to be nourished if it is to fully develop.

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RESEARCH ARTICLE

Patient and general practitioner perspectives of the Hospital Outreach Medication Review service at Monash Health

Mary Hanna[1], Ian Larmour[1], Sally Wilson[2], Karen O'Leary[3]

1 Department of Pharmacy, Monash Health, Melbourne, Australia
2 Research into Practice Pharmacist, The Society of Hospital Pharmacists of Australia, Melbourne, Australia*
3 Policy and Projects Manager, The Society of Hospital Pharmacists of Australia, Melbourne, Australia

Abstract

Background: The Hospital Outreach Medication Review (HOMR) service at Monash Health is a pharmacist-led service that targets patients at high risk of medication misadventure in the immediate post-discharge period.
Aim: To determine the views of patients and general practitioners (GPs) who were involved with a HOMR in 2012.
Method: A standardised risk assessment tool was used to identify patients at high risk of medication misadventure at Monash Health. A HOMR was provided by a clinical pharmacist from the Monash Health Pharmacy Department who undertook a structured evaluation of a patient's medications and produced a report on the issues identified and recommended management strategies. This report was disseminated to the patient's GP with a feedback questionnaire. Patient perceptions were determined using an anonymous self-administered, paper-based questionnaire.
Results: A total of 487 home visits were conducted in 2012 (49.7% male patients, 50.3% female, mean age 72.8 ± 14.1 years). A total of 217 patients (45%) returned feedback forms. About 99% of patients who responded felt the HOMR was worthwhile (very much 88%, partly 11%) and 84% indicated they were more confident and less confused about their medications. In all, 105 (21.6%) GPs of 487 responded to the feedback form. Ninety-six percent of GP respondents indicated they agreed with the recommendations made and 92% indicated they would adopt either some (44%) or all (48%) of the recommendations.
Conclusion: The positive views shared by patients and their GPs are indicative of the importance of medication reviews in promoting medication safety and encouraging autonomous medication adherence.

Keywords: HOMR, HMR, outreach, medication review.

INTRODUCTION

The Hospital Outreach Medication Review (HOMR) service at Monash Health was introduced in 2006 as part of the Victorian government's Hospital Admission Risk Program (HARP). The program targets patients in the immediate post-discharge period who are identified as being at high risk of medication misadventure and aims to promote the quality use of medications through an integrated response of hospital and community services. The service involves an experienced hospital-based clinical pharmacist visiting the patient's home to undertake a structured evaluation of a patient's medications, with the aim of optimising the use of medications and empowering and assisting patients to take greater control of their medication management and to encourage autonomous medication adherence. In-depth information and education are provided to the patient.

Inappropriate medication management and medication-related problems (MRPs) have been identified as major contributors to hospital readmissions.[1] Groups often at greatest risk of medication errors and adverse events, after discharge from hospital, are older people, those taking multiple medications, the culturally and linguistically diverse (CALD) and those taking high-risk medications.[2] Early evidence supporting the benefits of a pharmacist-led 'education outreach service' began to emerge from a study conducted within our institution (Alvarez *et al.*[3]) as part of a Commonwealth Department of Health and Aged Care national coordinated care trial aimed at testing new models of healthcare funding and delivery. This study examined ways in which a hospital pharmacist could provide support to general practitioners (GPs) during the critical post-

Address for correspondence: Mary Hanna, Department of Pharmacy, Monash Medical Centre, 246 Clayton Road, Clayton, Melbourne, Victoria 3167, Australia
E-mail: mary.hanna@monashhealth.org

*Currently at Centre for Medicine Use and Safety, Faculty of Pharmacy and Pharmaceutical Sciences, Monash University, Parkville, Australia.

discharge period via a variety of service initiatives, including providing follow-up education and medication reviews to patients. The experience gained offered an insight into the valuable contribution that hospital-based pharmacists could make in promoting the rational, safe, effective and economic use of medication. The evidence supporting the benefits of home medication reviews continues to expand.[4–6] However, there is a lack of knowledge regarding recipients' experiences with, perceptions of, and willingness to use such services in Australia. As part of a series of research activities reporting on the impact of the HOMR model, we aimed to determine the views of GPs and patients about the HOMR services received in 2012.

METHOD

Study Design and Participants

This study was conducted across all sites of Monash Health which consists of six major hospitals and more than 2216 acute, subacute, mental health and aged care beds. The study was undertaken during 2012 as part of the normal services provided by the HOMR service. Patients receiving a HOMR and their GPs were surveyed to determine their perceptions of the service.

Approval for this Continuous Quality Improvement Activity was granted by the Monash Health Human Research Ethics Committee.

Referral Process

Patients were identified as being at risk of medication misadventure through the use of a standard risk assessment tool that was developed through literature review and local expert consensus (Appendix). The tool assesses common risk factors associated with hospital readmissions such as polypharmacy concerns, chronic disease, renal or hepatic insufficiency, high-risk medications (e.g. warfarin, benzodiazepines, opiates, insulin), recent hospitalisation, multiple prescribers and language barriers.[2,7–9] Patients were prioritised by the number of risk factors present. A referral for a HOMR could be initiated by any healthcare provider, carer or the individual patient within the Monash Health network. Following receipt of each referral, the patient's medical record was reviewed to determine his or her eligibility for a HOMR (Table 1). Patients were deemed ineligible for the service for a variety of reasons (Table 1). Patients who were identified as having medication management issues but who were taking fewer than four medications received a telephone review as it was felt that most issues could be resolved over the telephone; these patients were not included in this study. Patients from outside the hospital catchment zone were referred to their GPs for consideration of a community-based Home Medicines Review (HMR).

Patients identified as being eligible for a HOMR were required to provide verbal consent prior to the visit. Professionally accredited interpreters were employed to facilitate communication if any language barriers were identified. Home visits were scheduled around carer availability where practicable. A safety risk assessment was performed on all eligible patients using a screening tool to ensure the safety of all outreach staff. Patients who were believed to be a safety risk received the medication review on hospital premises if appropriate.

Personal information was handled in accordance with the Information Privacy Act 2000 and the Health Records Act 2001.

The HOMR Process

A HOMR was delivered by registered pharmacists at Monash Health who have a minimum of 3 years hospital clinical pharmacy experience. There are three full-time equivalent pharmacists working within the service, namely a senior pharmacist in-charge and two clinical pharmacists.

Table 1 Inclusion and exclusion criteria for a Hospital Outreach Medication Review (HOMR)

Inclusion criteria
Lives alone and manages own medications
Recent medication changes
Multiple medications (≥4 regular medications/day)
Recent hospital admission
Chronic disease (cardiovascular, respiratory, diabetes, other)
Taking a medicine requiring dose modification
Use of high-risk medicines
More than one GP, no GP, multiple pharmacies
History of noncompliance (deliberate or unintentional)
Concerns regarding carer(s) ability to manage medications appropriately
Cognitive/intellectual impairment
Language/cultural barriers or beliefs
Falls risk (potential or documented)
Cannot read dispensing labels/impaired vision
Renal impairment (<30 mL/min) or hepatic impairment (>3× normal liver function tests)
Other (e.g. suspect a problem may exist)
Exclusion criteria
Client declined HOMR
Safety risk
Other appropriate services in place
Unable to contact
Low risk (<4 medications)
Resides in long-term care facility
Palliative (life expectancy <1 year)
Outside 20 km catchment area

All clinical pharmacists, with the exception of the pharmacist in-charge, are rotated in the area for a period of 6 to 9 months; a total of eight different clinical pharmacists provided HOMR services in 2012.

The HOMR consisted of:

- an assessment of all current medications taken by the patient
- gathering relevant information from the patient's record (electronic hospital notes, hospital pharmacist medication profiles, GP summaries, community pharmacy record)
- a comprehensive interview with the patient in his or her home environment (approximately 60 min in duration), which included identification of any patient concerns and MRPs. Examples of MRPs included unnecessary or inappropriate prescribing, dosing issues, medicine interactions, regimen complexities, under-prescribing, monitoring deficiencies or adherence issues. Where appropriate, any identified issues were resolved and education was provided to the patient and/or carer.

A report (using a standardised format) on the findings from the HOMR regarding medication compliance, actions taken, identified MRPs and recommended strategies to manage these problems, was faxed to the patient's GP, any relevant specialists and the patient's nominated community pharmacy, usually on the same day as the visit. If a patient had more than one GP, the report was faxed to each practitioner. All reports were scanned electronically into the hospital scanned medical record (SMR) and were accessible to any Monash Health healthcare provider.

Patient Feedback

Patient perceptions of the pharmacist's visit and the HOMR were determined using a self-administered, paper-based questionnaire (Figure 1). The questionnaire asked questions pertaining to the HOMR; for example, the patients' prior willingness to have a medication review in their homes, whether they felt the visit was worthwhile, if the review helped them better understand how their medications relate to their medical conditions and if they felt more confident and less confused about their medications following the review. The questionnaire asked patients to give their views about these questions on a 4-point scale, which included the following options: 'Yes very much', 'Yes partly', 'Unsure' or 'No'. It also invited patients to provide comment on the overall service or offer suggestions to help improve the service. At the conclusion of the home visit, the questionnaire, together with a stamped, self-addressed envelope was given to each patient to complete. To facilitate participation in the feedback process by patients with limited English, the questionnaire was translated into various common languages (Italian, Greek, Arabic, Russian and Chinese) by professionally accredited translators within Monash Health. Participation in the survey was voluntary. There was no follow-up to enhance response rate.

General Practitioner Feedback

The HOMR report and GP feedback questionnaire were both transmitted to the patient's GP via facsimile. The GP questionnaire explored the patient's perspectives on whether the report aided his or her understanding of any recent medication changes following recent hospitalisation and the rationale behind these changes and on how the patient was managing his or her medications at home (Figure 2). It also asked about recommendations made by the pharmacist regarding MRPs identified during the HOMR and whether they were appropriate to adopt. The questionnaire also invited GPs to provide comments on how the service or report could be improved. Each returned questionnaire was identifiable by a unique patient hospital identification number and could be linked to the relevant patient report if any follow-up was required. Participation in the GP questionnaire was voluntary and there was no follow-up to enhance response rate.

RESULTS

A total of 487 HOMRs were conducted in 2012. There was an even distribution of males to females receiving a HOMR (49.7% male, 50.3% female). The mean age of all participants was 72.8 ± 14.1 years (range 15 to 97 years).

The majority of patients resided at home with family (68%, $n = 331$) and 25.5% ($n = 124$) lived at home alone. Approximately half of all patients (49.9%, $n = 243$) stated that they had no carer, whereas 45.2% ($n = 220$) of patients had a family member, friend or professionally employed carer to assist with activities of daily living and/or medication management.

Patients originated from a variety of countries with various spoken languages. About 112 (23%) patients who received a HOMR ($n = 487$) required the assistance of an interpreter; the most common languages were Greek (49.1%), Italian (13.4%) and Dari (12.5%).

Patients who received a HOMR reported a range of medical conditions, with the most common being congestive heart failure, chronic obstructive pulmonary disease and ischaemic heart disease.

Out of 740 referrals, 253 patients were deemed ineligible to receive a HOMR during the study period in 2012 (Table 1). The most commonly identified reason for exclusion was refusal to provide consent for a home visit (51.8%). Possible reasons for refusing to engage

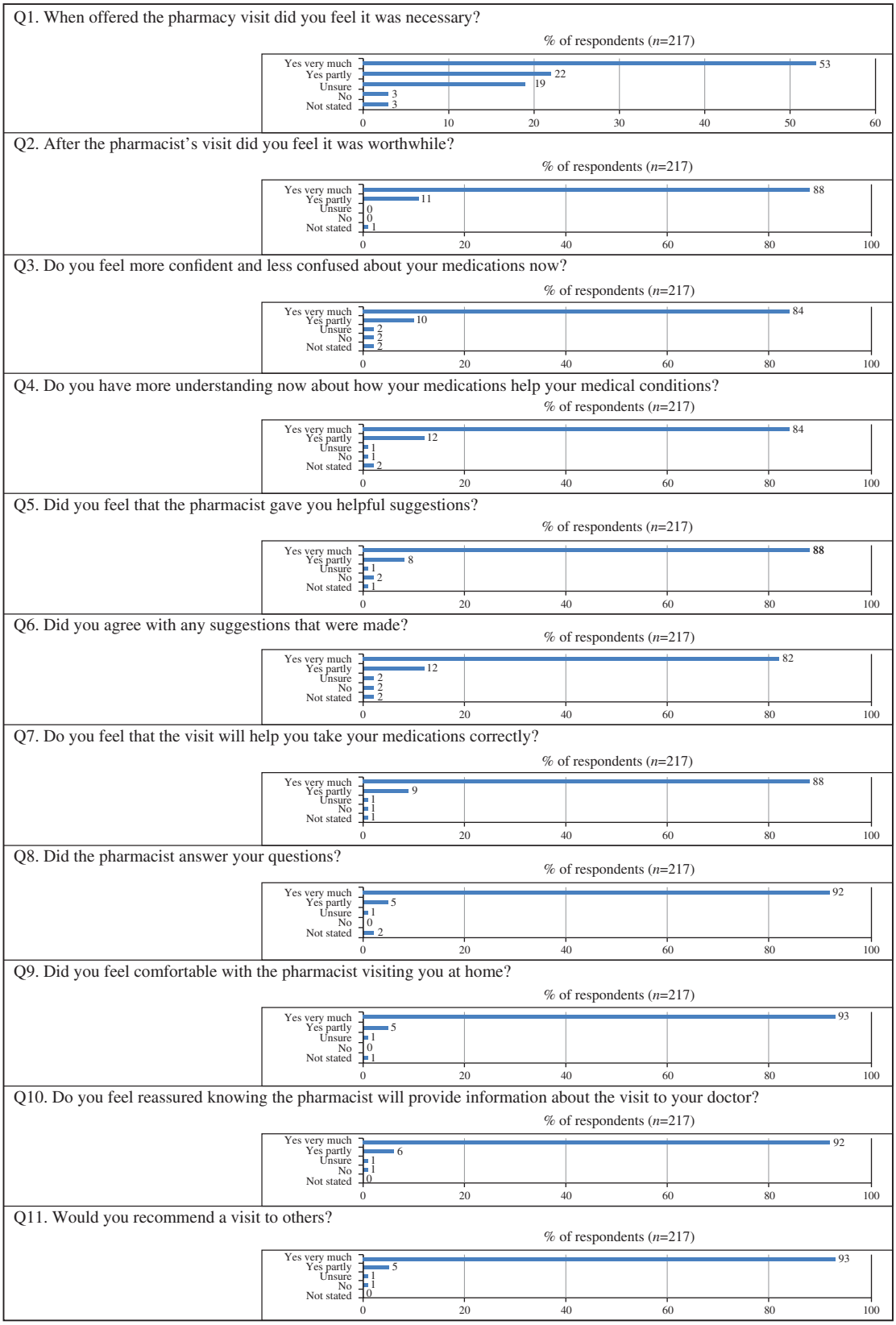

Figure 1 Patient feedback results.

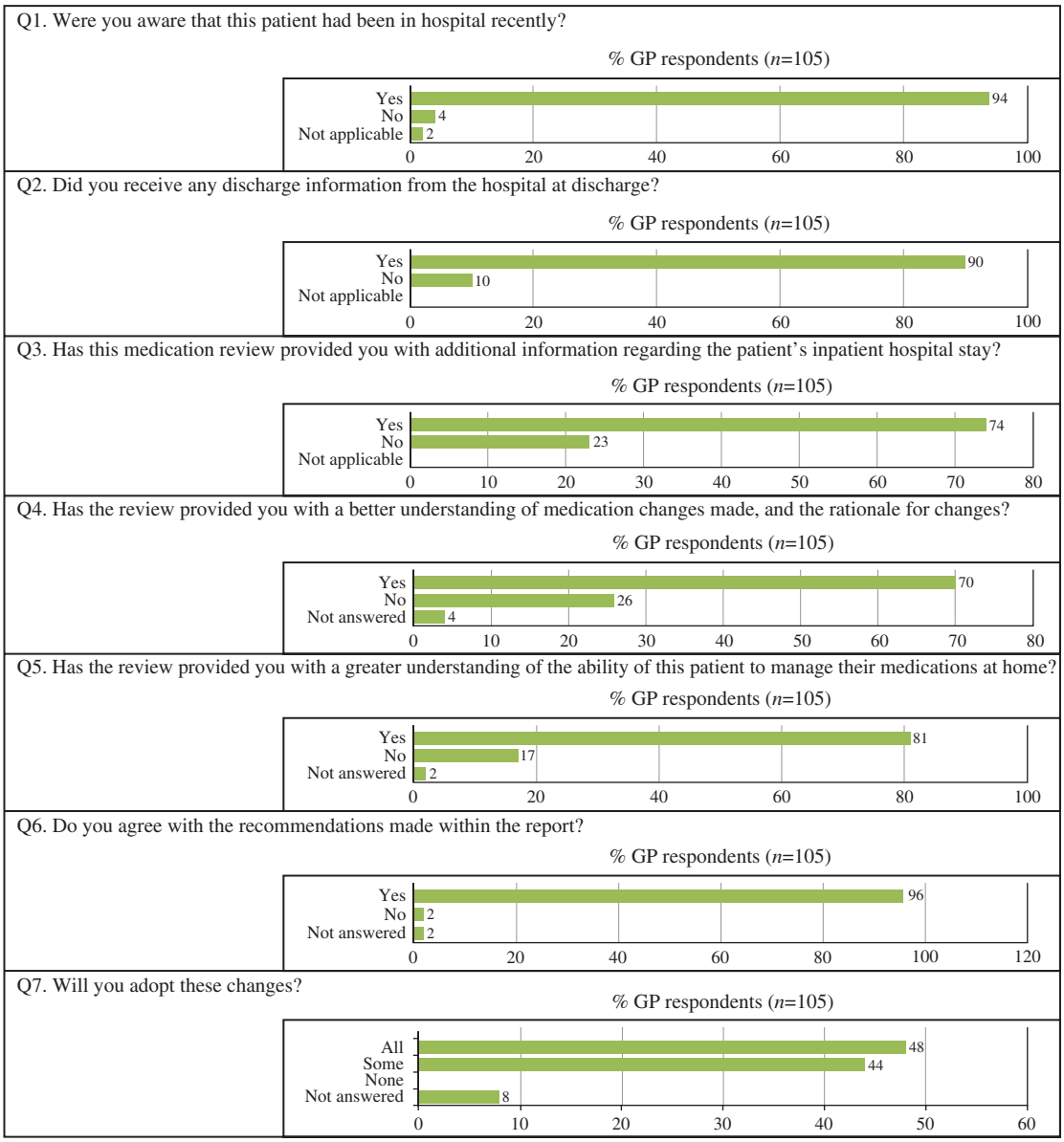

Figure 2 General practitioner feedback results.

in the service may have included the perception that there would be no benefit from a pharmacist visiting their home, a loyalty to their GP or community pharmacist or concerns regarding privacy and safety. In addition, 11.8% of patients could not be contacted, 11.1% had deceased before a HOMR could be scheduled, 9.5% were discharged to a support facility and 9.2% fell outside the catchment area.

Feedback from Patients Who Were Recipients of the HOMR Service

Of the 487 patients who received a HOMR in 2012, 217 (45%) returned feedback forms. Many patients (22% of 217 respondents) indicated they were initially unsure (19%) or did not feel the home visit was necessary (3%). However, once the visit had been completed, 99% of respondents indicated it was worthwhile (very much (88%) and partly (11%)). Patients indicated that they had an improved knowledge and understanding of their medications as a result of the HOMR; 84% of respondents indicated that they felt very much more confident and less confused about their medications and 84% indicated they had a greater understanding about how their medications help their medical conditions. About 88% of respondents felt that the pharmacist provided helpful suggestions for medication management and that the visit would enable

Table 2 Sample comments from patients and general practitioners (GPs) about the Hospital Outreach Medication Review (HOMR) service

Patient comments
The pharmacist was very patient and answered all our questions. He was very helpful and gave us very valuable advice. I hope other people will make use of this service.
We are very grateful for this service and any other services that would help me and my family better manage my diabetes.
This service of excellence keeps a bed free in hospital for one person in greater need.
It has given me more strength and confidence.
I feel I have more knowledge and confidence about the medications I am taking. The visit was the best thing I have done in years. The advice I received was sensational. I would highly recommend.
This was a very beneficial visit as it resolved issues with my tablets and provided information and confidence with taking my medications.
Very informative and empowering to patients.
Routine scheduled visits would be beneficial.
The pharmacy visit will be more helpful if it was within 1 week to reassure that the patient is taking the correct dose.
GP comments
Excellent service.
Well done, a comprehensive report and great service.
The first Hospital Outreach Medication Review I received in my 1.5 years as a GP here. Would be good if more patients received this beneficial service.
Quite comprehensive and useful.
Good thoughtful review.
Continue preparing these reports.

them to take their medications correctly. A summary of the responses from patients is shown in Figure 1. Responses from patients were overwhelmingly positive, often commenting on the professionalism of the pharmacist and the self-empowerment the visit provided (Table 2). Guiding patients on the timing of doses and introducing medication administration aids were identified by many patients as essential in aiding their confidence and understanding. Two patients commented on the need to ensure that the service is delivered in a timely manner so that issues can be addressed during the critical post-discharge period. Other patients requested regular follow-up visits to provide ongoing confidence and support with their medications.

General Practitioner Feedback

In all 115 GPs of 487 (21.6%) who received a faxed feedback form together with the HOMR report responded to the General Practitioner Feedback Form. The results are outlined in Figure 2. Most GPs who provided feedback (94%, $n = 99$) were aware that their patient had been in hospital and 10% ($n = 11$) indicated they did not receive any discharge information from the hospital. The 96% ($n = 101$) of GPs who responded indicated they agreed with the recommendations made in the HOMR report. Overall 92% indicated they would adopt either some (44%, $n = 46$) or all (48%, $n = 105$) of the recommendations made. In all 81% ($n = 85$) indicated the review provided them with a greater understanding of patients' abilities to manage their medications at home (Figure 2).

Responses from GPs tended to be positive, suggesting they recognise the benefit of a medication review in the patient's home. Several responders indicated that it would be 'good if more patients could receive this beneficial service' and be made aware that it was available. The positive response from GPs is reinforced by some of the comments in Table 2.

When invited to provide comment on any service improvements, one GP of the 105 indicated that the service was more beneficial to the patient rather than to themselves. Another thought that it duplicated their work. The importance of prompt delivery of a hospital discharge summary was raised by a number of GPs ($n = 8$).

DISCUSSION

Responses from GPs suggest they were receptive to the additional information provided regarding the patient's inpatient stay as it gave them an improved understanding of the associated medication changes and the rationale for these changes. The overwhelming majority of GPs agreed to adopt the recommendations made in the reports, highlighting the valued role of having an independent person review a patient's medications and support clinical decision-making. The hospital outreach pharmacists were uniquely placed to resolve and clarify any medication-related therapy problems as they had access to a patient's complete hospital admission history. Their experience allowed them to provide targeted, relevant information to the GPs. Direct communication with the appropriate treating unit, either before or after the HOMR, was likely to occur as necessary. This allowed the HOMR pharmacist to clarify and feedback any important medication-related issues to the patient's GP and members of the healthcare team.

Assessing how patients manage their medications in the home environment often provides the opportunity to obtain a realistic insight into the patient's ability to manage his or her medications independently. This view was supported by 81% of GP respondents, who agreed that the

home visit helped increase their understanding of how the patient was managing his or her medications at home. Improving the quality of information disseminated to GPs at discharge helps pharmacists meet their obligation in ensuring continuity of care in line with the Australian Pharmaceutical Advisory Council's 'Guiding principles to achieve continuity in medication management'.[10] Overall, responses from GPs seem to recognise the potential benefit of integrating an outreach pharmacist into the primary care setting.

Many of the concerns that were raised by GPs were related to the inadequate information relayed to them by the treating unit immediately following the discharge of the patient from hospital. Transmission of prompt discharge summaries, including medication changes, is paramount in ensuring continuity of care in the community setting.[10] In this study, we have been able to demonstrate that outreach services are appropriately placed to help bridge this information deficit. This, however, relies on the timely delivery of such services amidst limited resources and increasing demand on the public health sector.

Patients had an overwhelmingly positive view of the value of the HOMR service (Figure 1), and frequently commented on the professionalism of the pharmacist and the self-empowerment the visit provided. Patients almost unanimously agreed that the medication review provided a greater understanding of their medications and improved their confidence in self-management of their medications. These findings are comparable to a similar study by Carter *et al*. in 2012 who found that overall 91% of recipients were satisfied with the Home Medicines Review service. We also found that most patients were reassured that the pharmacist would provide their GPs with information about the HOMR visit. The testimonies highlight the considerable gains that can be made in improving the quality use of medications in an environment that is conducive to information sharing and education. It also illustrates the importance of the collaborative and interdisciplinary component to patient care between pharmacists, GPs and other members of the healthcare team.

Medication review services seek to improve medication adherence and the quality use of medications but they also:

- involve patients in making decisions about proposed changes to their treatment[11]
- help patients to better manage their medication by improving the patients' knowledge and understanding about their medications
- simplify dosage regimens
- minimise MRPs by helping patients to recognise MRPs and to seek help if they experience any problems,[12]
- promote good communication between the healthcare professionals involved in the patient's care[12]
- help patients make informed decisions about their health.[13]

Medication review services are provided by pharmacists as a collaborative, proactive service to prevent further or unnecessary MRPs and morbidity and reduce unnecessary presentations to emergency departments or admission to hospital.[1,14]

The Cochrane Collaboration has recently published global research on the different interventions that can improve the safe and effective use of medications. The review makes specific comment on the international evidence supporting pharmacists providing 'medicines reviews (with positive effects on medicines adherence and use, medicines problems and clinical outcomes) and pharmaceutical care services (consultation between pharmacist and consumer to resolve medicines problems, develop a care plan and provide follow-up; with positive effects on adherence and knowledge)'.[11,15]

Despite the widespread acceptance for a HOMR among patients referred to the service, there were a total of 131 patients who refused to provide consent for a home visit. Reasons for refusing to engage in the service were varied, but included a perceived loyalty to their GPs, pride and autonomy, privacy and safety concerns. This perhaps illustrates inadequate promotion or understanding of the service. Some patients find it difficult to see the potential benefits that can be gained from a HOMR, possibly due to the lack of understanding about the clinical role of a pharmacist. Studies have shown that patients who typically refuse a medication review service are more often in need of the service (i.e. culturally and linguistically diverse, the aged and Indigenous Australians).[16] Patients from a culturally and linguistically diverse background are reported to have twice the rate of medication errors when compared to individuals who have English as a first language.[17] This may in part be due to language barriers, as well as cultural variations in perceptions towards medications. Refining communication and improving promotion of the service by educating patients and their GPs about the potential benefits of a medication review is paramount in obviating some of these barriers.

A total of 217 of 487 (45%) patients who were recipients of a HOMR responded to the questionnaire. This is a greater response rate than the quantitative research conducted by Carter *et al*. in 2012, which observed a 31% response rate.[18] It was expected that patients were more likely to respond to the patient questionnaire if they reported positive experiences with the HOMR service. The anonymity of the questionnaire aimed to avoid some of this response bias, but it did not curtail it entirely. Indeed

one of the limitations of this study was the inability to distinguish between responders and non-responders and their various characteristics. Patients who may have been least likely to respond may have suffered from greater comorbidities, had significant language barriers or were visually impaired. Establishing their various views on the service will be a valuable part of any future work in this area. The low response rate (22%) seen by GPs could be attributable, in part, to time constraints. Due to the voluntary nature of the feedback process, we would also expect a bias towards the extremes of a positive or a negative view of the service. Future research will seek to explore some of the views held by both patients and GPs who did not participate in the feedback process and address any potential response bias. Follow-up telephone calls may be a means of achieving this. We also aim to explore some of the barriers to participation so that service improvements may be made and targeted education be provided in future.

CONCLUSION

Overall, this study highlights the positive views shared among many patients and their GPs towards the HOMR service offered by the Monash Health Pharmacy Department. It also demonstrates the gains that can be realised by collaborative efforts among members of the healthcare team, in order to achieve the rational, safe and effective use of medications. The feedback received from both patients and their GPs indicates that there is a strong belief that the HOMR provides a valuable service and fills an existing gap in patient care. This suggests that there are positive benefits in promoting and developing HOMR services by hospitals.

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Competing interests

None declared.

ENDNOTES

1. Internal data, to be published.

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APPENDIX

Hospital Admissions Risk Program
HOSPITAL OUTREACH MEDICATION REVIEW SERVICE

For Office Use Only	**DC / OP**
Pharmacist Profile Faxed □ Original □	M.R. Request □ Date Req _____
Discharge Script □ Merlin printout □	Discharge Summary □
Referrer client information CIC/other □	Report in MR □ HMS database □ 02/08

HOMR Referral/Risk Assessment Tool

Attach Bradma Label here:
UR:_____
Name:_____
Address:_____
_____
Tel: _____ DOB:_____

Expected discharge date: ____/____/____
Discharge destination: _____
Referrer: _____
Referrer role: _____
Contact Details: _____
Referral date: _____
Recruitment date: _____

Tick criteria which apply. One or more ticks qualifies for a referral

□	Lives alone and manages own medications	□	History of non-compliance (deliberate or unintentional)
□	Recent medication changes	□	Concerns regarding carer ability to manage medications appropriately
□	Multiple Medications (≥4 regular medications/day)	□	Cognitive/intellectual impairment and managing own medications
□	Recent hospital admission	□	Language/Cultural barrier or beliefs
□	Chronic disease (cardiovascular, respiratory, diabetes, other)	□	Falls risk (potential or documented)
□	Taking a drug requiring dose modification (eg. warfarin, insulin, prednisolone, antiepileptics)	□	Cannot read dispensing labels/impaired vision
□	Use of High Risk Drugs (eg NSAIDS, benzodiazepines, opiates)	□	Renal impairment (<30ml/min) or Hepatic impairment (>3x normal LFTs)
□	More than one GP, no GP, multiple pharmacies	□	Other eg; suspect a problem may exist

Additional information:

Signature: _____ Date: ____/____/____

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RESEARCH ARTICLE

The impact of a hospital outreach medication review service on hospital readmission and emergency department attendances

Mary Hanna, B.BiomedSc(Hons), BPharm(Hons), GradCertPharmPract[1], Ian Larmour, FSHP, BPharm, MSc(Pharmacology)[1], Sally Wilson, BPharm, GradDipHospPharm, PhD[2], Karen O'Leary, BPharm[3]

1 Department of Pharmacy, Monash Health, Melbourne, Australia
2 Research into Practice Pharmacist, The Society of Hospital Pharmacists of Australia, Melbourne, Australia*
3 Policy and Projects Manager, The Society of Hospital Pharmacists of Australia, Melbourne, Australia

Abstract

Background: The Monash Health Hospital Outreach Medication Review (HOMR) service is a pharmacist-led service that targets patients at high risk of medication misadventure in the immediate post-discharge period.
Aim: To study the impact of a HOMR service on emergency department attendances and hospital admissions within an Australian hospital network.
Method: Information was collected on the total number of emergency department attendances and hospital admissions during the 12-month period prior to, and after, the date a HOMR service was provided to the study group between 1 January 2012 and 22 November 2012. This was compared to a control group who were referred to the service and were eligible, but rejected the service. Patients were stratified by age (≤50, 51–65 and >65 years) to determine any age-related variations and tõhen investigated excluding regular, planned admissions (dialysis, chemotherapy or transfusion-related).
Results: The 398 patients in the study group had a total of 1691 admissions in the 12-month period pre-HOMR. The total number of admissions in the 12-month period post-HOMR was higher than during the pre-HOMR period for both the control and study groups. When an age subanalysis was conducted and regular planned admissions were excluded, patients aged 51–65 years exhibited a 25% reduction in hospital admissions ($\chi^2 = 6.14$, $p < 0.05$). There was no significant reduction in admissions for the other age groups or in emergency department attendances.
Conclusion: The provision of HOMR outreach services has a valuable role to play in a clearly identified population that is at high risk of medication misadventure.

Keywords: HOMR, medication review, HMR, outreach.

BACKGROUND

Medication misadventure leading to unplanned hospital admissions constitutes a significant public health burden. Medication misadventure, defined as a medication error, adverse event or inappropriate use of a medicine, contributes to increased healthcare costs and poor quality of life. An earlier prospective study conducted within the Monash Health network looked at adverse drug reactions as a cause of hospital-related admissions and found that 1.6% of admissions were attributable to medication-related adverse events.[1] A number of reviews examining medication safety in Australia collectively report that approximately 2–3% of hospital admissions are medication related.[2] Variations in such studies often reflect different methodologies and patient categories. This figure rises considerably to 30% among the elderly population and may be preventable in many cases.[3–7]

There are many elements of the medication process that contribute to medication misadventure. The Australian Commission on Safety and Quality in Health Care identifies recent discharge from hospital as a significant risk for medication-related adverse events.[8] The number of errors that occur during the transfer of care are especially high.[9] Inadequate communication to patients and primary healthcare providers is found to be a common contributing factor.[10] Some reports indicate that up to 78% of general practitioners (GP) do not

Address for correspondence: Mary Hanna, Pharmacy Department, Monash Medical Centre, 246 Clayton Road, Clayton, Melbourne, Victoria 3167, Australia.
E-mail: mary.hanna@monashhealth.org

*Currently at Centre for Medicine Use and Safety, Faculty of Pharmacy and Pharmaceutical Sciences, Monash University, Parkville, Australia.

receive discharge summary information, and of those that do, 52–88% of summaries are reported to have errors.[11] Furthermore, hospitalisation and discharge from hospital are critical junctures at which multiple medication changes are made, treatment options are re-evaluated and ongoing monitoring of therapy is required. This increases the risk of medication-related harm during the immediate post-discharge period[12] and highlights the need for strategies that aim to reduce preventable medication-related harm.

The *Guiding Principles to Achieve Continuity in Medication Management*, developed by the Australian Pharmaceutical Advisory Committee, aim to address the issue of 'continuity in medication management' as patients transition from one episode of care to another.[13] The guiding principles highlight the obligations of health professionals to practice in a collaborative manner in order to enhance patient care. Home medication reviews are an example of how pharmacists can facilitate a seamless transition from the hospital to the home by reviewing medication therapy and providing education, communication and support to patients. Early evidence supporting the benefits of a pharmacist-led 'education outreach service' emerged from a study conducted by Alvarez *et al*. in 2001,[14] as part of a Commonwealth Department of Health and Aged Care national coordinated care trial, aimed to test new models of healthcare funding and delivery. This study examined ways in which a hospital pharmacy could support GPs and patients during the post-discharge period via a variety of program initiatives, including follow-up patient education and medication reviews. The experience gained in this study offered an insight into the valuable contribution hospital pharmacists could make in promoting the rational, safe, effective and economic use of medications. The Medication Alert Project subsequently commenced as part of a collaboration of four hospitals in Melbourne, Australia, between February 2004 and June 2005, which aimed at reducing medication-related hospital readmissions.[15] The project was funded by the Victorian government as part of its Hospital Admission Risk Program, and its success has led to the establishment of a well-defined Hospital Outreach Medication Review (HOMR) service at Monash Health. Alongside this has been the development of the Home Medicines Review (HMR) Program in the community setting, which was introduced by the Australian Government through the Department of Health and Ageing in 2001.[16] The medication review is seen as a tool to deliver a structured evaluation of a patient's medications, with the aim of optimising the use of medications, providing information and continued education.

The evidence supporting the benefits of home medication reviews continues to expand,[17,18] and medication reviews are now a funded non-admitted patient service in Australia's public hospitals (provided in an outpatient clinic or as an outreach service).[19] Studies have demonstrated a capacity for such services to identify and resolve pharmaceutical care issues as well as improve patient medication knowledge and adherence.[20] However, many questions remain as to whether such interventions have a significant impact on patient outcomes, such as reducing mortality and unplanned hospital admission rates. This paper studies the impact of the Monash Health pharmacist-led HOMR service on the utilisation of acute health services, namely emergency department (ED) attendances and combined hospital admissions. It is one of two papers that aim to demonstrate key interventions, canvass the viewpoints from key stakeholders and determine whether such a service meets its key objective of improving patient outcomes.

METHOD

Study Design and Participants

This study was conducted across all sites of Monash Health, a major metropolitan health network that provides health care in the southeast region of Melbourne, Victoria. Monash Health consists of six hospitals and more than 2216 acute, sub-acute, mental health and aged care beds. The study was undertaken during 2012 as part of the normal services provided by the pharmacy department through the HOMR service.

All personal information was handled in accordance with the Information Privacy Act 2000 and the Health Records Act 2001. Approval for this continuous quality improvement activity was granted by the Monash Health Human Research and Ethics Committee.

Patients were identified as being at risk of medication-related problems through a standard risk assessment tool that was developed through literature review and local expert consensus. Concern regarding the patient or carer's abilities to manage medications combined with one other risk factor listed in Table was used to determine patients at risk of medication-related problems. These included, but were not limited to, patients who had a history of non-adherence, identified language/cultural barriers, multiple medications (≥4 medications/day) or patients who had a chronic disease (where 50% do not take their medications as prescribed). There is also a higher risk of medication-related problems in patients who see multiple doctors or who have multiple conditions and do not have a regular doctor.[21] A referral for a HOMR could be activated by any healthcare provider within the hospital network. The outreach pharmacist reviewed the patient's medical

Table 1 Eligibility criteria for a Hospital Outreach Medication Review (HOMR)

Inclusion criteria (concerns regarding carer or patient's ability to manage medications independently plus *one* other risk factor listed below)	Exclusion criteria
Lives alone and manages own medications	Patient declined HOMR
Recent medication changes	Safety risk
Multiple medications (≥4 regular medications/day)	Other appropriate services in place
Recent hospital admission	Unable to contact
Chronic disease (cardiovascular, respiratory, diabetes, other)	Low risk (<4 medications)
Taking a medication requiring dose modification	Resides in long-term care facility
Use of high risk medications	Palliative (life expectancy <1 year)
More than one GP, no GP, multiple pharmacies	Outside 20 km catchment area
History of non-compliance (deliberate or unintentional)	
Cognitive/intellectual impairment	
Language/cultural barriers or beliefs	
Falls risk (potential or documented)	
Cannot read dispensing labels/impaired vision	
Renal impairment (creatinine clearance <30 mL/min) or hepatic impairment (>3 × normal liver function tests)	
Other (e.g. suspect a problem may exist)	

record to verify eligibility (Table 1) and verbal consent was required prior to each visit. Patients who were considered to be a safety risk using a safety risk assessment tool received a review on hospital premises where appropriate. Patients deemed to be at a low risk of medication misadventure (i.e. taking < 4 medications) received a telephone review and were not included in this study. Patients who fell outside the catchment zone (>20 km) were referred to their GP for a community-based HMR. Professionally accredited interpreters were employed to facilitate communication if any language barriers were identified.

The Intervention

A HOMR was delivered by registered pharmacists at Monash Health who have a minimum of 3 years hospital clinical pharmacy experience. There are 3.0 full-time equivalent pharmacists working within the service, namely a senior pharmacist in-charge and two clinical pharmacists. All clinical pharmacists, with the exception of the pharmacist in-charge, are rotated to the area for a period of 6–9 months; this forms an integral component of the clinical pharmacists training program at Monash Health. All pharmacists were required to complete a general-level competency framework to ensure ongoing development of their competencies by self-directed and problem-based learning, in line with the original concept of Clinical Pharmacy Peer Review developed by Larmour *et al*.[22]

The HOMR involved three main components: (a) an assessment of all current medications taken by the patient; (b) gathering of relevant information from the patient's medical record (electronic hospital record, medication profiles compiled by ward pharmacists, GP summaries, community pharmacy records); and (c) a comprehensive, structured interview with the patient in their home environment (approximately 60 min duration), which involved the identification of any medication-related problems (MRPs). Where appropriate, any identified MRPs were resolved during the visit and education was provided.

A report on the findings from the medication review regarding medication adherence, actions taken and medication management goals (using a standardised format) was faxed to the patient's GP and community pharmacy, usually on the same day of the visit. The report was also scanned electronically into the hospital's scanned medical record.

The risk of medication misadventure is known to be high in the immediate post-discharge period, usually within 7–10 days.[23] We aimed to facilitate each visit within 10 days of hospital discharge or receipt of referral. Patients who were assessed subjectively as being at very 'high risk' of medication misadventure (e.g. recurrent admissions related to medications, patients who discharge against medical advice) had their review expedited within 5 days.

Hospital Utilisation Data

Hospital utilisation data were obtained from the Monash Health patient administration computer database with assistance from data analysts. Information on acute

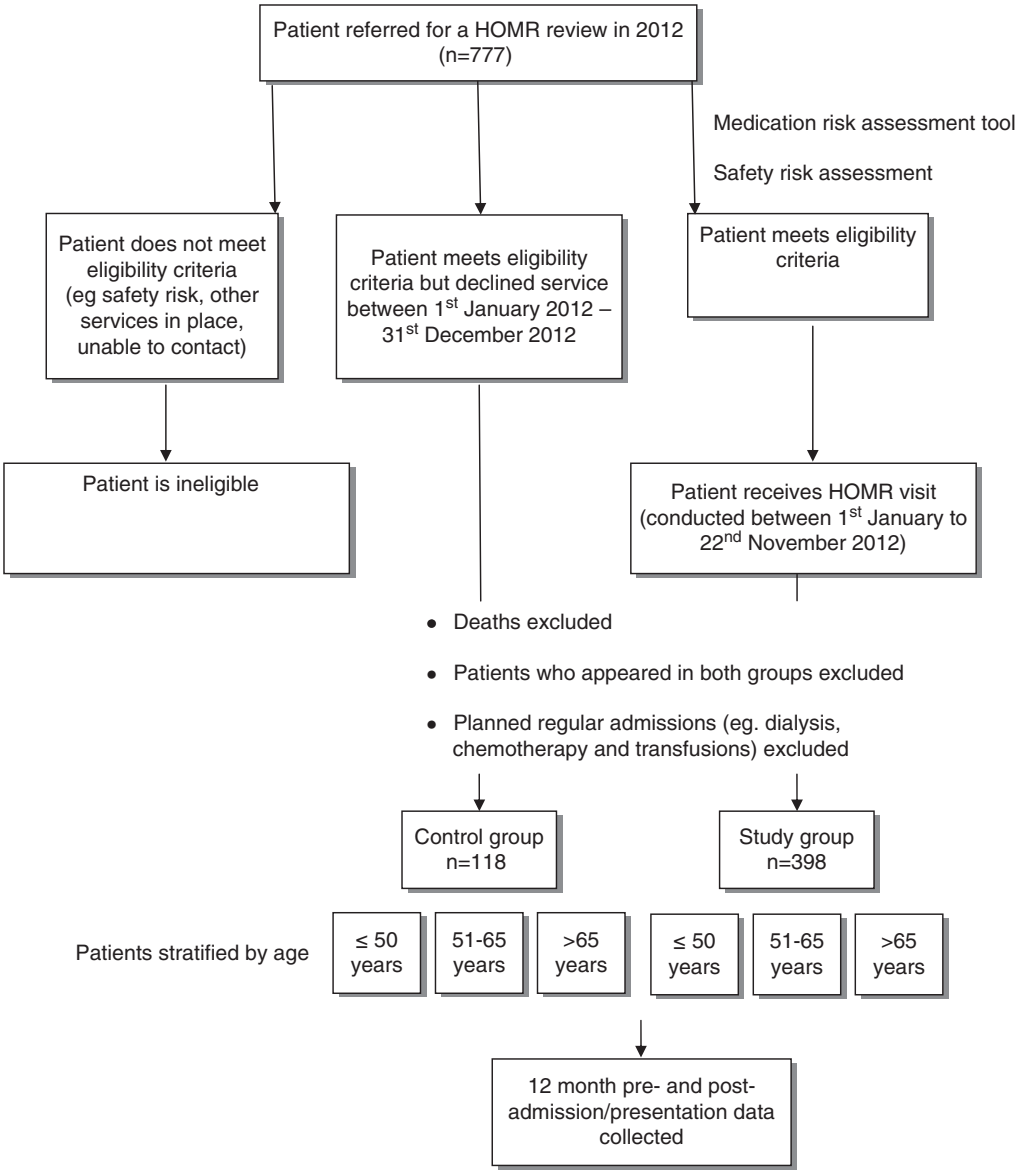

Figure 1 Recruitment of patients for study.

health service utilisation was collated for all patients who were recipients of a HOMR between 1 January 2012 and 22 November 2012 and compared to a control group consisting of patients who were referred to and were eligible for the service but who rejected the service between 1 January 2012 and 31 December 2012. Patients were stratified into specific age categories (≤50 years; 51–65 years and >65 years), and admission rates were reanalysed to determine whether age was an independent predictor of benefit (as measured by reduced admission rates) from a HOMR (see Figure 1). Information was collected on the total number of emergency department attendances and hospital inpatient admissions during the 12-month period prior to, and after, the date of the HOMR (study group) and date of rejection (control group). Patients who died during the study period or who appeared in both study and control groups were excluded from the analysis.

Patients who required regular admissions as part of their planned and regular care (e.g. patients requiring dialysis, chemotherapy and transfusions) were assigned specific diagnosis-related codes (DRGs): haemodialysis (L61Z), chemotherapy (R63Z) and red blood cell

disorders (Q61B); a HOMR would unlikely influence their attendance at a hospital, and these patients were identified and assessed as a separate cohort.

A chi-squared test was carried out at the 5% significance level to determine change in hospital admission data. The software package, SPSS statistics (version 22.0), was used for the analysis.

RESULTS

Participants

A total of 777 patients were referred to the HOMR service during the period 1 January 2012 to 31 December 2012 (Table 2). Referrals for a HOMR were received from a variety of acute and sub-acute settings across the health network. Over half (68.5%) the referrals were from the acute inpatient setting from either Clayton, Dandenong or Casey Hospitals. A total of 75 (9.7%) referrals was received from one of the emergency departments. Thirty-seven patients remained on the waiting list for a HOMR and were followed up in 2013 (awaiting discharge, respite, rehab, contact). Therefore, the adjusted number of referrals in 2012 (patients who were referred and either received the service (487) or were excluded (253)) was 777–37 = 740 patients.

Of a total of 740 referrals, 487 home visits (66%) (adjusted) were conducted in 2012. There was an even distribution of males to females among patients receiving a HOMR (49.7% males, 50.3% females) (Table 3). This compared to the control groups, which comprised 45.8% males and 54.2% females. The mean age of patients receiving a HOMR and those who declined a HOMR was 72.1±14.2 years and 73.7±13.3 years, respectively. The majority of patients receiving a HOMR resided at home with family (68%). Approximately half of all patients stated that they had no carer. Patients originated from a variety of countries with various spoken languages. One hundred and twelve patients (23%) in the study group required the assistance of an interpreter with the majority speaking Greek (49.1%), Italian (13.4%) or Dari (12.5%).

All eligible patients who received a HOMR reported a range of medical conditions: congestive cardiac failure (CCF), diabetes, chronic obstructive pulmonary disease (COPD) and ischaemic heart disease (IHD) were the most commonly recorded conditions.

Two hundred and fifty-three patients were deemed ineligible to receive a HOMR during the study period. The most commonly identified reason for exclusion was refusal to provide consent for a home visit (51.8%). Nine percent of patients fell outside the catchment area, 12% could not be contacted, 10% were discharged to a support facility and approximately 11% were deceased at the time of recruitment. Patients who died during the study period or appeared in both the study and control groups were excluded. The final study group comprised 398 patients and the control group comprised 118 patients.

Sixty-two percent of visits occurred within 10 days of discharge from hospital or referral, and 58% of patients who rejected a HOMR did so within 10 days of discharge. The similar percentages observed tend to suggest that the risk of medication misadventure is comparable between groups.

Impact of Home Medication Reviews on the Frequency of Hospital Readmissions and Emergency Department Attendances

Local admission data showed a total of 1691 hospital admissions for the study group in the 12-month period

Table 2 Hospital Outreach Medication Review (HOMR) referral source

Referral source	Total patient referrals 2012 ($n = 777$)
Inpatient hospital ward[†]	532 (68.5%)
Clayton hospital	339 (43.6%)
Dandenong hospital	189 (24.3%)
Casey hospital	4 (0.5%)
Emergency department	75 (9.7%)
Clayton hospital	67 (8.6%)
Dandenong hospital	8 (1.0%)
Referrals from other sources[‡]	170 (21.9%)

[†]Inpatient ward includes an admission into Clayton, Dandenong or Casey Hospitals. This may include an admission into a general or specialty ward, short-stay unit, intensive care or the acute assessment unit.
[‡]Referrals from other sources include outpatient clinics (any campus), Kingston hospital, Moorabbin hospital or patients enrolled under the Hospital Admission Risk Program.

Table 3 Characteristics of patients receiving a Hospital Outreach Medication Review (HOMR) in 2012

Characteristics	All HOMR patients visited between 1 January 2012 and 31 December 2012 ($n = 487$)	HOMR patients in study group[†] ($n = 439$)	Patient control group[‡] ($n = 131$)
Gender			
Male	242 (49.7%)	215 (49.0%)	60 (45.8%)
Female	245 (50.3%)	224 (51.0%)	71 (54.2%)
Mean age (years)	72.8±14.1 (range: 15–97 years)	72.1±14.2 (range: 15–96 years)	73.7±13.3 (range: 26–97 years)
Residence			
Home alone	124 (25.5%)	108 (24.6%)	21 (16.0%)
Home with family	331 (68.0%)	302 (68.8%)	48 (36.6%)
Other	24 (4.9%)	22 (5.0%)	3 (2.5%)
Not stated/inadequately defined	8 (1.6%)	7 (1.6%)	59 (45.0%) (Incomplete data)
Carer status			
Has a carer[§]	220 (45.2%)	209 (47.6%)	32 (24.4%)
Has no carer	243 (49.9%)	198 (45.1%)	25 (19.1%)
Not stated/inadequately defined	24 (4.9%)	32 (7.3%)	74 (56.5%) (Incomplete data)
Interpreter requirements			
Requiring an interpreter	112 (23.0%)	97 (22.1%)	11 (8.4%)
Not requiring an interpreter	372 (76.4%)	339 (77.2%)	60 (45.8%)
Not stated/inadequately defined	3 (0.6%)	3 (0.7%)	60 (45.8%) (Incomplete data)

[†]Study group: cohort of patients seen by a HOMR pharmacist between 1 January 2012 and 22 November 2012 (for analysis of hospital admission data).
[‡]Control group: cohort of patients who were referred to the HOMR service but rejected the service between 1 January 2012 and 31 December 2012 (for analysis of hospital admission data). Incomplete data collected on place of residence, carer status and interpreter requirements.
[§]Having a carer refers to a family/friend/relative who assists with activities of daily living (ADLs) or medication management. Home visits were scheduled around carer availability where practicable.

preceding the HOMR. This increased to 1850 admissions in the 12-month period post-HOMR (Table 4). A similar increase in admissions was seen within our control group from 798 to 913 over the study period.

Once regular, planned admissions such as those for dialysis, chemotherapy or transfusions were excluded, an age sub-analysis was performed to determine any impact of a HOMR on hospital readmission rates. Patients who were 50 years of age or under showed a significant increase in hospital admissions following a HOMR compared to the control group (Table 4). Patients aged between 51 and 65 years had a 25% reduction in hospital admissions from 200 to 150 compared to the control group, which showed an increase in admissions from 77 to 92 ($\chi^2 = 6.14$, $p < 0.05$). There was a similar trend in patients aged over 65 years, but this was not statistically significant. It is worth noting that only two patients in the 51–65 year age category died during the study period (one from heart failure and the other from a variceal bleed secondary to ethanol).

There was a reduction in emergency department attendances for both the control and study groups, but there was no statistically significant difference between the two cohorts (Table 4).

DISCUSSION

Pharmacist-led hospital outreach medication review services have the capacity to identify and resolve MRPs in the immediate post-discharge period. The current study suggests that a HOMR appears to be associated with a

Table 4 Total number of hospital inpatient admissions and emergency department attendances in the 12-month period pre- and post-Hospital Outreach Medication Review (HOMR)

Hospital inpatient admissions									
	Study group†				Control group‡				
	Number of patients (*n*)	Pre-intervention admissions (observed and expected) (*n*)	Post-intervention admissions (observed and expected) (*n*)	Difference (%)	Number of patients (*n*)	Pre-referral admissions (observed and expected) (*n*)	Post-referral admissions (observed and expected) (*n*)	Difference (%)	p-value (between study and control groups)
Total	398	1691 1678.13	1850 1862.87	+9.4%	118	798 810.87	913 900.13	+14.4	$\chi^2 = 0.58$ $p = 0.45$
Total excluding regular, planned admissions (DRGs L61Z, R63Z, Q61B)									
≤50 years	31	140 168.08	376 347.92	+168.6%	8	46 17.92	9 37.08	−80.4	$p < 0.0001$ $\chi^2 = 72.25$
51–65 years	76	200 186.8	150 163.2	−25%	21	77 90.2	92 78.8	+19.5	$p < 0.05$ $\chi^2 = 6.14$
>65 years	287	783 793.14	481 470.86	−38.6%	89	226 215.86	118 128.14	−40.7	$p = 0.20$ $\chi^2 = 1.63$
Emergency department attendances									
	Study group†				Control group‡				
	n	Pre-intervention attendances (observed and expected) (*n*=)	Post-intervention attendances (observed and expected) (*n*=)	Difference (%)	*n*	Pre-referral attendances (observed and expected) (*n*)	Post-referral attendances (observed and expected) (*n*)	Difference (%)	p-value (between groups)
Total	389	1057 1069.58	690 677.42	−34.7%	115	274 261.42	153 165.58	−44.2	$p = 0.16$ $\chi^2 = 1.94$
≤50 years	25	70 70.95	44 43.05	−26.0%	8	19 18.05	10 10.95	−47.4	$p = 0.68$ $\chi^2 = 0.17$
51–65 years	77	280 280.87	150 149.13	−46.4%	21	59 58.13	30 30.87	−49.2	$p = 0.83$ $\chi^2 = 0.05$
>65 years	357	847 852.52	536 530.48	−36.7%	86	196 190.48	113 118.52	−42.3	$p = 0.47$ $\chi^2 = 0.51$

NB = emergency short-stay admissions are reported as inpatient admissions.

†Study group refers to patients who received a HOMR between 1 January 2012 and 22 November 2012.

‡Control group consists of patients who were referred to and were eligible for a HOMR but rejected the service between 1 January 2012 and 31 December 2012. A total of 19 patients died in the study group, and three patients died in the control group in the 12 months post-intervention or referral; these patients were excluded from the analysis. Patients who featured in both the control and study groups ($n = 6$) were also excluded. Patients who appeared in either the study or control group on more than one occasion had their readmission dates counted from the time of initial presentation or referral.

25% reduction in hospital readmissions in patients aged between 51 and 65 years of age. Further research is required to confirm this apparent benefit. There was a similar trend in patients aged over 65 years who were in the study and control groups, but this was not statistically significant. While there may be some benefit from delivering a HOMR service to this age group, there may be other factors contributing to this observed result which warrant further investigation; these may include the influence of other chronic disease management programs, admissions that are not related to medication use, or the complexity of disease or disease progression that is not solely influenced by the benefits of a HOMR. This is in contrast to patients aged between 51 and 65 years of age who may be in a better position to undertake their own medication management and therefore maximise the benefits of a HOMR. We were unable to demonstrate a similar benefit in patients who were 50 years of age or under. While this may be a reflection of attitudinal differences in the younger age group, it is difficult to come to a conclusion given the limited sample size.

A recent study by Roth *et al*.[24] reported the impact of an individualised medication assessment and planning program embedded into a primary care practice. Patients received comprehensive medication therapy management at repeated intervals over a 6-month period by a clinical pharmacist. Their study demonstrated a significant reduction in the number of MRPs for patients participating in the program and a comparable reduction in acute health services utilisation of 35%. While it may not be possible in many cases to eliminate medication misadventure entirely, the current study demonstrates the pivotal role outreach services play in supporting continuity of care, enhancing patient care and providing essential medication counselling services in individuals who are at high risk of medication misadventure.

MRPs were identified in all patients who received a HOMR. The reasons for the high incidence of MRPs observed in this group of referred patients are varied but may in part be due to a substantial chronic disease burden requiring a number of pharmacological therapies. In addition, a relatively high number of patients relied on a carer and required an interpreter during the HOMR service; both of these factors are identified risk factors for medication misadventure. Australian studies have reported an average of five to seven medication changes per hospital admission.[25] This is commonly seen in chronic diseases such as CCF, COPD, diabetes and IHD, where evidence exists for the use of multimedication regimens. Approximately 43% of patients receiving a HOMR between 2009 and 2012 exhibited one or more of these chronic medical conditions, highlighting the potential confusion that may arise from the complexity of therapy and care and the need for focused preventability targets. Other factors may also predispose patients to MRPs. Prescribers may be inadequately informed about a patient's entire repertoire of medications; this is especially the case in the elderly population who are the highest users of the hospital system and who may often see multiple prescribers for multiple chronic conditions. There is also the risk that they may self-medicate with complementary and alternative medications. The use of medications with multiple trade names often leads to confusion and contributes to MRPs such as inadvertent duplication, medication interactions and adverse drug events.

There is a clear need for reliable systems of care to improve medication safety and improve medication management and adherence. Pharmacists are suitably qualified to understand how medications are typically used by patients, to recognise the problems that exist and to recommend ways to overcome these issues in order to minimise harm. Hospital outreach medication reviews are one way a pharmacist's expertise can be utilised to avoid or minimise preventable hospital admissions. Timely access to such services is essential to address patient concerns and prevent treatment failure. HOMRs also facilitate direct communication with the patient's GP, provide a list of medications on discharge with corresponding therapy changes and reasons for change and identify any relevant MRPs and action required.

Despite the widespread acceptance of a HOMR among patients referred to the service at Monash Health, there were a total of 131 patients who refused to provide consent. Reasons for refusing to engage in the service are varied but may include the perception that there would be no benefit from a pharmacist visiting their home, a loyalty to their GP or community pharmacist, a sense of pride and autonomy, privacy and safety concerns and poor understanding of the service. Studies have shown that patients who typically refuse the service are more often the most in need of it, with higher hospitalisation rates related to medication misadventure. Some of these patients include, for example, the aged, culturally and linguistically diverse (CALD) populations and indigenous Australians.[26,27] Language is the largest barrier for access to many healthcare services in CALD communities. This emphasises the need for engaging trained interpreters to assist in better informing patients and their carers. In addition, the elderly population may become overwhelmed or confused by the amount of information they receive or may be fearful of losing their independence. Improving communication with patients and better promotion of the HOMR service are paramount in obviating some of these misconceptions.

There are many variables that may contribute to our observed reduction in hospital admissions in the 51–65 year age group, including the provision of other services during the study period (e.g. chronic heart failure program, care coordination, diabetes support services) or other medical interventions that may have been implemented within the inpatient setting to improve patient care. It is likely that a complex interplay of factors is responsible for the trends observed. Further studies may help to clarify this. The authors further analysed the mortality data and found that only two patients in the 51–65 year age category died during the study period (one from heart failure and the other from a variceal bleed secondary to ethanol). Due to the very low numbers, the authors feel that this is unlikely to bias significantly the effect estimate.

This study did not include an economic analysis of the HOMR service. We investigated two key performance measures of the HOMR service: hospital readmissions and emergency department attendances. Based on this data, we believe that well-targeted and appropriately delivered medication review hospital outreach services should continue to be provided by Monash Health and ideally offered by other hospital pharmacy services in Australia.

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Competing interests

None declared.

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Chapter Five

Examining the Benefits of Research Collaboration between Hospital Pharmacy and Medical Departments

25. Kempster P, Iansek R, Larmour I (1991); Intermittent Subcutaneous Apomorphine Injection Treatment for Parkinsonian Motor Oscillations, ANZ Journal of Medicine 21, 314 – 318. Citations 22

Intermittent subcutaneous apomorphine injection treatment for Parkinsonian motor oscillations

P. A. Kempster
Neurologist, Monash Medical Centre, Melbourne, Vic.

R. Iansek
Neurologist, Monash Medical Centre, Melbourne, Vic.

I. Larmour
Manager of Pharmaceutical Services, Monash Medical Centre, Melbourne, Vic.

Abstract:
Eight patients with severe Parkinsonian motor oscillations have been treated with the dopamine receptor agonist apomorphine by intermittent subcutaneous self-injection as an adjunct to oral anti-Parkinsonian medication. The dopamine receptor antagonist domperidone was also given by mouth to prevent nausea. Six patients remain on chronic treatment (mean period 6.5 months) with improved control of motor function in each case. Four have had major enhancement of their quality of life. Benefits of this treatment stem from the training of patients to use intelligent behaviour to administer a promptly acting and effective pharmacological agent, thereby exercising a degree of direct control over previously unpredictable variations in motor performance. (Aust NZ J Med 1991; 21: 314-318.)

Key words: Parkinson's disease, apomorphine, domperidone, motor oscillations.

INTRODUCTION

Fluctuation of motor function is a common development in patients receiving long term L-dopa medication for Parkinson's disease. After more than five years of treatment, clinically significant fluctuations will have developed in over 50% of patients and are a major clinical problem in 10% ('on-off' syndrome).[1] When motor oscillations are severe, patients alternate between incapacitating Parkinsonian motor disability and relative motor improvement marred by dyskinetic involuntary movements. Swings of motor function between these states may occur many times per day, with obscuration of the relationship between individual L-dopa doses and motor response. The resultant unpredictability often causes these patients to become housebound despite periods of quite independent motor function.

Motor fluctuations are seen in patients who have prominent Parkinsonian motor deficits when pharmacological agents are temporarily withheld but who retain capacity to respond strongly to dopamine receptor stimulating treatment (L-dopa and dopamine receptor agonists). In this situation, severe deficiency of endogenous striatal dopamine release causes a critical dependence on exogenous pharmacological dopaminergic stimulation. Although L-dopa remains the best and most physiological treatment for Parkinson's disease, vagaries of L-dopa absorption and peripheral pharmacokinetics lead to fluctuating delivery of the drug to the brain. This produces motor fluctuations in susceptible patients. Once established, motor fluctuations are notoriously difficult to ameliorate with conventional anti-Parkinsonian medication.

Apomorphine is a polycyclic compound with potent dopamine receptor agonist properties. Its dopaminergic pharmacodynamic effects more closely match those of dopamine than ergolide dopamine receptor agonists

Reprint requests to: Dr P. A. Kempster, Neurology Department, Prince Henry's Hospital, St Kilda Road, Melbourne, Vic. 3004, Australia.

such as bromocriptine and lisuride.[2] Previous placebo controlled single dose studies show unequivocal responsiveness of motor deficits to apomorphine in patients with L-dopa related motor fluctuations.[3,4] When objective parameters of motor function are compared, apomorphine produces motor responses virtually indistinguishable from those of L-dopa in individual patients.[5]

Apomorphine, by virtue of its previously established clinical efficacy, can be used as an adjunct to oral pharmacological therapy in patients with erratic response to L-dopa. Attempts to use apomorphine by the oral route have been limited by renal toxicity[6] but subcutaneous administration by intermittent injection or continuous diurnal infusion has been shown to be an effective and well tolerated treatment for motor oscillations.[7-10] Here we describe our experience with intermittent subcutaneous apomorphine injection treatment in eight patients with disabling Parkinsonian motor fluctuations. The aim of this report is to illustrate the indications, mode of action and clinical benefits of this form of pharmacological management.

PATIENTS

Eight patients (five male and three female) on long term L-dopa treatment for idiopathic Parkinson's disease have been treated with subcutaneous apomorphine by intermittent self-injection. Mean age was 59.9 years and mean duration of disease was 16.1 years. All had established motor oscillations which had been present for a number of years. All fulfilled the following criteria:

☐ Loss of independent mobility in 'off' periods, with or without unpleasant positive motor phenomena (tremor, painful dystonic spasm);

☐ restoration of independent motor function during 'on' periods despite the presence of dyskinetic involuntary movements;

☐ greater than three 'off' phases per day with resultant unpredictability of motor performance;

☐ well preserved cognitive function and/or a close relative able to supervise delivery techniques.

This treatment programme was approved by the Prince Henry's Hospital Research Advisory and Ethics Committee and all patients gave their informed consent.

METHODS

Patients were admitted to hospital for a period of assessment and initiation of apomorphine treatment. Previous clinical impressions regarding the amplitude of motor oscillations were confirmed by observations of 'on' and 'off' motor states in relation to a single oral L-dopa/decarboxylase inhibitor dose while fasting.

Treatment with domperidone, a peripherally acting dopamine receptor antagonist, was commenced at a dose of 20mg three times daily by mouth at least 24 hours prior to the first dose of apomorphine to prevent nausea and vomiting. Apomorphine was initially administered at a test dosage of 1mg subcutaneously during an 'off' period following temporary withholding of normal L-dopa medication. A further 2mg bolus was given after 20 minutes if no response was seen and this was repeated if necessary until a motor response approximating previously observed 'on' phase motor function occurred. Intermittent subcutaneous apomorphine injections were then commenced at a dosage determined by the sensitivity to the test doses (usually 2.4-3.6mg).

Apomorphine was administered via a disposable 1ml insulin syringe mounted in a Penject (Hypoguard Ltd, Melton, Suffolk, UK) device. This is a simple plastic dose metering device which is pre-set to ensure correct dosage delivery and is easily carried in pocket or handbag for ambulatory use. Patients were educated in the technique of self-injection and were taught to give injections during, or in anticipation of, 'off' phases. Spouses were also taught about injections and the delivery device; the task of periodically drawing up apomorphine from glass ampoules required considerable dexterity and in general had to be performed by a relative.

While in hospital, patients' understanding of delivery technology and timing of self-administration were monitored. If necessary, the bolus dose was adjusted so that nearly all doses resulted in an 'on' state of equal quality to L-dopa motor response without excessive dyskinesia. Significant alteration of dosage and timing of oral anti-Parkinsonian agents was not attempted.

After discharge from hospital, patients were reviewed at monthly intervals and had blood tests to monitor plasma electrolytes, urea, creatinine, liver function tests and full blood count. Optimum frequency of self-injection was determined on a trial and error basis by patients once they had returned to their normal environment and routine. Patients were encouraged to reduce their dosage of domperidone gradually after a few weeks as tolerance to the emetic effects of apomorphine developed.

Objective Motor Assessments

When apomorphine dosage was optimised, response to a single injection was quantified by scoring of 'on' and 'off' states using a modified Webster disability scale[11] (grading for 12 domains of motor function giving a maximum disability score of 36). Other medication was temporarily withheld for this assessment. Latency to onset of response and duration of response were also ascertained.

On admission to hospital, patients were instructed to fill in diary records of motor function at hourly intervals while awake to assess fluctuations in motor

TABLE 1
Characteristics of Motor Response to Subcutaneous Apomorphine Injections

Case No.	Optimum dose (mg)	Latency to onset (min)	Duration of response (min)	Modified 'off'	Webster score 'on'
1	2.8	7.5	60	23	6
2	2.8	7.5	60	23	2
3	1.4	5	60-75	22	12
4	3.6	10	50-60	25	3
5	3.6	10-15	75	22	7
6	2.0	2.5-5	60	25	13
7	3.6	5-10	60	20	1
8	2.8	10	60-70	26	8

function. Severity of motor disability when 'off' and of dyskinetic involuntary movements when 'on' were recorded according to simple three point scales. Motor diary recording was continued for one week prior to initiation of regular apomorphine treatment.

RESULTS

Apomorphine Dose Response Characteristics

All patients showed motor responses to apomorphine which were approximately equal in magnitude to those of their usual oral L-dopa doses. Mean 'on' phase modified Webster scale score after apomorphine was 6.5 (one-13) and mean modified Webster scale amplitude of apomorphine motor response ('off' minus 'on' score) was 17 (12-22). Magnitude and pattern of dyskinetic involuntary movements following apomorphine and L-dopa doses were generally similar in individual patients. Optimum apomorphine subcutaneous doses ranged between 2.0 and 3.6mg (mean 2.8). Onset of dose responses to apomorphine occurred after a mean period of 9 minutes (2.5-13) and mean duration of response was 63 minutes (55-75). Details of dose response characteristics are shown in Table 1.

Long Term Treatment

Six patients have continued on subcutaneous apomorphine injection treatment for a mean period of 6.5 months. The mean dose of apomorphine required for an optimum response has not changed significantly (2.8mg after six months). Mean number of injections per day is 3.8 and mean total daily apomorphine dose is 11.6mg (four-25). Clinical details for all patients on long term treatment are shown in Table 2.

All six patients have shown sustained improvement in control of motor function since commencing apomorphine. In four patients (Cases 1, 2, 4 and 5) apomorphine has led to a major improvement in quality of life, manifested by increased independence in activities of daily living, greater confidence to travel outside their homes and enhanced social functioning. Quite frequent apomorphine injections were used in Cases 2 and 4 to reduce unpleasant 'off' phase motor phenomena of disabling tremor and painful dystonia. Patients 1 and 5 experienced less intrusive 'off' phase symptoms. They found less frequent apomorphine doses to be satisfactory, resorting to injections only when loss of mobility threatened to interfere with daily personal motor tasks or social activities.

Moderate motor benefits were observed in two more disabled patients. Case 3 had severe swings in motor function with severe 'off' periods associated with painful truncal muscle spasm and hypoventilation. She initially required eight injections per day with reasonable control of daytime symptoms, but continued to experience prolonged and unpleasant nocturnal 'off' manifestations. Her pattern of motor

TABLE 2
Clinical Features of Patients on Chronic Treatment

Case No.	Age and Sex	Disease duration (years)	Other treatment	Injection frequency (doses/day)	Associated clinical features
1	41M	12	M,B	2	
2	53F	17	S,B	6	severe 'off' phase tremor and painful dystonia
3	69F	21	S,H	3	'off' phase truncal dystonia and hypoventilation
4	58M	16	S,B,A	6-8	violent 'off' phase tremor
5	68M	16	S,B,A	2	
6	68M	10	S	2	cognitive impairment autonomic insufficiency

Legend to other treatment abbreviations: S-L-dopa/carbidopa, M-L-dopa/benserazide, B-bromocriptine, H-controlled release L-dopa/benserazide, A-anticholinergic.

disability would have been better managed by continuous apomorphine subcutaneous infusion therapy, but she declined this treatment. The subsequent addition of evening and daytime slow-release L-dopa medication reduced nocturnal disabilities and allowed satisfactory control of daytime symptoms with on average three apomorphine doses per day. Case 6 had very advanced Parkinson's disease associated with moderate dementia and cardiovascular autonomic dysfunction. Prior to apomorphine treatment, oral L-dopa medication produced few periods of satisfactory motor function and his wife was having increasing difficulty in caring for him. Apomorphine injections provided reliable periods of independent motor function which greatly facilitated his care at home although significant motor disabilities remained.

Four patients (Cases 3 and 6 were unable to complete diary records adequately) filled out motor diary charts for one week after a mean treatment period of five months. These were compared to pre-treatment records. Before apomorphine mean total 'off' time was 5.9 hours per day (4.0-6.8) with 2.9 hours (2.1-4.5) of that time spent in severe 'off' states (loss of independent mobility). On apomorphine treatment, mean daily 'off' time was 5.4 hours (3.8-8.8) with 1.7 hours (1.1-2.2) of incapacitating 'off' time. Ninety-four per cent of apomorphine doses resulted in clinical motor response according to the diary records. Reduction in daily 'off' time was related to the number of daily injections used and was most marked in the patients using greater than five injections per day (Cases 2 and 4).

Treatment Withdrawals

Shortly after commencing apomorphine, Case 7, who had a history of chronic stable angina, experienced further anginal chest pain and apomorphine was withdrawn as a precautionary measure. Subsequently, he has continued to experience infrequent similar episodic chest pain.

Case 8 had severe motor oscillations associated with cognitive impairment, but demonstrated satisfactory mobility after apomorphine injections which facilitated her care at home by her husband. L-dopa induced dyskinesia had previously been a prominent source of symptoms and apomorphine dose responses were accompanied by similar involuntary movements. Treatment was withdrawn when her husband, who had been administering apomorphine, developed a serious medical illness.

Side-Effects

Domperidone prevented nausea and vomiting in all cases. Mean daily dosage of domperidone after long term treatment was 17mg; one patient was able to stop this medication completely. Case 6 had symptomatic postural hypotension prior to the initiation of apomorphine for which he was prescribed fludrocortisone. He experienced several syncopal episodes after morning injections of apomorphine when domperidone dosage was tapered. These were subsequently prevented by increasing the morning domperidone dose to 20mg.

No neuropsychiatric toxicity was observed in relation to apomorphine treatment, although Cases 6 and 8 had previously had episodic confusion in relation to other anti-Parkinsonian agents.

Biochemical and Haematological Monitoring

Monthly blood test results showed no evidence of apomorphine related toxicity. No patient showed peripheral blood eosinophilia, in contrast to previous experience with subcutaneous infusion administration of apomorphine.[7,10]

DISCUSSION

In agreement with previous observations, we found that single subcutaneous injections of apomorphine act promptly and reliably in patients with Parkinsonian motor fluctuations.[3-5] Our results suggest that the management of intractable motor oscillations can be improved by self administration of apomorphine via simple delivery technology which enables patients to restore 'on' phase motor function during periods of decline in action of oral L-dopa medication. In this study, patients received apomorphine in an open, unblinded manner. However, all patients alternated between distinct 'off' and 'on' motor states, the difference clearly obvious to both patients and observers. Conversion from 'off' to 'on' state occurs in response to dopaminergic pharmacological agents but not placebo.[4] In conjunction with the objectively quantified time to onset, duration and magnitude of response to injected doses, we believe that patients' accounts and diary recordings concerning the time course of pharmacologically induced 'on' phases provide a reliable indication of the effectiveness of apomorphine treatment. Total 'off' state duration can be reduced roughly in proportion to the number of daily injections used. However, most patients commented that an important benefit of subcutaneous apomorphine was that it provided a direct means of control over previously erratic variations of motor performance. Whereas previously journeys beyond the confines of the home were complicated by the hazard of unpredictable loss of mobility, patients were always confident that mobility could in any event be restored within five to ten minutes by an apomorphine injection. Intelligent behaviour is obviously an important determinant of effectiveness of this treatment. Best results are obtained in patients who have insight into their motor fluctuations and can acquire an understanding of the delivery technology and the optimum timing of injections during, or in anticipation of, 'off' phases. The

assistance of a spouse to administer injections was invaluable in patients who had marked impairment of manipulative ability during 'off' phases. However, most patients showed a practice effect over several months as they learnt to integrate apomorphine injection treatment with their usual oral medication and daily routine. Patients were thus more independent with injection administration as they became adept at anticipatory use of apomorphine.

Patients were allowed to determine the optimum frequency of apomorphine injections on their return to the home environment after the initial training in self-administration technique. In general, injection frequency was strongly influenced by patients' perception of 'off' phase motor function. When 'off' periods produced loss of independent mobility which could be tolerated reasonably well, as long as this did not occur at inconvenient times, two or three injections per day could be ample. However, when 'off' phases were extremely unpleasant because of painful dystonic spasms or violent tremor, patients tended to use at least six injections per day.

It needs to be emphasised that this treatment is not suitable for all Parkinsonian patients who have developed an unsatisfactory response to oral L-dopa or dopamine receptor agonist medication. Simple observations of amplitude of motor response to an L-dopa dose help to establish the goals of pharmacological treatment in individual patients. Use of apomorphine can increase overall 'on' phase duration and allow patients greater influence over the time course of 'on' phases, but will not significantly improve the quality of 'on' phase motor function.[5] Patients who respond weakly to test doses of L-dopa are unlikely to benefit from apomorphine treatment. Similarly, aspects of Parkinsonian motor disability resistant to L-dopa in an individual patient (such as gait freezing or postural instability) will not be corrected by the use of apomorphine.

An ideal pharmacological treatment for Parkinson's disease would entail constant and reliable delivery to the brain of adequate amounts of a drug with pharmacodynamic properties similar to dopamine. Such a treatment is not currently available. The strategy of apomorphine treatment by intermittent subcutaneous self-administration accepts the inevitability of fluctuating L-dopa levels within the nervous system. It provides patients with a technique to produce additional prompt and reliable phasic central dopamine receptor stimulation allowing them to exercise control over previously capricious swings in motor function with a relatively small increase in overall pharmacological therapy. The treatment is well tolerated, relatively easy to initiate and uses simple technology. A trial of subcutaneous apomorphine is recommended for Parkinsonian patients who, despite periodically satisfactory motor function, are disabled by unpredictable motor fluctuations. ■

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Chemotherapy Delays Progression of Motor Neuron Disease in the SOD1 G93A Transgenic Mouse

K.M. Bruce[a] K. Narayan[b] H.C. Kong[c] I. Larmour[c] E.C. Lopes[a]
B.J. Turner[a] J.F. Bertram[a] S.S. Cheema[a]

[a]Department of Anatomy and Cell Biology, Monash University, [b]Department of Pharmacy, Monash Medical Centre, [c]Peter MacCallum Cancer Institute, Melbourne, Australia

Key Words
Amyotrophic lateral sclerosis · Astrocyte · Histology · Microglia · Vincristine

Abstract
Background: A significant proliferation of glial cells occurs in the spinal cord and brainstem of SOD1 G93A transgenic mice with familial amyotrophic lateral sclerosis (ALS). Since activated glia may contribute to motor neuron degeneration, we tested whether inhibition of gliosis using low-dose chemotherapy is beneficial in this mouse model. ***Methods:*** Mice were administered fortnightly intraperitoneal injections of 0.1 mg/kg vincristine (VIN) or saline commencing at postnatal day 68 before disease onset. Mice were sacrificed at end-stage disease, and spinal cords were examined for histology. ***Results:*** Survival of VIN-treated mice was significantly increased at 132.0 ± 4.1 days compared to control animals at 117.8 ± 2.1 days ($p < 0.05$). Furthermore, analysis of microglia and astrocyte populations suggests a reduction in the former following VIN therapy. ***Conclusion:*** This study suggests that chemotherapy may offer an alternative therapy or co-therapy for ALS.

Introduction

Amyotrophic lateral sclerosis (ALS) is the most common form of motor neuron disease. This adult-onset disorder is characterised by progressive muscle weakness, atrophy and paralysis due to progressive loss of spinal, brainstem and cortical motor neurons. In 50–70% of ALS patients, death occurs within 3–5 years from symptom onset, usually from respiratory failure [1].

Mutant superoxide dismutase 1 (SOD1) mice provide an excellent model for the familial form of ALS. These transgenic mice develop many of the clinical and pathological phenotypes found in human ALS [2]. Spinal motor neurons decrease in number with disease progression [3]. At end-stage disease, this extensive motor neuron loss is accompanied by gliosis [4]. Proliferation and activation of microglia and astrocytes may be involved in ALS neurodegeneration [5–7]. These glial cells are also implicated in many other neurodegenerative diseases including Parkinson's disease, Alzheimer's disease, Huntington's disease and multiple sclerosis [8]. Astrocyte damage can occur through the release of glutamate, which exerts excitotoxic effects and causes neuronal degeneration in vivo and in vitro [9]. Microglia can contribute to the neurodegeneration by release of glutamate and pro-inflammatory cytokines including TNF-α, IL-1 and IL-6 [6]. Microglia

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Assoc. Prof. S.S. Cheema
Howard Florey Institute
University of Melbourne
Victoria 3010 (Australia)
Tel. +61 3 8344 1959, Fax +61 3 9348 1707, E-Mail s.cheema@hfi.unimelb.edu.au

are also a major source of nitric oxide (NO) and superoxide anion (O_2^-), which combine to form the potent neurotoxin peroxynitrite ($ONOO^-$) [7].

In the present study, we hypothesised that inhibition of gliosis may be an effective strategy for ALS therapy. We treated SOD1 G93A transgenic mice with vincristine (VIN), a chemotherapeutic agent that halts mitosis at metaphase and therefore arrests proliferating cells [10]. VIN has demonstrated activity against tumours involving glial cells (i.e. gliomas) and is currently used as part of a multiagent regimen for the treatment of tumours [11].

Materials and Methods

Transgenic Mice

SOD1 G93A transgenic mice derived from the B6SJL-TgN(SOD1-G93A)1Gur line (Jackson Laboratory, Me., USA) and B6SJL non-transgenic wild types were PCR-genotyped using standard protocols. For histochemical studies, mice (n = 3 per genotype) were sacrificed at postnatal day 120 (Lethabarb sodium pentobarbitone, 200 mg/kg, intraperitoneal) and processed as stated below.

Treatment Regimen

This double-blind study on SOD1 G93A transgenic mice was approved by a Monash University Animals Ethics and Experimentation Committee (permit number BAM/A/2001/4). Treatments began prior to disease onset at postnatal day 68 and continued until a predefined end point was reached. Mice were injected with a 0.1 mg/kg dose of VIN (n = 6) or an isovolume of a saline vehicle (VEH) (n = 4) solution via intraperitoneal injection once every 2 weeks. This dose and dosage frequency was extrapolated from clinical paediatric practice. Disease progression was scored as follows: stage I, onset of hind-limb tremor; stage II, onset of hind-limb paresis; stage III, severe hind-limb paresis, and stage IV, end point. The end point was defined to be when one or more hind limbs became completely paralysed, at which stage mice were sacrificed. Disease progression was compared between treatment groups using a two-tailed t test (GraphPad Prism 3.02).

Histology and Histochemistry

Mice were transcardially perfused with mouse tonicity phosphate-buffered saline (MT-PBS), pH 7.4, followed by 4% (w/v) paraformaldehyde (Sigma, Australia) in 0.1 *M* sodium phosphate buffer, pH 7.4. The lumbar enlargement of the spinal cord (L4 and L5 segments) was dissected, post-fixed in 4% (w/v) paraformaldehyde overnight at 4°C, dehydrated and embedded in paraffin wax. Transverse serial 4-μm sections were cut using a microtome and immunostained to visualise astrocytes and microglia.

For astrocyte immunostaining, sections were blocked using a 1:200 dilution of normal goat serum in 1% (v/v) fetal calf serum (FCS) in MT-PBS for 1 h at room temperature. Sections were incubated overnight with a rabbit anti-bovine glial fibrillary acidic protein (GFAP) antibody (DAKO) diluted 1:500 in 1% (v/v) FCS in MT-PBS then biotinylated goat anti-rabbit antibodies (Vector Laboratories) diluted 1:200 in 1% FCS (v/v) and MT-PBS for 1 h. Sections were treated with avidin-biotin conjugated to peroxidase diluted 1:100 in MT-PBS for 1 h and visualised with 3,3′-diaminobenzidine tetrahydrochloride (DAB) chromogen (DAKO) in 0.3% (v/v) H_2O_2 in MT-PBS.

For microglial staining, sections were incubated for 2 days at room temperature with biotinylated *Ricinus communis* agglutinin I (RCA-120, Vector Laboratories) diluted 1:2,000 in 1% (v/v) Triton-X 100 in MT-PBS. Tissues were then incubated with avidin-biotin conjugated to peroxidase diluted 1:100 for 1 h and visualised using DAB in 0.3% (v/v) H_2O_2 in MT-PBS. All sections were counterstained for motor neurons using cresyl violet.

Quantification

Morphometric analysis estimating the number of nucleated astrocyte and microglial profiles per unit area of section (mm^2) was performed on every tenth slide at a final magnification of ×1,095. An unbiased two-dimensional counting frame was employed [12]. Results were then analysed using a two-tailed t test to determine any significant changes that occur in glial numbers with chemotherapy.

Results

We first determined qualitative changes in spinal cord glial cell number and appearance in SOD1 G93A transgenic mice at end-stage disease. Using GFAP immunostaining, small and few astrocytes were identified in spinal cords of age-matched wild-type mice (fig. 1A). Extensive proliferation and hypertrophy of astrocytes was prominent in SOD1 G93A transgenic mice (fig. 1B), accompanied by other degenerative changes including motor neuron atrophy and vacuolation. Microglia shown by RCA-120 lectin staining were not visible in wild-type mouse spinal cord (fig. 1C). In contrast, many elongated microglia with thin processes were present in spinal cords of SOD1 G93A transgenic mice (fig. 1D). These data suggest that increased proliferation of glial cells accompanies motor neuron degeneration in SOD1 G93A transgenic mice.

Based on these observations, we therefore assessed the effects of low-dose chemotherapy on SOD1 G93A transgenic mouse survival using the anti-mitotic agent VIN. Animals treated with VIN did not exhibit any adverse reactions as revealed by regular monitoring of both body weight and physical activity. Mice in the VIN group consistently showed a delay in disease onset and progression compared to VEH-treated mice (fig. 2A). While this trend was noted at all stages, only at clinical stage IV was there a statistically significant difference ($p < 0.05$).

Kaplan-Meier survival analysis of the two groups is shown in figure 2B. There was a significant increase ($p < 0.05$) in survival of mice in the VIN group compared to the VEH group. The VIN-treated mice had a mean sur-

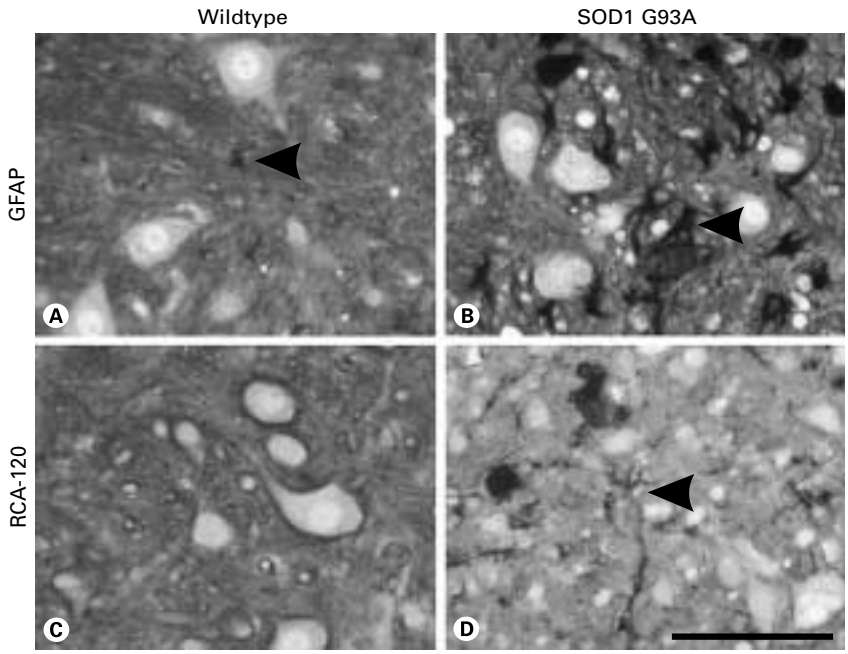

Fig. 1. Photomicrographs of spinal cord sections from the lumbar enlargement of postnatal day 120 wild-type mice and SOD1 G93A transgenic mice. Tissues were immunostained with GFAP antibodies to detect the presence of astrocytes (**A**, **B**) and RCA-120 lectin to detect microglia (**C**, **D**). Extensive proliferation of glial cells can be seen in transgenic mice (**B**, **D**). Astrocytes display swollen and enlarged cell bodies and processes (**B**, arrowhead) compared to the few small astrocytes in wild-type mice (**A**, arrowhead). Microglia display a more elongated appearance with long processes (**D**, arrowhead). Scale bar: 50 μm.

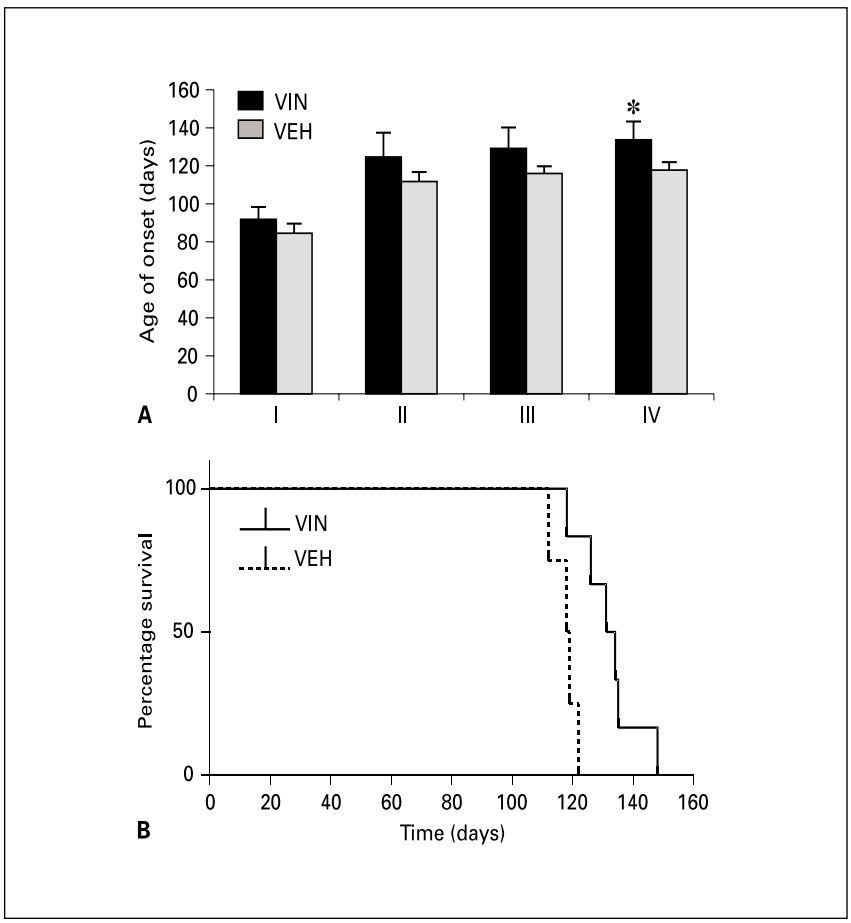

Fig. 2. Effects of VIN on disease progression. **A** Average time (days) of onset of clinical stages for the VIN and VEH treatment groups. Statistical significance (* $p < 0.05$) was observed in the delay of stage IV disease in VIN-treated mice. **B** Kaplan-Meier analysis showing a significant increase ($p < 0.05$) in survival in animals with VIN treatment. The mean survival for VIN-treated animals was 132.0 ± 4.1 days. In comparison, VEH-treated animals had a mean survival of 117.8 ± 2.1 days. The hazard ratio of the curve was 3.8, indicating that the rate of deaths in the VEH-treated group was approximately 4 times that in the VIN treatment group. Values represent means ± SEM.

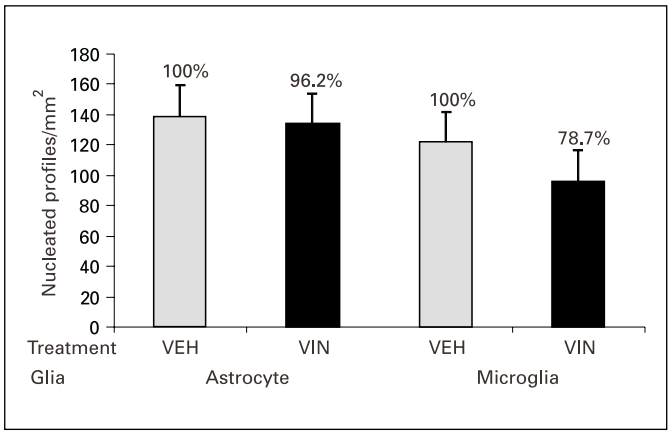

Fig. 3. Quantification of numbers of nucleated astrocyte and microglial profiles per mm^2 of section in the lumbar enlargement of the spinal cord. No significant differences in counts of nucleated glial cell profiles were observed after chemotherapy, although a 21% decrease in the numbers of microglia in the VIN-treated group was achieved. Values represent means ± SEM.

vival of 132.0 ± 4.1 days, while VEH-treated animals had a mean survival of 117.8 ± 2.1 days. The hazard ratio, which measures the rate of mortality, indicated that the rate of deaths in the VEH group was approximately 3.8 times that of the VIN group.

Following treatment, GFAP-positive astrocytes and RCA-120-positive microglia were identified and counted in spinal cord sections (fig. 3). Using an unbiased counting system, there was a 4% decrease in nucleated astrocyte profiles per unit area of spinal cord section in the VIN group compared to the VEH group, although this was statistically insignificant ($p = 0.649$). A large 21% reduction in microglial numbers was determined after VIN treatment compared to the VEH group. However, this difference was not statistically significant ($p = 0.086$).

Discussion

Proliferation of glial cells in the spinal cord of the SOD1 G93A transgenic mouse model of ALS has been well-documented [2, 4]. These studies have focused predominantly on astrocytes and their role in response to neurodegeneration. Recent evidence suggests that microglia may play an active role in the neurodegenerative pathways associated with trauma and injury in the CNS [6, 8].

Here, we show that VIN therapy delays the onset of hind-limb paralysis and prolongs survival of SOD1 G93A transgenic mice. These findings suggest that agents that reduce cellular proliferation may provide a novel therapy on their own or as co-therapy in the treatment of human motor neuron diseases such as familial ALS. Treatment with the anti-proliferative agent hydroxyurea also increased survival in this mouse model of ALS [13]. It is important to note that in this study, the beneficial effects were achieved with a low dose of VIN administered fortnightly. Whether further benefits can be obtained with higher and more frequent dosages needs to be clarified. However, possible benefits of higher dosages of chemotherapeutic agents must be balanced with adverse effects on existing healthy neurons through the disruption of microtubules. Having said this, VIN is currently used for the treatment of gliomas at much higher doses than were used in this study. It is noteworthy that the results of this study suggest a reduction in the numbers of microglia ($p = 0.086$) in the VIN group. We suggest that even a small non-significant decrease in microglia counts may sufficiently delay motor neuron disease as observed here. In addition, this preliminary finding deserves further analysis using unbiased stereological techniques. Microglia can secrete neurotoxins that result in neurodegeneration [6]. Indeed, minocycline, an inhibitor of microglial proliferation and mitochondrial cytochrome c release, delays disease onset and progression in this mouse model of ALS [14, 15]. Thus, a combination of low-dose chemotherapy and specific inhibitors of microglial proliferation may provide a novel approach in the prevention of neurodegeneration associated with ALS and other conditions.

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Citations 6

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Assessment of aminoglycoside dosing and estimated glomerular filtration rate in determining gentamicin and tobramycin area under the curve and clearance

A. K. H. Lim,[1,2,3] G. Mathanasenarajah[2] and I. Larmour[4]

[1]Department of Nephrology, [2]General Medicine, [3]Monash University Department of Medicine, [4]Pharmacy, Monash Health, Melbourne, Victoria, Australia

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aminoglycoside clearance, estimated glomerular filtration rate, gentamicin, tobramycin, Cockroft–Gault, antibiotic guideline.

Correspondence
Andy K. H. Lim, Department of Nephrology, Monash Medical Centre, 246 Clayton Road, Clayton, Vic. 3168, Australia.
Email: andy.lim@monash.edu

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Abstract

Background: Aminoglycoside clearance depends on kidney function, but the Australian Therapeutic Guidelines for antibiotics (version 14, 2010) recommend initial dosing based on weight without consideration of kidney function. Other guidelines that modify dosing based on kidney function estimates often use the Cockroft–Gault equation, but the role of the estimated glomerular filtration rate equations for this purpose is unclear.

Aim: To determine the performance of current guideline dosing in achieving target area-under-the-curve and examine the relative precision of the estimated glomerular filtration rate equations compared with traditional Cockroft–Gault creatinine clearance in predicting aminoglycoside clearance.

Methods: We analysed 496 aminoglycoside treatment episodes involving 1377 infusions in adult patients. Conformity with antibiotic guideline dosing was achieved if the discrepancy between prescribed and recommended dose was less than 15%. Aminoglycoside clearance was determined from linear regression using a one compartment model with the Aminoglycoside Levels and Daily Dose Indicator programme. We assessed the precision of the Cockroft–Gault, Modification of Diet in renal Disease Study and Chronic Kidney Disease–Epidemiology Collaboration (CKD–EPI) equations in predicting aminoglycoside clearance by correlation and linear regression.

Results: Conformity with guideline dosing was not associated with achieving target area-under-the-curve. The CKD-EPI estimated glomerular filtration rate adjusted for body surface area showed the highest correlation (gentamicin, $r = 0.66$; tobramycin, $r = 0.82$) and best predictive model for aminoglycoside clearance.

Conclusion: Current guideline dosing may be suboptimal for achieving target area-under-the-curve. The CKD-EPI equation adjusted for patient body surface area best predicts aminoglycoside clearance, and could be evaluated as a covariate in determining initial aminoglycoside dosing.

Introduction

Aminoglycosides, such as gentamicin (GEN), tobramycin (TOB) and amikacin (AMI) are bactericidal antibiotics mostly used to treat severe Gram-negative infections. The Australian Antibiotic Guidelines (version 14, 2010) classify aminoglycoside treatment as either empirical or directed therapy.[1] With empirical therapy, the duration is limited to two or three daily doses without therapeutic drug monitoring. On the other hand, therapeutic drug monitoring is advised for patients receiving directed therapy. The initial guideline recommended daily dose is based on the patient's bodyweight and age: 10–29 years (6 mg/kg, maximum 560 mg), 30–60 years (5 mg/kg, maximum 480 mg) and > 60 years (4 mg/kg, maximum 400 mg); and is not directly adjusted for kidney function.[1]

Aminoglycosides are predominantly excreted by the kidneys and their clearance (CL) is influenced by kidney function. They are freely filtered through the glomerulus, but some reabsorption occurs in the proximal tubule by megalin-mediated endocytosis. Aminoglycosides are nephrotoxic as high concentrations may lead to tubular

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necrosis, intra-renal vasoconstriction and mesangial contraction, resulting in acute kidney injury (AKI).[2] Ototoxicity and neuromuscular toxicity are other possible side effects, and high doses and prolonged treatment are risk factors for toxicity. Therefore, some guidelines recommend reducing the initial aminoglycoside dose in patients with reduced kidney function.

Balancing the risk of toxicity, under-dosing needs to be avoided as achieving target concentrations is important for antibacterial efficacy. The main pharmacokinetic and pharmacodynamic parameters related to aminoglycoside efficacy are the area under the curve : minimum inhibitory concentration (AUC : MIC) ratio and the maximum concentration (Cmax) : MIC ratio.[3] Hence, the target AUC is a useful parameter in clinical practice to base doses on. There are several methods of dose individualisation that can be utilised to target these parameters, including linear regression, population methods and Bayesian estimation.[4] In many Australian hospitals, including ours, an AUC-based computerised method is utilised, as recommended by the Antibiotic Guidelines. The Aminoglycoside Levels and Daily Dose Indicator (ALADDIN) is one such method. ALADDIN is based on the linear regression method and assumes a one compartment model. It requires two serum levels, one immediately after the end of the infusion, and the second, 6–8 h later.

Early achievement of target concentrations may be associated with improved clinical outcomes. However, the current Antibiotic Guidelines do not recommend therapeutic drug monitoring for the initial 2 or 3 days of empirical therapy. There is a risk that patients may not achieve target concentrations for several days, and patients with reduced kidney function may experience cumulative toxicity. Given the importance of kidney function in aminoglycoside CL, an estimate of kidney function may help us predict CL and thus optimise initial dosing better to achieve target AUC early on. Overestimates of kidney function may result in inappropriately high doses and toxicity, while underestimates may result in inefficacy.

Radionuclide determination of glomerular filtration rate (GFR) is the gold standard for measuring kidney function, but would not be practical in routine practice. Most guidelines that recommend reducing the initial aminoglycoside dose in patients with reduced kidney function suggest using the Cockroft–Gault (CG) equation to estimate creatinine clearance (eCL_{CR}) as a surrogate for GFR. The CG equation can be modified to compensate for obesity by using ideal bodyweight (IBW) or adjusted bodyweight (ABW) in place of total bodyweight (TBW). Most laboratories now routinely report the estimated GFR (eGFR), which are kidney function estimates based on equations derived from population studies. The eGFR equations include the four-variable Modification of Diet in Renal Disease Study (MDRD) and Chronic Kidney Disease–Epidemiology Collaboration (CKD-EPI), which are normalised to a body surface area (BSA) of 1.73 m^2.[5,6] The eGFR equations were intended to detect and stage chronic kidney disease (CKD), but may represent an alternative to the CG equation for drug dosing. However, these estimates are not interchangeable for the purpose of drug dosing. Studies have shown 20–36% discordance in hypothetical dosing recommendations based on the CG, MDRD or CKD-EPI estimates of kidney function for several non-aminoglycoside antimicrobials.[7–9] In one study, the CG and MDRD equations produce discordant eGFR in over 60% of patients, with only one-third classified as having the same stage of CKD.[10]

We sought to determine if current guideline recommended doses are associated with achieving target AUC and if a weight-adjusted dosing protocol was hypothetically better. We also aimed to determine which of the various kidney function estimates (CG-TBW, CG-IBW, CG-ABW, MDRD and CKD-EPI) would best correlate with aminoglycoside CL. Finally, we attempted to determine any changes in aminoglycoside CL after multiple infusions.

Methods

ALADDIN database

An analysis of the ALADDIN database at Monash Health was performed from April 2010 to December 2012. The database only includes patients receiving daily intravenous aminoglycoside infusions (GEN, TOB, AMI), with some patients receiving multiple courses (treatment episodes) at different times. Only adults (age ≥18 years) were included in the analysis, and the information gathered included age, sex, weight, height, serum creatinine, infusion number, prescribed dose, timing of infusions, aminoglycoside levels, baseline kidney function and indication for treatment. All serum creatinine measurements during this period were standardised to isotope-dilution mass spectrometry (IDMS) traceable creatinine assays. Data were fitted to a one compartment model by the ALADDIN programme to determine CL. As most TOB and some GEN patients had multiple treatment episodes, the selection of a unique first infusion dataset to assess the relationship between eGFR and aminoglycoside CL used the following algorithm: (i) exclude infusions with suboptimal treatment or measurement of levels, as this may increase the error in AUC_{24} calculation (infusion time <15 min, first level >60 min after end of infusion, second level <1.0 mg/L or <6 h after the first level), (ii)

exclude infusions associated with serum creatinine >25% below baseline and (iii) of the remaining treatment episodes, a random first infusion is selected.

Definitions

IBW was determined by the Devine formula (IBW = 50.0 + 0.9 kg/cm over 152 cm [male] or 45.5 + 0.9 kg/cm over 152 cm [female]). ABW applied the 0.40 correction factor (ABW = IBW + 0.4 × (TBW-IBW)). Obesity was defined as TBW greater than 20% over the patient's IBW as suggested by the Antibiotic Guidelines. BSA was calculated from the Dubois formula (BSA = height$^{0.725}$ × weight$^{0.425}$ × 0.007184). AKI was defined as a rise in serum creatinine of 0.3 mg/dL (equivalent to 27 μmol/L) or 1.5 × greater than baseline, as described by the Acute Kidney Injury Network (AKIN) criteria.[11] In this study, severe AKI is defined as a rise in serum creatinine greater than 2 × baseline values (AKIN stage 2 or more). Baseline creatinine was determined by a nephrologist and is generally defined as the best stable creatinine value in the last 12 months. Where multiple preadmission creatinine values are available, the most recent lowest value that demonstrates minimal fluctuation (stability) over 3 months is used. The standard CG equation, CG = (140 – age, in years) × weight (kg) × (0.85 if female) / (0.814 × serum creatinine, in μmol/L). The eCL_{CR} was calculated using the CG equation by replacing the *Weight* parameter with TBW, IBW and ABW (CG-TBW, CG-IBW and CG-ABW). The four-variable IDMS-aligned MDRD and CKD-EPI equations have been previously described.[5,6] To determine BSA-adjusted MDRD and CKD-EPI eGFR, the normalised eGFR (mL/min/1.73 m^2) was divided by 1.73 and multiplied by the patient's BSA, to give the $MDRD_A$ and $CKD\text{-}EPI_A$ eGFR (mL/min) respectively.

Guideline dosing

To calculate the guideline recommended initial dose for each patient, the Antibiotics Guidelines version 14 criteria were applied.[1] Three weight-based protocols were derived based on TBW, IBW and ABW. In the latter two protocols, obese patients used their IBW or ABW to determine guideline dosing. Conformity to guidelines is defined as a prescribed dose being less than 15% different to the guideline dose. The 24 h AUC (AUC_{24}) is generated by the ALADDIN programme, with the target AUC_{24} for non-cystic fibrosis patients defined as 80 ± 10 mg.h/L and 100 ± 10 mg.h/L for cystic fibrosis patients.[12]

Treatment duration and aminoglycoside CL

The change in aminoglycoside CL for patients receiving ≥2 infusions was calculated as the difference in the subsequent CL compared with the baseline CL (first infusion). Negative values represent a decline in CL. The mean change in CL for the group is calculated for each time point to determine an overall change in CL over time, with the infusion number as a surrogate for treatment duration in days, as all infusion intervals are 24 h.

Statistics

All analysis was performed on IBM SPSS version 20. A $P < 0.05$ was considered significant. Standard deviation (SD) is reported with the data mean values (mean ± SD) unless specified otherwise. A significant difference in means between two groups for continuous variables was determined by a paired-samples *t*-test or Wilcoxon Signed Rank test (comparing protocols), and independent samples *t*-test (comparing subgroups of same protocol). To compare categorical variables, Chi-squared (subgroups of same protocol) or McNemar's test (comparing protocols, same patients) was performed. Correlation analysis was performed with Pearson's correlation coefficient (r). Analysis of dosing conformity with guidelines and relationship with AUC was done on data from all treatment episodes. Correlation and regression on renal function estimates were done on unique patient data (multiple treatment episodes eliminated as described in the methods section). The 95% confidence interval (CI) for Pearson's correlation was determined by bootstrapping, based on 1000 bootstrap samples. The coefficient of determination (R^2) was used to determine the precision of the regression model.

Results

Patient characteristics

The database contained 1406 infusions from 342 patients for GEN and TOB. There were insufficient entries in the database for AMI to allow a meaningful analysis. TBW was available for 1377 infusions involving 496 treatment episodes from 319 patients. Of these, TOB was used in 216 episodes (60 patients, of which BSA could be calculated for all episodes) and GEN in 280 episodes (259 patients, of which BSA could be calculated in 246 episodes from 221 patients). The GEN and TOB patient characteristics are shown in Table 1. There were equal males and females, but TOB patients were younger, with lower weights and serum creatinine. There were more obese patients receiving GEN than TOB. TOB patients were mostly Caucasians, reflecting a high proportion of patients with cystic fibrosis. GEN was commonly used for genitourinary or intra-abdominal infection and bacteraemia. The prevalence of AKI was low with both TOB and

Table 1 Patient characteristics

Characteristic	TOB (n = 60)	GEN (n = 282)
Age (years)	31.6 ± 16.9	54.7 ± 19.4
Male sex (%)	48.3	51.1
Caucasian (%)	98.3	83.7
Total bodyweight (kg)	62.1 ± 16.0	73.7 ± 18.6†
Obese (%)	11.7%	33.2%†
Height (cm)	168 ± 11	166 ± 11‡
Ideal bodyweight (kg)	63.2 ± 10.8	61.0 ± 10.1‡
Adjusted bodyweight (kg)	62.2 ± 11.3	66.3 ± 11.8‡
Serum creatinine (μmol/L)	67 ± 16	74 ± 24
CG-TBW eCL_{CR} (mL/min) [range]	118 ± 6 [40–288]	105 ± 49† [26–342]
MDRD eGFR (mL/min/1.73 m^2) [range]	112 ± 4 [46–208]	94 ± 38 [26–348]
CKD-EPI eGFR (mL/min/1.73 m^2) [range]	114 ± 3 [52–152]	93 ± 32 [27–321]
Indication for aminoglycoside	Cystic fibrosis 86.7% Bronchiectasis§ 11.7% Osteomyelitis 1.6%	Genitourinary 35.5% Gastrointestinal 33.7% Bacteraemia¶ 16.3% Pulmonary 8.3% Soft tissue 4.7% Other 1.4%

Results are mean ± standard deviation except for reported percentages. †n = 259. ‡n = 221. §Not related to cystic fibrosis. ¶Proven or suspected, including febrile neutropenia. CG, Cockroft–Gault; CKD-EPI, Chronic Kidney Disease–Epidemiology Collaboration; eCLCR, estimated creatinine clearance; eGFR, estimated glomerular filtration rate; GEN, gentamicin; MDRD, Modification of Diet in Renal Disease; TOB, tobramycin; TBW, total bodyweight.

GEN (1.7% vs 6.4%, P = 0.26). There were no patients with stage 4 or 5 CKD in the database.

Conformity with guideline dosing and target AUC

TOB prescribed doses were normally distributed, but GEN prescribed doses had notable peaks (Fig. S1), reflecting commonly prescribed doses of 240 mg (36.4%) and 320 mg (16.1%). A comparison between prescribed and guideline recommended doses is shown in Table 2. About 40–50% of patients in the database conformed to guideline dosing. However, the IBW protocol demonstrated the smallest dose discrepancy between prescribed and guideline doses, and bears closest resemblance to actual prescribing patterns.

The AUC_{GEN} and AUC_{TOB} showed a normal distribution and a positive correlation with prescribed dose, r = 0.32 and 0.36 (P < 0.001) respectively. The percentages of patients achieving target AUC on the initial infusion for all treatment episodes are gentamicin 29.6% (n = 280) and tobramycin 33.0% (n = 216). However, conformity with any of the protocols did not affect the proportion or likelihood of patients achieving target AUC_{GEN} (Table 3). The TBW protocol compatible group had higher AUC_{GEN} compared with the weight-adjusted protocols, consistent with the higher doses received. TBW dosing was also associated with achieving AUC_{GEN} above the target range (P = 0.001). For TOB, there appeared to be a higher proportion of patients achieving target AUC_{24} if they conformed to guideline dosing (Table 4). However, this was only statistically significant for the ABW protocol. The odds ratio for achieving target AUC_{TOB} with ABW protocol conformity compared with non-conformity in dosing was 1.99 (95% CI: 1.09, 3.63).

Table 2 Prescribed and guideline recommended doses by weight protocols

	Prescribed	TBW	IBW	ABW
GEN, n = 246				
Mean ± SD (mg)	274 ± 73	336 ± 92†	287 ± 75‡,§	309 ± 80†,§
Median (mg)	240	337†	272§,¶	300†,§
Range (mg)	80 – 540	140 – 580	140 – 564	140 – 471
Conformity (%)		41.5	48.8††	45.5
TOB, n = 216				
Mean ± SD (mg)	315 ± 73	332 ± 66¶	317 ± 58	324 ± 59
Median (mg)	320	330	312	324
Range (mg)	100 – 560	156 – 546	156 – 546	156 – 546
Conformity (%)		54.0	56.7	58.1

†P < 0.001 compared with prescribed dosing. ‡P = 0.020 compared with prescribed dosing. §P < 0.001 compared with TBW protocol dosing. ¶P = 0.029 compared with prescribed dosing. ††P = 0.042 compared with TBW protocol dosing. ABW, adjusted bodyweight; GEN, gentamicin; IBW, ideal bodyweight; SD, standard deviation; TBW, total bodyweight; TOB, tobramycin.

Comparison of CG and eGFR

Extreme outliers (eCL_{CR} or eGFR >3 × interquartile range above 75th percentile) were excluded (n = 4, mean age 19 ± 1 years, mean serum creatinine 32 ± 1 μmol/L). Patients with severe AKI (serum creatinine >2 × baseline) were also excluded (n = 2). Mean serum creatinine for the entire cohort was 72.6 ± 21.0 μmol/L. Figure 1 compares the eCL_{CR} and eGFR derived from the various equations. The CG-TBW gave the highest estimates with the most variation and skew in distribution (mean, 105 ± 44 mL/min). This was attenuated with the CG-IBW (mean, 90 ± 35 mL/min) and CG-ABW (mean, 96 ± 36 mL/min). The CKD-EPI equation gave the least variation and outliers, and had a normal distribution (mean, 95 ± 24 mL/min/1.73 m^2).

Table 3 GEN dose and AUC_{GEN} by conformity with hypothetical protocols

	TBW protocol		IBW protocol		ABW protocol	
	Conform (n = 99)	Others (n = 144)	Conform (n = 118)	Others (n = 125)	Conform (n = 110)	Others (n = 133)
Mean ± SD dose (mg)	295 ± 72	260 ± 70	275 ± 62	274 ± 82	289 ± 65	262 ± 76
Median dose (mg)	300	240	240	240	300	240
Dose range (mg)	160–540	80–520	160–540	80–520	160–540	80–520
Mean ± SD AUC_{24} (mg.h/L)	89.7 + 25.9	77.3 ± 28.9	84.2 ± 25.2	80.6 ± 31.0	86.4 ± 24.7	79.0 ± 30.8
Median AUC_{24} (mg.h/L)	88.4	72.3	81.0	79.7	86.0	73.1
AUC_{24} range (mg.h/L)	42.3–198.8	25.3 – 160.7	41.7 – 160.7	25.3 – 198.8	42.3 – 174.5	25.3 – 198.8
Target AUC_{24} (%)	31.3	26.4	28.0	28.8	30.9	26.3
Above target AUC_{24} (%)	45.5	28.5	38.9	32.0	40.9	30.9
Below target AUC_{24} (%)	23.2	45.1	33.1	39.2	28.2	42.8
Chi-squared†	0.700		0.021		0.625	
Significance	P = 0.403		P = 0.885		P = 0.429	

†Association between protocol conformity and achieving AUC_{24} target. ABW, adjusted bodyweight; AUC, area under the curve; GEN, gentamicin; IBW, ideal bodyweight; SD, standard deviation; TBW, total bodyweight.

Correlation between GFR estimates and aminoglycoside CL

CL_{GEN} and CL_{TOB} were normally distributed. The mean CL_{TOB} was 53.6 ± 15.7 (range, 18.6 – 95.9) mL/min. The mean CL_{GEN} was 60.0 ± 20.8 (range, 20.0–119.9) mL/min. The correlation analysis is shown in Table 5. The MDRD eGFR showed the lowest correlation with CL_{GEN} and CL_{TOB}. The CKD-EPI did not perform well when normalised to 1.73 m^2, but demonstrated the best correlation with CL_{GEN} and CL_{TOB} when adjusted using actual patient BSA, as the CKD-EPI_A. In the obese subgroup, the weight-adjusted CG equations and BSA-adjusted eGFR equations correlated better with CL_{GEN} than their native (unadjusted) counterparts, and the CG-IBW was almost equivalent to the CKD-EPI_A (Table 5). For patients with mild AKI (n = 13), the correlation between GFR estimates and CL_{GEN} is preserved except for the MDRD equation (Table 5). However, the large confidence intervals due to the small numbers limit our conclusion on the validity of using eGFR to predict aminoglycoside CL in mild AKI.

Linear regression

Regression diagnostics with a probability–probability (P–P) and standardised residuals plot confirm normally distributed data. Given the small number of TOB patients, further analysis of normality included the Kolmogorov–Smirnov test. The CKD-EPI_A eGFR (D = 0.094, df = 59, P = 0.20) and CL_{TOB} (D = 0.076, df = 59, P = 0.20) did not deviate significantly from normal. The linear regression models to determine CL_{GEN} and CL_{TOB} from the CKD-EPI_A eGFR (Fig. 2) is detailed in Table 6.

Table 4 TOB dose and AUC_{TOB} by conformity with hypothetical protocols

	TBW protocol		IBW protocol		ABW protocol	
	Conform (n = 116)	Others (n = 99)	Conform (n = 122)	Others (n = 93)	Conform (n = 125)	Others (n = 90)
Mean ± SD dose (mg)	322 ± 56	306 ± 88	316 ± 59	313 ± 90	321 ± 55	306 ± 91
Median dose (mg)	320	300	320	300	320	320
Dose range (mg)	160–440	100–560	160–440	100–560	160–440	100–560
Mean ± SD AUC_{24} (mg.h/L)	106.6 ± 31.8	95.7 ± 30.2	104.6 ± 30.7	97.7 ± 32.3	104.8 ± 29.9	97.2 ± 33.2
Median AUC_{24} (mg.h/L)	103.9	90.8	102.0	91.6	100.8	91.2
AUC_{24} range (mg.h/L)	58.9–293.8	40.7–193.9	51.8–293.8	40.7–212.6	58.9–293.8	40.7–212.6
Target AUC_{24} (%)	37.1	28.3	36.9	28.0	39.2	24.4
Above target AUC_{24} (%)	35.3	25.2	33.6	26.8	32.8	27.8
Below target AUC_{24} (%)	27.6	46.5	29.5	45.2	28.0	47.8
Chi-squared*	1.864		1.902		5.151	
Significance	P = 0.172		P = 0.168		P = 0.023	

†Association between protocol conformity and achieving AUC_{24} target. ABW, adjusted bodyweight; AUC, area under the curve; SD, standard deviation; IBW, ideal bodyweight; TBW, total bodyweight; TOB, tobramycin.

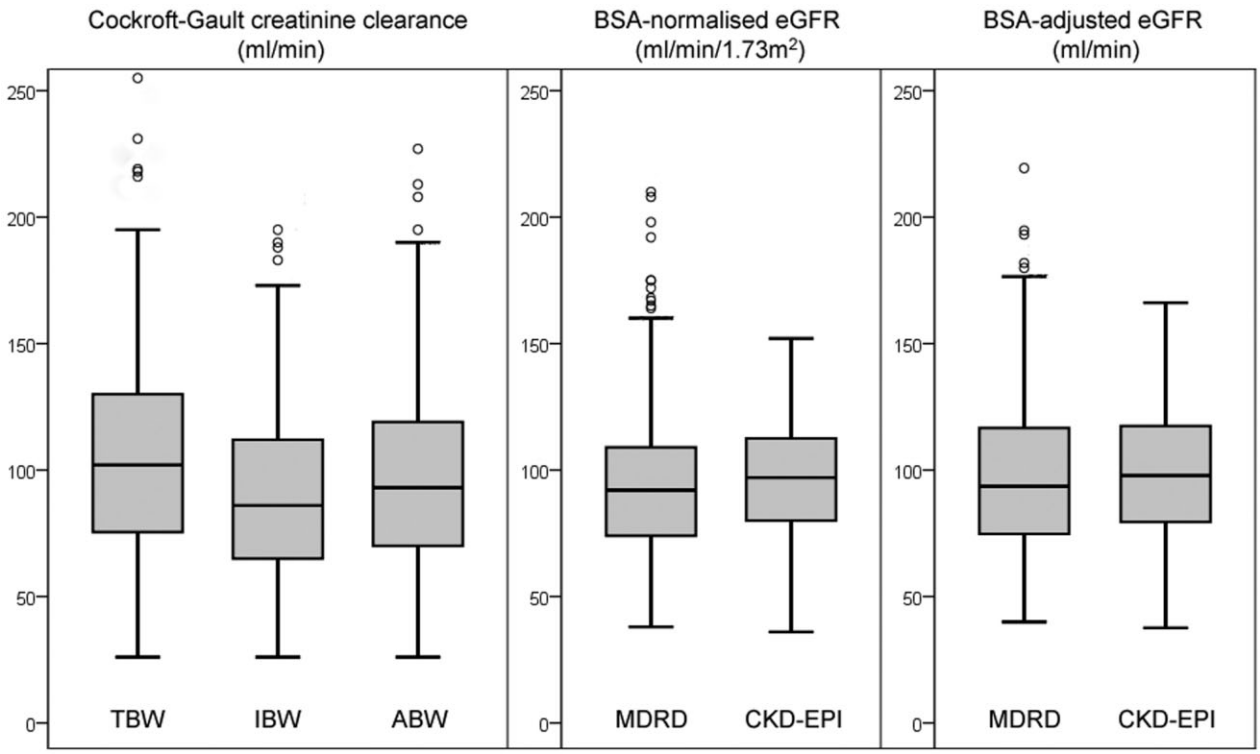

Figure 1 Box plots of kidney function estimates from the Cockroft–Gault and estimated glomerular filtration rate (eGFR) equations. The body surface area (BSA) adjusted Chronic Kidney Disease–Epidemiology Collaboration (CKD-EPI) equation provides estimates with the smallest range, and without skew or outliers. The edge of the boxes represents the 25th and 75th percentiles, with the box representing the interquartile range. The line between the quartiles represents the median. The box whiskers represent the upper and lower bound ranges. Circles represent mild outliers (between 1.5 and 3 times the interquartile range). Combined data from gentamicin and tobramycin patients presented (n = 275). ABW, adjusted bodyweight; IBW, ideal bodyweight; MDRD, Modification of Diet in Renal Disease; TBW, total bodyweight.

The aminoglycoside dose can be calculated from the target AUC_{24} and predicted CL: Dose = Target AUC_{24} × 0.06 × ((Coefficient × CKD-EPI_A eGFR) + Constant). With the regression models, the CKD-EPI_A eGFR accounted for 44% of the variance in CL_{GEN} and 67% of the variance in CL_{TOB}. In GEN patients with CKD-EPI_A eGFR <60 mL/min (11% of GEN patients), the regression line is steeper and approaches unity, associated with a lowering of the intercept (constant). This could not be analysed for TOB patients due to insufficient cases.

Aminoglycoside CL and treatment duration

The change in CL_{GEN} was negatively correlated with the infusion number (r = −0.34, P < 0.001). However, the mean change in CL_{GEN} was minimal for the first eight infusions (<10%), thereafter there was a more obvious drop (Fig. 3). Patients with eGFR <60 mL/min did not appear to have a higher risk of declining CL_{GEN} (>20% from baseline) during a treatment episode of up to 14 infusions compared with patients with eGFR ≥60 mL/min (Chi-squared 0.04, P = 0.95). In contrast, CL_{TOB} appears stable over time, and there was no difference in the change in CL_{TOB} compared with baseline. There appeared to be no correlation between the change in CL_{TOB} and the number of infusions (r = −0.05, P = 0.57). Furthermore, the average AUC_{24} for GEN was lower than TOB for the initial eight infusions, arguing against a greater drug exposure as the cause of the decline in CL_{GEN} compared with CL_{TOB} (Fig. S2). Data beyond 14 infusions were not analysed as there were <10 patients for each infusion time point and wide error bars.

Discussion

Our data indicated that one third of patients achieve target AUC_{24} when aminoglycoside therapy is initiated. However, even patients who received doses conforming to the antibiotic guidelines (half the cohort) were *not* more likely to achieve target AUC_{24}. It can be argued that dosing with the IBW protocol could potentially reduce toxicity, given it is associated with smaller overall doses

Table 5 Correlation between GFR estimate and aminoglycoside CL

	CG-TBW	CG-IBW	CG-ABW	MDRD	$MDRD_A$†	CKD-EPI	$CKD\text{-}EPI_A$‡
GEN *n* = 221							
Pearson's r	0.60	0.55	0.60	0.28	0.50	0.48	0.66
95% CI	0.52, 0.67	0.46, 0.65	0.52, 0.68	0.15, 0.41	0.39, 0.60	0.35, 0.58	0.58, 0.73
Significance	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001
Obese *n* = 97							
Pearson's r	0.54	0.61	0.59	0.40	0.52	0.56	0.63
95% CI	0.40, 0.66	0.48, 0.72	0.46, 0.71	0.23, 0.57	0.36, 0.66	0.40, 0.69	0.50, 0.75
Significance	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001
AKI *n* = 13							
Pearson's r	0.76	0.84	0.84	0.44	0.78	0.62	0.83
95% CI	–0.31, 0.97	0.15, 0.98	0.06, 0.97	–0.31, 0.87	–0.36, 0.94	–0.17, 0.90	–0.16, 0.96
Significance	*P* = 0.002	*P* < 0.001	*P* < 0.001	*P* = 0.13	*P* = 0.002	*P* = 0.024	*P* < 0.001
TOB *n* = 60							
Pearson's r	0.75	0.75	0.76	0.50	0.72	0.54	0.82
95% CI	0.63, 0.85	0.62, 0.86	0.65, 0.86	0.29, 0.69	0.59, 0.82	0.30, 0.73	0.70, 0.89
Significance	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001	*P* < 0.001
Obese *n* = 8							
Pearson's r	0.85	0.85	0.85	0.61	0.81	0.76	0.95
95% CI	0.45, 1.00	0.42, 0.97	0.45, 1.00	–0.17, 1.00	0.26, 1.00	–0.07, 0.99	0.78, 1.00
Significance	*P* = 0.002	*P* = 0.004	*P* = 0.002	*P* = 0.110	*P* = 0.015	*P* = 0.047	*P* = 0.002

†Body surface area-adjusted MDRD. ‡Body surface area-adjusted CKD-EPI. ABW, adjusted bodyweight; CG, Cockroft–Gault; CI, confidence interval; CKD-EPI, Chronic Kidney Disease–Epidemiology Collaboration; IBW, ideal bodyweight; MDRD, Modification of Diet in Renal Disease; TBW, total bodyweight.

compared with the TBW protocol. The TBW protocol may also be associated with a higher risk of achieving GEN AUC_{24} above the recommended target. These results also suggest that there is room to improve our approach to aminoglycoside dosing. In that respect, there is a good argument for incorporating the assessment of renal function into dosing algorithms. Studies have demonstrated that utilising kidney function as a covariate in estimating

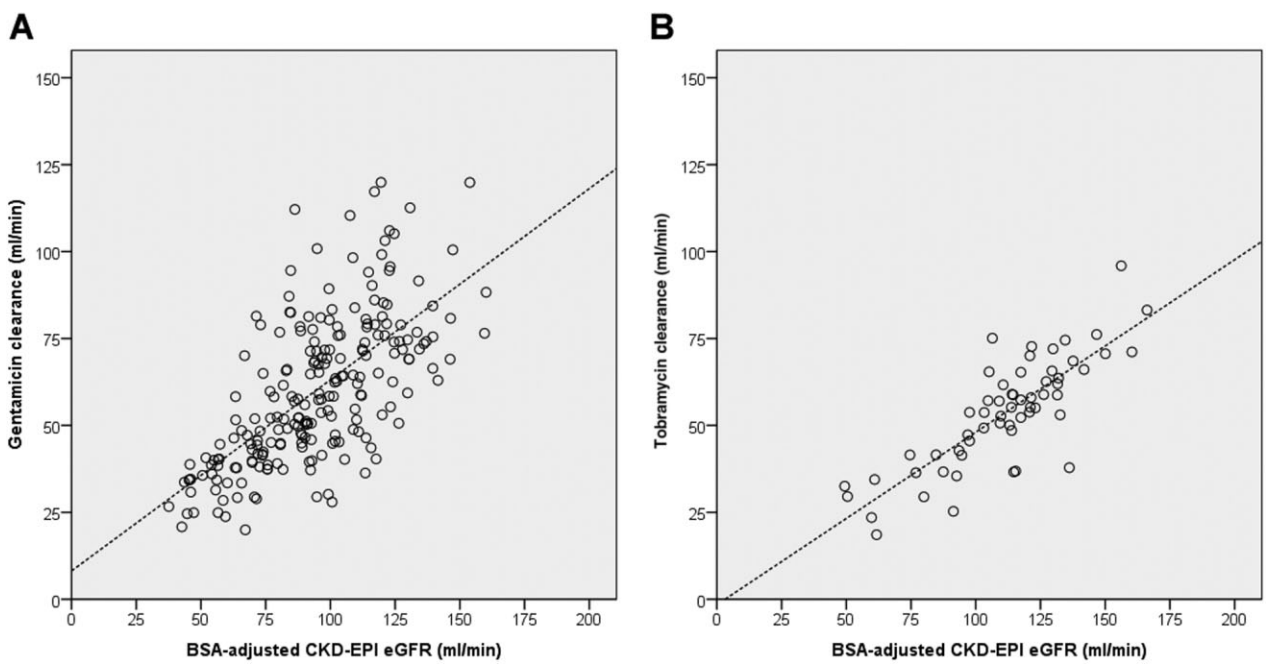

Figure 2 Scatterplot of the body surface area (BSA) adjusted Chronic Kidney Disease–Epidemiology Collaboration (CKD-EPI) estimated glomerular filtration rate (eGFR) versus gentamicin clearance (A) and tobramycin clearance (B). A linear regression line is fitted for each aminoglycoside (dotted lines).

Table 6 Linear regression models of estimated glomerular filtration rate (eGFR) as predictors of aminoglycoside clearance

Aminoglycoside/eGFR	Coefficient (95% CI)	Constant (95% CI)	R^2
GEN			
CKD-EPI	0.46 (0.34, 0.57)	18.62 (7.85, 29.39)	0.22
<60 mL/min/1.73 m^2	0.74 (0.05, 1.44)	–1.67 (–37.38, 34.05)	0.19
≥60 mL/min/1.73 m^2	0.36 (0.21, 0.52)	28.36 (13.49, 43.23)	0.10
$CKD\text{-}EPI_A$†	0.55 (0.47, 0.63)	8.14 (–0.07, 16.29)	0.44
<60 mL/min	0.92 (0.46, 1.38)	–11.84 (–36.34, 12.65)	0.45
≥60 mL/min	0.54 (0.43, 0.64)	9.40 (–1.37, 20.16)	0.34
TOB‡			
CKD-EPI mL/min/1.73 m^2	0.39 (0.23, 0.55)	9.58 (–9.03, 28.19)	0.29
$CKD\text{-}EPI_A$† mL/min	0.50 (0.40, 0.59)	–1.56 (–12.17, 9.05)	0.67

†Body surface area-adjusted CKD-EPI. ‡Insufficient cases of eGFR <60 for subgroup analysis. CI, confidence interval; CKD-EPI, Chronic Kidney Disease–Epidemiology Collaboration; GEN, gentamicin; TOB, tobramycin.

aminoglycoside CL results in better model fit and predictive value.[13,14]

In our study, the BSA-adjusted CKD-EPI eGFR ($CKD\text{-}EPI_A$) showed the best correlation with aminoglycoside CL, with the least variability and better consistency in obesity. Incorporating the $CKD\text{-}EPI_A$ into a linear regression prediction model for aminoglycoside CL provided the best precision among the variables examined. These findings are in keeping with two previous studies. Chin *et al*. noted that the CKD-EPI equation (based on IDMS-aligned creatinine assays) corrected for individual BSA provided the best estimate of CL_{GEN} and was superior to the CKD-EPI equation normalised to 1.73 m^2.[15] Pai *et al*. reported that eGFR was better than CG in estimating aminoglycoside CL, and CKD-EPI outperformed MDRD for precision in patients with eGFR >60 mL/min.[16] The performance of the two eGFR equations was similar with eGFR <60 mL/min. In this particular study however, there was a marginal reduction in the precision of the prediction model when BSA-normalised eGFR was corrected from mL/min/1.73 m^2 to mL/min using patient BSA. Nonetheless, CKD-EPI still clearly outperformed the CG equations.

Our study also noted that the CKD-EPI eGFR was normally distributed and had the least spread of values and hardly any outliers. In contrast, the CG-TBW eCL_{CR} gave the highest kidney function estimates with the most variability and outliers. It has been previously noted that a GFR determined by inulin CL was a more precise estimate of aminoglycoside CL than CL_{CR}.[17] It is also well

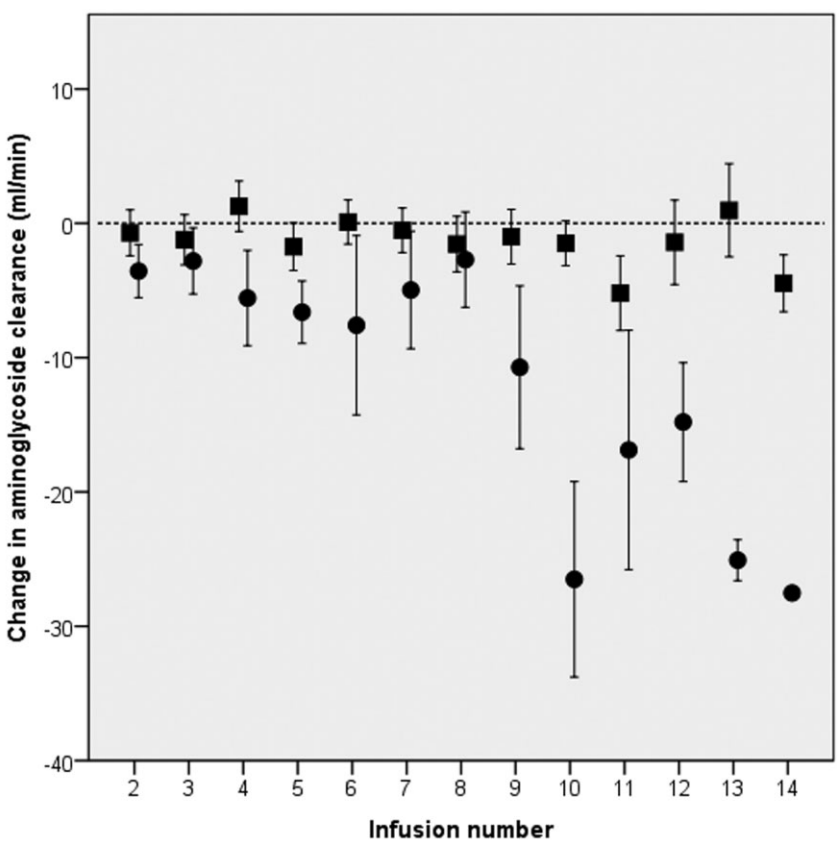

Figure 3 Change in aminoglycoside clearance for gentamicin (circles) and tobramycin (squares) over time relative to baseline (dotted line). The infusion number on the x-axis represents a surrogate for the duration of treatment in days, given the dosing intervals of 24 h. Tobramycin clearance is preserved over 14 days of treatment, but gentamicin clearance declines after 8 days. Data shown are mean ± SEM.

known that tubular secretion of creatinine may lead to overestimation of CL_{CR} by the CG equation. Our data support this finding, with the eGFR giving lower estimates of kidney function than CG. We also noted that not adjusting for bodyweight in dosing obese patients is associated with higher treatment doses and AUC_{24} above the target range, implying a propensity for overdosing. Furthermore, in obese patients, the weight-adjusted CG equations demonstrated superior correlation to aminoglycoside CL than CG-TBW and were comparable to the CKD-EPI_A equation. This is consistent with previous studies, which showed that using the lower of TBW and lean bodyweight was a better predictor of the volume of distribution (V_d) than either independently.[18] Furthermore, using the lower bodyweight in the CG equation resulted in a better correlation with CL_{GEN}. Similar results were noted even if obesity was defined as a body mass index >30 kg/m^2 per World Health Organisation (data not shown).

We found that the MDRD eGFR showed the poorest correlation with aminoglycoside CL. This is consistent with previous studies, which noted that the MDRD-based prediction model was inferior to CG-based models.[15,19,20] The MDRD equation also produced higher estimates than CG and would have resulted in higher recommended doses for some antimicrobials.[7–9] A study by Bookstaver *et al*. noted that the MDRD was better at predicting aminoglycoside CL than BSA-adjusted CG.[21] However, this study used a six-variable MDRD equation, and the serum creatinines were derived from assays that were not IDMS-aligned.

Increasing duration of treatment is correlated with a reduction in CL_{GEN}, which occurred after 1 week. Thus, cumulative nephrotoxicity may be a greater concern, and vigilance is advised if patients require GEN for more than 1 week. Due to small numbers, we could not demonstrate that patients with CKD were more likely than non-CKD patients to develop reduced CL_{GEN} during a treatment episode. On the other hand, TOB treatment for up to 2 weeks was not associated with a decline in CL_{TOB} in this cohort. Although there appears to be a lifetime risk of declining CL_{CR} with repeated TOB treatment episodes,[22] a recent study in patients with cystic fibrosis did not find a significant change in CL_{TOB} over many years.[23] It may be that TOB is less nephrotoxic than GEN.[24,25] Alternatively, TOB patients may be less sick, with less comorbidity and concurrent kidney insults, which may lower GFR. Thus, multiple TOB doses seem less problematic than GEN.

There are several limitations of this study. The severity of the illness is not considered in calculating guideline dosing, in that critically ill patients may have a larger V_d. Pharmacokinetic parameters other than AUC are also important in antimicrobial therapy. A high Cmax is required for optimal bactericidal activity and a low Cmin (minimum concentration) to minimise adaptive resistance. The first dose parameters were not always available for empirical GEN treatment. However, as our analysis shows, CL_{GEN} varies little within the first week. In some patients, selecting an accurate baseline serum creatinine in order to define AKI was limited by the availability of a recent measurement or serial measurements to determine stability. In accepting creatinine values up to 12 months prior as baseline, there may be have been an interim decline in renal function that has been undetected or a previous episode of AKI that has resolved. There are also general limitations of using serum creatinine as a filtration marker in patients with extremes of muscle mass, unusual diet or rapidly changing serum creatinine. Large volume fluid infusion may lower serum creatinine by haemodilution and artefactually increase the eGFR. In some cystic fibrosis patients, the serum creatinine values were transiently below the lower limit of the laboratory reference range that significantly impacted the accuracy of eGFR equations. In selecting the unique data from multiple TOB treatment episodes, we attempted to minimise this potential confounding by excluding treatment episodes where the first infusion was associated with a serum creatinine >25% lower than baseline. The results of our study may not be valid for patients with severe AKI, serum creatinine <35 μmol/L or stages 4–5 CKD as these patients were not represented in the analysis.

It is not entirely clear why the predicted aminoglycoside CL of our CKD-EPI_A models is lower than the expected 70–90% of CL_{CR}. However, recent studies have suggested that the eGFR equations perform differently at higher values as a predictor of aminoglycoside CL. Pai *et al*. noted that the coefficient (slope) and constant (intercept) in their linear regression model were different for patients with eGFR ≥60 compared with <60 mL/min.[16] We observed similar findings, with the slope approaching unity in patients with eGFR <60, but was substantially less in patients with eGFR ≥60 mL/min. In addition, Chin *et al*. described the eGFR based models as systematically underestimating CL_{GEN} as CL_{GEN} increased.[15] Only 11% of our GEN patients had eGFR <60 mL/min, and we speculate that this may be partly explain the flatter slope of the regression line, which is even more pronounced for TOB as many cystic fibrosis patients have high eGFR due to low serum creatinines and young age. These models need to be validated in another cohort of similar patients, and prospective studies would be useful to assess the utility of this approach in dosing algorithms. The need to stratify

patients by eGFR levels to determine which equations are optimal will also need to be further explored.

Conclusion

Our data support the use of IBW in calculating initial doses of aminoglycosides for obese patients. There is merit in including a kidney function estimate in calculating initial dosing, and the CKD-EPI$_A$ eGFR shows the greatest precision as an estimate of aminoglycoside CL. This approach requires validation, and further studies are needed to determine if a dosing protocol incorporating a CKD-EPI$_A$ eGFR-based estimation of aminoglycoside CL improves the achievement of target AUC or other important pharmacokinetic parameters.

Acknowledgements

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Figure S1 Frequency distribution histogram of gentamicin (A) and tobramycin (B) initial.
Infusion doses, with superimposed normal distribution curve (dotted lines). Each bar on the x-axis represents a 40 mg dose interval.

Figure S2 Overall aminoglycoside exposure as demonstrated by the mean 24-hour area under-the-curve for gentamicin (dark columns) and tobramycin (light columns).

Is post-pneumonia chest X-ray for lung malignancy useful? Results of an audit of current practice

C. Macdonald,[1] S. Jayathissa[1] and M. Leadbetter[2]

[1]Department of Medicine, Hutt Hospital and [2]Pacific Radiology, Boulcott Hospital, Wellington, New Zealand

Key words
lung neoplasm, pneumonia, mass screening, chest X-ray.

Correspondence
Sisira Jayathissa, Department of Medicine, Hutt Hospital, High Street, Lower Hutt, Wellington 5010, New Zealand.
Email: sisira.jayathissa@huttvalleydhb.org.nz

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Abstract

Background/Aim: Patients with community-acquired pneumonia (CAP) are often screened with repeat chest X-ray within 6–12 weeks following an admission. This practice is aimed to detect underlying lung malignancy, which can be difficult to identify initially when an acute infiltrate is present on X-ray. We conducted a study on the use of follow-up chest X-rays after an admission with CAP to determine the yield of suspected or diagnosed cancer.
Methods: During the 2-year period, January 2010–January 2012, we evaluated all patients over the age of 50 who had no previous history of lung cancer and were admitted to Hutt Hospital with CAP.
Results: A total of 302 patients was included. Of these, 53% received a follow-up chest X-ray within 6–12 weeks after admission. A total of six patients (2.0%) was diagnosed with lung cancer based on a chest X-ray within 6–12 weeks after admission. After a median period of follow up of 19.5 months, a further five patients who had normal chest X-ray were diagnosed with lung malignancy.
Conclusion: The majority of patients were screened with follow-up X-rays. The yield from a 6- to 12-week chest X-ray following CAP is low, which is consistent with previous studies. The development of clear guidelines to ensure identification of patient groups at significantly high risk of lung cancer is important to increase the sensitivity of screening. High yielding strategies, such as low-dose computed tomography, should be considered as an alternative.

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Original Full Length Article

Deferasirox at therapeutic doses is associated with dose-dependent hypercalciuria

Phillip Wong [a,b,c,*], Kevan Polkinghorne [c,d], Peter G. Kerr [c,d], James C.G. Doery [c,f], Matthew T. Gillespie [a,e], I. Larmour [g], Peter J. Fuller [a,b,c,e], Donald K. Bowden [h], Frances Milat [a,b,c]

[a] Hudson Institute of Medical Research, Victoria, Australia
[b] Department of Endocrinology, Monash Health, Victoria, Australia
[c] Department of Medicine, Monash University, Victoria, Australia
[d] Department of Nephrology, Monash Health, Victoria, Australia
[e] Department of Biochemistry and Molecular Biology, Monash University, Victoria, Australia
[f] Department of Pathology, Monash Health, Victoria, Australia
[g] Department of Pharmacy, Monash Health, Victoria, Australia
[h] Thalassemia Service, Monash Health, Victoria, Australia

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Iron overload

ABSTRACT

Deferasirox is an oral iron chelator used widely in the treatment of thalassemia major and other transfusion-dependent hemoglobinopathies. Whilst initial long-term studies established the renal safety of deferasirox, there are now increasing reports of hypercalciuria and renal tubular dysfunction. In addition, urolithiasis with rapid loss of bone density in patients with β thalassemia major has been reported. We conducted a cross-sectional cohort study enrolling 152 adult patients comprising of β thalassemia major (81.5%), sickle cell disease (8%), thalassemia intermedia (2%), HbH disease (6.5%) and E/β thalassemia (2%). Cases were matched with normal control subjects on age, gender and serum creatinine. Iron chelator use was documented and urine calcium to creatinine ratios measured. At the time of analysis, 88.8% of patients were receiving deferasirox and 11.2% were on deferoxamine. Hypercalciuria was present in 91.9% of subjects on deferasirox in a positive dose-dependent relationship. This was not seen with subjects receiving deferoxamine. At a mean dose of 30.2 ± 8.8 mg/kg/day, deferasirox was associated with an almost 4 fold increase in urine calcium to creatinine ratio (UCa/Cr). Hypercalciuria was present at therapeutic doses of deferasirox in a dose-dependent manner and warrants further investigation and vigilance for osteoporosis, urolithiasis and other markers of renal dysfunction.

1. Introduction

Thalassemia is a disorder of ineffective erythropoiesis and in its most severe form requires chronic blood transfusion and concomitant iron chelation treatment to prevent the complications of iron overload [1]. Thalassemia bone disease is a highly prevalent and severe complication with multiple risk factors including hypogonadism, marrow expansion, kidney stones, iron toxicity and iron chelators [2–4]. Deferasirox is an oral iron chelating agent used widely in the treatment of transfusion-dependent anemia's such as thalassemia major, sickle cell, myelodysplastic syndrome, aplastic and other rare anaemias.

Deferoxamine, the standard of care for the past 40 years, requires subcutaneous or intravenous administration and is associated with poor patient compliance [5]. Deferasirox is highly efficacious and safe in the treatment of iron overload in thalassemia major as demonstrated in large prospective [6,7] and extension studies of up to 5 years duration [8]. A mild dose-dependent reversible increase in serum creatinine was reported in one third of subjects [6,7], but the renal safety was confirmed at deferasirox doses greater than 30 mg/kg/day [9]. However, testing for renal tubulopathy and in particular hypercalciuria was not routinely performed in these early pivotal studies.

Increasing and worrying reports of renal tubular dysfunction including hypercalciuria have emerged with deferasirox [4,10], but this has not been examined systematically. Moreover, hypercalciuria is a possible mechanism linking recent findings of increased urolithiasis with severe osteoporosis in thalassemia major [2,3,11]. We sought to determine the prevalence of hypercalciuria in subjects with transfusion-dependent

* Corresponding author at: Hudson Institute of Medical Research, 27-31 Wright Street, Clayton, VIC 3168, Australia.
E-mail address: phillip.wong@hudson.org.au (P. Wong).

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hemoglobinopathies treated with deferasirox or deferoxamine compared to normal controls.

2. Methods

2.1. Cases

We enrolled 152 subjects with transfusion-dependent haemoglobinopathies from a single academic center in Melbourne in 2014. Iron chelator use was documented and dosage expressed as mg/kg/day. Synchronous urine and serum biochemistry was obtained. These comprised of serum creatinine, calcium, phosphate, parathyroid hormone (PTH) and 25(OH)VitD levels. Urine testing for UCa/Cr and tubular protein to creatinine ratios were measured on 2 separate occasions, and the mean value derived. Hypercalciuria was defined as a UCa/Cr greater than 0.40 mol/mol [12]. Hypercalciuria severity was separated into 3 tertiles (normal <0.4 mol/mol, moderate 0.5–1.5 mol/mol and severe 1.5 mol/mol and above). Increased urine protein excretion was defined as a urine protein to creatinine ratio > 0.3 [13].

Bone mineral density was measured using dual energy X-ray absorptiometry (DXA) at a single center. Fractures and kidney stones were defined as those confirmed based on radiological reports or through the medical records as was bisphosphonates use. In the majority of cases, kidney stones were diagnosed radiologically by plain abdominal X-ray or computer tomography (particularly if symptomatic) and abdominal ultrasound. A history of hypogonadism and hypoparathyroidism was documented based on biochemistry [14,15].

2.2. Controls

A control population was selected from subjects in the baseline cohort of the Australian Diabetes, Obesity and Lifestyle (AusDiab) study. Details of the study are described elsewhere [16]. Cases were matched with controls subjects on age, gender and serum creatinine; UCa/Cr was assessed in the same laboratory for both the cases and control subjects.

2.3. Statistics

One-way ANOVA was used to determine the difference between hypercalciuria severity with clinical and biochemical variables; post hoc analysis was performed using the Tukey test. A Kernel density estimation was used to derive a probability distribution of urine Ca/Cr ratio in the deferasirox, deferoxamine and control groups. The relationship between hypercalciuria and iron chelator dosage was determined using uni- and multivariate regression with adjustments for potential confounders (sex, age, creatinine, ferritin, calcium, PTH). Multicollinearity was determined to be present if the variance inflation factor was greater than 10. Analyses were conducted using using Stata 13 (College Station, Texas) and SPSS 20 (IBM, Armonk, NY).

3. Results

The study cohort of 152 subjects comprised of patients with β thalassemia major (81.5%), sickle cell disease (8%), thalassemia intermedia (2%), HbH (6.5%) and E/β thalassemia (2%). The mean age was 34 years and 42% were males. At the time of analysis, 88.8% of patients were receiving deferasirox (mean dose 23.2 mg/kg/day) and 11.2% deferoxamine (mean dose 44.1 mg/kg/day). All subjects had received deferoxamine prior to 2007. Subjects in the deferasirox arm had received continuous deferasirox since 2007; those in the deferoxamine arm were treated with deferoxamine for an average of 5 ± 2 (years ± SD) prior to the commencement of the study in 2014. There was no significant difference in transfusion parameters, serum calcium and vitamin D, hypogonadism, hypoparathyroidism, kidney stones, fractures or bone density between those on deferasirox or deferoxamine at baseline (Table 1).

Table 1
Baseline patient characteristics.

	Deferasirox (n = 134)	Deferoxamine (n = 18)	P value
Gender	M(44%) F(56%)	M(24%) F(76%)	0.1
Age (yrs)	33.5 ± 12.5	37.8 ± 9.1	0.35
Hemoglobin (120–160 g/L)	108.3 ± 10.2	103.1 ± 9.7	0.06
Creatinine (55–105 μmol/L)	67.9 ± 20.2	76.7 ± 47.6	0.69
Ferritin (15–180 μg/L)	1237.4 ± 1401	1738.6 ± 1714	0.1
Calcium (2.20–2.60 mmol/L)	2.28 ± 0.13	2.28 ± 0.10	0.99
Phosphate (0.8–1.5 mmol/L)	1.2 ± 0.25	1.2 ± 0.20	0.79
Parathyroid hormone (1.5–7.0 pmol/L)	1.98 ± 1.24	2.1 ± 1.02	0.56
25 (OH) vitamin D (75–250 nmol/L)	65.4 ± 18.1	72.3 ± 23.9	0.31
Urine calcium/creatinine (≤0.4)	1.20 ± 0.74	0.95 ± 0.66	0.12
Urine tubular protein/creatinine (≤0.3)	0.041 ± 0.08	0.033 ± 0.033	0.34
Fracture	15%	12%	0.74
Hypogonadism	38%	35%	0.84
Hypoparathyroidism	15%	29%	0.21
Kidney stones	23%	18%	0.62
Bisphosphonates	19%	24%	0.62
Lumbar spine Z score	−1.72 ± 1.29	−1.74 ± 1.44	0.6
Femoral neck Z score	−0.93 ± 1.14	−1.138 ± 0.84	0.07

The distribution of UCa/Cr was significantly different in the control, deferasirox and deferoxamine treated subjects (Fig. 1). Hypercalciuria was present in 91.9% of subjects on deferasirox and 83.4% on deferoxamine in the presence of a normal serum creatinine. There was a significant positive association between weight-adjusted deferasirox dosage and hypercalciuria severity which was maintained after adjusting for confounding factors. In contrast, the relationship between deferoxamine dose and hypercalciuria was not significant (Table 2).

4. Discussion

Deferasirox when used in therapeutic dosage is associated with dose-dependent hypercalciuria in patients with thalassemia major. The findings of significant hypercalciuria may explain the increased prevalence of kidney stones [3,11] and associated accelerated bone loss [2] described in the thalassemia cohort since the introduction of deferasirox.

Renal tubular and glomerular dysfunction has been described in the pediatric thalassemia population on deferoxamine and deferasirox [10,17]. Indeed, cases of reversible Fanconi's syndrome, increased

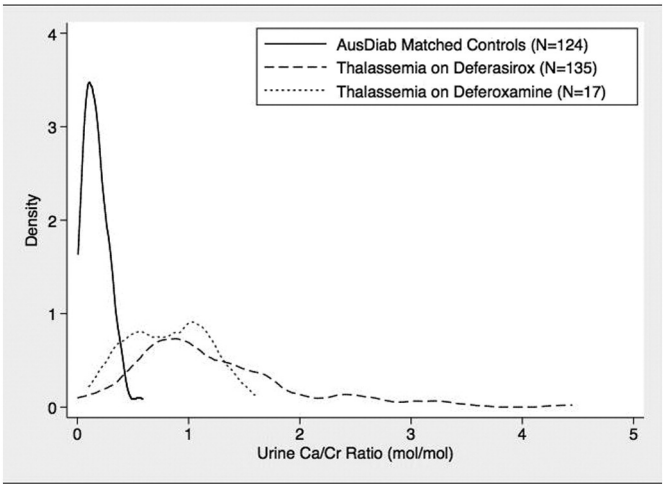

Fig. 1. Kernel density estimation of urine Ca/Cr ratio in subjects treated with either deferasirox or deferoxamine compared to controls.

Table 2
Patient characteristics based on urine Ca/Cr ratio.

Urine Ca/Cr ratio (mol/mol)	Gender (M/F)	Age (yrs)	Weight (kg)	Creatinine (μmol/L)	Ferritin (μg/L)	Calcium (mmol/L)	PTH (pmol/L)	‡ Deferasirox dose (mg/kg/day) (n = 134)	Deferoxamine dose (mg/kg/day) (n = 18)
Normal: <0.4	M (11%) F (8%)	36.5 ± 12.7	62.4 ± 20.1	87.5 ± 54.5	2326.7 ± 2352.9	2.2 ± 0.2	3.0 ± 2.4	17.7 ± 10.4 (n = 11)	39.7 ± 23.6 (n = 3)
Moderate: >0.4 and <1.5	M (72%) F (64%)	34.3 ± 12.1	57.4 ± 15.6	67.4 ± 19.7	1210.1 ± 1406.8	2.3 ± 0.1	1.9 ± 0.9	21.3 ± 10.9 (n = 89)	45.6 ± 14.4 (n = 13)
Severe: >1.5	M (17%) F (28%)	32.3 ± 12.5	54.0 ± 14.2	66.3 ± 18.5	1157.0 ± 931.2	2.3 ± 0.1	2.0 ± 1.3	30.2 ± 8.8 (n = 34)	30.6 ± 4.0 (n = 2)
All	M (n = 64) F (n = 88)	34.0 ± 12.2	57.0 ± 15.8	68.9 ± 24.9	1294.1 ± 1442.3	2.3 ± 0.1	2.0 ± 1.2	23.2 ± 11.2 (n = 134)	43.0 ± 15.5 (n = 18)
P value*	0.26	0.58	0.27	0.7	0.17	0.94	0.19	0.001	0.47

* Kruskall wallis test, chi square for gender.
‡ $P < 0.05$ on Post-Tukey.

markers of proximal renal tubule dysfunction and hypercalciuria are associated with deferasirox use [4,10]. In patients using deferoxamine, hypercalciuria has been reported in 1/3 of cases with an abnormal UCa/Cr range of (0.21–0.57, normal < 0.21) [18]. In our patient cohort on deferasirox, hypercalciuria was more prevalent (91.8%), severe (UCa/Cr range (0.41–4.2, normal < 0.4)) and associated with a significant dose-dependent relationship. Whilst the number of subjects treated with deferoxamine was small, its relationship with hypercalciuria and other markers of renal tubular function was not dose-dependent and is consistent with findings from previous studies [17,18].

The mechanisms underlying renal tubular damage in thalassemia major are likely to be multifactorial. Chronic anemia, iron overload or iron chelators causing relative iron depletion or direct toxicity may be implicated [19]. Relative intracellular iron depletion can compromise the function of the proximal renal tubule which accounts for 80% of renal calcium handling. This site is rich in Na^+/K^+-ATPase activity and iron is an important intermediary for ATP production [20]. Deferasirox is able to readily enter cells due to its lipophilicity and form a highly charged complex with iron; this negative charged complex is less lipophilic and may account for the nephrotoxic potential of deferasirox [19]. Indeed, the absence of other markers of proximal renal tubular dysfunction such as phosphate or significant protein excretion, suggests calcium loss may be due to a specific rather than broader defect in renal tubular function. However, we did not routinely screen for hyperuricemia which is a risk factor for kidney stones.

Deferasirox exacerbates hypercalciuria which may already be pre-existing due to other factors. Hypercalciuria is an established risk factor for osteoporosis and urolithiasis. Our previous study had confirmed urolithiasis and osteoporosis to be highly prevalent in thalassemia subjects treated with deferasirox [3]. In the 4 year extension registration study, optimal iron chelation was achieved with deferasirox at doses between 15 and 35 mg/kg/day in 76.1% of patients [8]. Our findings confirm deferasirox at a mean dose of 30.2 ± 8.8 mg/kg/day was associated with a UCa/Cr of almost 4 fold the upper limit of normal. Although we did not find a significant difference in the prevalence of kidney stones, BMD or fractures in our cohort, we did not actively screen for kidney stones or fractures radiologically. Therefore, asymptomatic kidney stones and vertebral fractures were likely to be underestimated in this study.

The bone and renal disease in thalassemia is a composite of multiple risk factors and elucidating their unique effect on the skeleton and kidney is challenging. Deferasirox has been shown to decrease both tartrate-resistant acid phosphatase and cathepsin K expression, as well as osteoclast activity in-vitro [21]. In a retrospective cohort study of combined pediatric and adult patients (age 5–49) with thalassemia major treated with deferasirox, improvements in lumbar spine BMD and stability in femoral neck BMD were seen during a mean study duration of 6.5 years, but this study lacked a control arm [22]. Further work is needed to elucidate the effect of deferasirox on bone health and BMD in patients with transfusion-dependent thalassemia. From a renal perspective, in a retrospective cohort in patients receiving deferasirox compared to deferoxamine the presence of kidney stones (as confirmed by abdominal ultrasound) was not significantly different [23]. However, as the majority of kidney stones are asymptomatic, the true incidence of kidney stones in thalassemia is unknown.

We are mindful of the limitations of this study. Whilst a dose-dependent effect of a drug may support causation, this study was cross-sectional and observational in nature. The selection of an appropriate control group is difficult as the inclusion of untreated thalassemia major subjects to act as controls would be unethical. Therefore, comparing deferasirox to subjects treated with deferoxamine (active comparator) is necessary. Whilst the number of subjects on deferoxamine was small, the failure of other studies to demonstrate a dose-dependent relationship between deferoxamine, hypercalciuria and other markers of renal tubular function [17,18], validates our own findings.

Deferasirox at therapeutic doses leads to an exacerbation of hypercalciuria in a dose-dependent manner and requires vigilance for osteoporosis, urolithiasis and other markers of renal dysfunction. In the presence of urolithiasis and/or loss of significant bone mineral density, consideration should be given where possible to either reducing the dose of deferasirox or switching to an alternative iron chelator. The clinical sequelae and reversibility of hypercalciuria in patients exposed to deferasirox needs to be confirmed in a prospective longitudinal study.

Disclosures

All authors declare that they have no conflicts of interest.

Author contribution

Study concept and design (PW, DKB, FM, PJF, MTG), acquisition (PW, DKB, JCGD), interpretation (PW, PGK, KP) of data and revision of manuscript (PW, KP, PGK, MTG, IL, JCGD, PJF, DKB, FM).

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Appendix

The Changing Role of Hospital and the Need for a Four-Year Pharmacy Undergraduate Course

Written by Ian Larmour June 1989

Executive Summary

Prepared for the SHPA and the Joint Four-Year Course Working Party and presented at the Heads of Pharmacy Schools Conference in 1990.

THE CHANGING ROLE OF HOSPITAL PHARMACISTS AND THE NEED FOR A FOUR YEAR PHARMACY UNDERGRADUATE COURSE.

PREPARED FOR THE SHPA FEDERAL COUNCIL

BY IAN LARMOUR

JUNE 1989

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EXECUTIVE SUMMARY

The role of the hospital pharmacist has changed dramatically over the past 15 years. This has occurred in response to the rapid increase in the number of useful, therapeutically active drugs and their potential risks. The associated proliferation of information, technology, community expectations and the increased complexity of treatment have also been major stimulus for this development.

The traditional skills and roles of the pharmacist are required. However, the changing role of hospital pharmacists has led to an extension of many of these roles plus the incorporation of new roles.

A review of the following roles is presented in the submission:

- Clinical Pharmacy Practice
- Patient Education and Medication Counselling
- Drug Information Services
- Intravenous Admixture Services
- Parenteral Nutrition Services
- Sterile Product Manufacturing
- Manufacturing of Non Sterile Products and Packaging Services
- Clinical Drug Trials
- Influencer of Prescribing
- Quality Assurance
- Teaching and Research
- Radio-pharmacy Services

It is likely that these roles will continue to develop in scope and sophistication.

This changing role requires changes in the undergraduate training of pharmacists.

In particular, there is a need to develop the clinical skills of pharmacists, especially clinical judgment and communication skills. These generic skills are equally as important for community pharmacists.

[redacted]

The problems with the current course are outlined and suggestions for changes are included. In particular, changes in didactic emphasis and content, skills development, active teaching methods, greater use of practitioner/educator and student/patient contact, especially off campus.

The increased time component due to changes in both methods of teaching and didactic content points to the urgent need for a 4 year undergraduate course for pharmacists.

The benefits to the community from this change in training are discussed. The benefits in summary are perceived to be:

1. The development of useful data bases on the use and safety of medication.

2. Decreasing the incidence of avoidable drug induced toxicity.

3. The education of patients, and others, to avoid medication problems and improve compliance.

4. The promotion of rational, cost effective prescribing, including appropriate Therapeutic Drug Monitoring programmes.

1. INTRODUCTION

The role of the pharmacist is not well understood by the general community. This makes it extremely difficult to illustrate the roles and needs of the profession to those outside the profession. This submission therefore aims to outline the roles, of hospital pharmacists, with particular emphasis on the role development of the past two decades.

This changing role illustrates the need for change in the undergraduate training of pharmacists. These changes will be of considerable benefit to the community.

2. THE CAUSE OF CHANGE

2.1 Increase in the Number of Useful Drugs

Since the 1950's there has been a dramatic rise in the number of therapeutically active drugs, together with significantly more stringent product registration requirements. This has been accompanied by a rapid proliferation in research and the growth of knowledge and information on pharmaceutical products and their therapeutic use. There has also been dramatic changes in drug technology, treatment sophistication and, as a consequence, an enormous range of potential complications. Hospital pharmacists have seen the need to become more actively involved in patient treatment in an attempt to reduce the adverse complications of drug therapy.

The complications of modern drug therapy include adverse drug reactions, drug interactions, incorrect use of serum drug assays/levels and inappropriate use of drugs. The pharmacist's intervention role is outlined in latter sections of this document.

2.2 Consumer Pressure

The increased expectations of the general public, especially well organised consumer groups, with respect to their treatment has also placed an increasing emphasis on the interaction between patients and pharmacists and on the thoroughness of the service provided. This has led to greater emphasis being placed on quality assurance programmes.

2.3 Manufacturing Technology

The need for high quality, safe pharmaceutical products has led to the development of strict manufacturing guidelines, as outlined under the Code of Good Manufacturing Practice. this has had a significant impact on the traditional manufacturing practices of hospital pharmacists.

2.4 Computer Technology

The development of computer technology has increased the scope of many activities and, at the same time, opened the opportunity for new and important roles e.g. Drug Utilisation Reviews (Pharmaco-epidemiology).

3. TRADITIONAL ROLE OF HOSPITAL PHARMACISTS

Hospital pharmacists have traditionally performed the following roles:

3.1 Review of prescriptions for dosage safety and drug interactions

3.2 Dispensed prescriptions, including labelling and records. The need for accurate dispensing being absolute.

3.3 Ensure legal and ethical aspects of professional pharmacy practice are carried out, in particular, for drugs of addiction or abuse.

3.4 Advise patients on dosage instructions, drug administration and general common ailments.

3.5 Formulate special pharmaceutical products.

3.6 Manufacture sterile and non sterile products, including extemporaneous dispensing.

3.7 Packaging and labelling bulk products in suitable patient use packs, thus increasing the efficacy of dispensing.

3.8 Budgeting, personnel and general administration, including involvement in a number of hospital committees and drug formularies.

3.9 Purchasing of pharmaceutical and related products, plus stock control and financial procedures.

4. NEW ROLES FOR HOSPITAL PHARMACISTS

Hospital pharmacists are still required to carry out these traditional roles. However the role of the hospital pharmacist has changed dramatically over the past two decades, not only in the type of activities, but particularly the depth and scope of traditional activities.

The most dominant feature of this development has been the evolution of the clinical roles of the pharmacists, and with this has developed the need for a more sophisticated approach to quality assurance.

These new roles are outlined below and cover

- Clinical Pharmacy Practice (Sect 4.1)
- Patient Education and Medication Counselling (Sect 4.2)
- Drug Information Services (Sect 4.3)
- Intravenous Admixture Services (Sect 4.4)
- Parenteral Nutrition Services (Sect 4.5)
- Sterile Product Manufacturing (Sect 4.6)
- Manufacturing of Non Sterile Products and Packaging Services (Sect 4.7)
- Clinical Drug Trials (Sect 4.8)
- Influencer of Prescribing (Sect 4.9)
- Quality Assurance (Sect 4.10)
- Teaching and Research (Sect 4.11)
- Radiopharmacy Services (Sect 4.12)

4.1 Clinical Pharmacy Practice

This has predominantly developed in the wards of hospitals, but there is a gradual shift to clinical practice in outpatient clinics e.g. epilepsy and pain control clinics. This clinical role also has considerable relevance to community pharmacy practice.

The tasks include

(i) Prescription or Drug Chart Review

This covers

- Dosage regime safety
- The relevance of patient diseases which affect drug dosage e.g. renal, hepatic and cardiac failure. This also involves judgment on whether alternative drugs would be safer in this patient

- Drug interactions, including monitoring for the appearance of rarer interactions and the formulation of approaches to avoid or minimise such interactions

- Avoiding contraindications to the medication

- Checking for previous drug hypersensitivity

- Checking against previous medication for errors in transcription or omission. This is also important for prescriptions issued to patients upon discharge from hospital

The problems detected are discussed with the relevant medical/nursing staff to ensure appropriate steps are taken.

(ii) Patient Parameter Monitoring

The pharmacist must be able to make judgments on which patients need monitoring, the parameters to be monitored and the frequency of monitoring. This monitoring should be seen in relation to the patient's medication and disease type.

This is relevant in determining

- Whether dosage should be adjusted e.g. due to the development of renal failure

- Detection of early signs of drug induced toxicity e.g. adverse drug reactions or drug interactions. Thus minimising the consequences of the adverse drug reaction or interaction by enabling the drug to be ceased at an early stage and ensure early relevant treatment

The parameters monitored are biochemistry reports (e.g. renal and hepatic indicators), microbiology reports, haematology reports, ward urinalysis charts, ward blood pressure/temperature/pulse charts and other records.

It also obviously involves close liaison with medical and nursing staff. This latter aspect is also important in the detection of skin rashes and other potentially drug related effects.

Pharmacists must also be familiar with the format and content of patient medical history records.

(iii) Therapeutic Drug Monitoring and Pharmacokinetic Dosage Advice Services

This role is to assist in the optimising of a specific patient's medication. It is performed in conjunction with the Biochemistry Department (serum drug assay reports) and the patient's medical practitioner.

The relationship between drug efficacy or toxicity and serum drug levels has not been established for all drugs, although the number is likely to substantially increase in the next decade. The drugs now most frequently involved in Australian hospitals are Anti-epileptic drugs, Aminoglycoside antibiotics, Vancomycin, Theophylline, Cyclosporin A and antiarrythmic drugs. Oral Anti-coagulants (Warfarin) also fall into this category, except that Prothrombin Time ratios are monitored.

The clinical pharmacist has a monitoring and educational role to ensure that therapeutic drug monitoring is conducted rationally in order to avoid inappropriate serum drug assays or erroneous interpretations.

This role includes:

- Promoting correct sampling, especially in the timing of sampling for trough or peak levels

- Ensuring drug therapy is at a steady state. This is related to the drug's half life and, in some cases, patient specific factors e.g. renal diseases

- Assisting in the interpretation of serum drug assay results. This includes consideration of drug interactions, drug assay interference, sampling errors and patient specific factors e.g. renal, hepatic or cardiac disease, age, medication compliance and whether the patient is a smoker or not. A knowledge of bioavailability factors is also relevant

- advise on dosage or dosage adjustments and follow up

This requires a practical knowledge of pharmacokinetic principles and the specific relevant drug parameters. The use of bayesian pharmacokinetic computerised dosage prediction methods is becoming increasingly important in this area. Thus a knowledge of computer applications and mathematics is required.

(iv) Documentation of Adverse Drug Reactions

The clinical pharmacist is in an ideal position to co-ordinate and supervise the reporting of Adverse Drug Reactions (ADR's). Generally this relates to spontaneous reporting systems, but it is also relevant for Intensive Monitoring Programmes in the wards of hospitals.

The appropriately trained pharmacist is also an ideal member of the health care team to co-ordinate post marketing surveillance programmes e.g. drug related hospital admissions and ADR's found in outpatient clinics. Such programmes may also involve joint projects between hospital and community pharmacists. This role is important in that it can assist in the development of useful data on the safety of drugs, especially the comparative incidence of ADR's. This is particularly relevant for new drugs, where pre-marketing clinical trials and evaluations, although extensive, are not able to detect all problems. The reasons for this include the limited number of patients tested, a number of patient groups are largely excluded (e.g. elderly, children and pregnant females) and the low incidence or long lead time associated with many ADR's.

This documentation of ADR's is also important in helping to elucidate patient risk factors.

This role requires an understanding of therapeutics, disease states, human pharmacology, pharmacokinetics and epidemiology, together with data analysis and statistical skills.

(v) Drug Information Source

The clinical pharmacist must be able to provide accurate, relevant and timely drug information, which may include:

- dosage and dosage adjustment
- drug selection
- side effects
- pharmacokinetics
- drug interactions
- intravenous imcompatibilities
- drug administration methods and routes
- contraindications
- indications
- therapeutic aspects

(vi) Educational Role

In addition to the education of pharmacy students, the clinical pharmacist also acts as a valuable resource for medical students, junior medical staff, nursing staff and other relevant student groups.

(vii) Member of the Health Team

To operate effectively, clinical pharmacists must be an integral member of the health care team. This in turn, requires effective communication skills and requires the pharmacist to attend ward/unit meetings/rounds.

4.2 Patient Education and Medication Counselling

The role of a pharmacist has always included advice on medication to patients. However, in recent years this role has become more extensive. This includes taking patient medication histories and discussions on the importance of compliance. For example, training in the use of inhalers, advice on methods/systems to help patients to remember to take their medication and providing relevant drug information according to the patients needs. The patients involvement is encouraged. In some cases pharmacists visit the homes of patients. This includes specialised home patient training e.g. Parenteral Nutrition, Home Dialysis and Home Antibiotic programmes.

This developing role places a greater emphasis on communication skills and a knowledge of relevant patient psychology. The development of these communication skills requires practical training and patient contact, not merely didactic information.

4.3 Drug Information Service Centres

This section deals mainly with the specialised support services provided at major hospitals. However, all pharmacists, including community pharmacists, are required to be able to provide accurate, relevant and timely drug information. It also covers Poison Information Centres.

The rapid increase in the number of therapeutically useful drugs has brought with it a proliferation of information sources. No longer is a standard list of textbooks adequate for the needs of a hospital pharmacy department. The diversity of requests requires access to numerous relevant journal articles and the use of sophisticated computerised data retrieval systems.

Apart from the normal clerical duties required to maintain retrievable and relevant material, the pharmacist requires an ability to make judgments on the accuracy and relevance of information. There is also an absolute need for effective verbal and oral communication skills.

In order to make relevant clinical judgment on the information being assessed and to provide the appropriate answer the pharmacist must

- Have an adequate knowledge of disease states and therapeutics (to enable the question to be understood). It is also necessary for the answer to be useful and be conveyed in a manner that the enquirer understands
- Have a knowledge on the design requirements of useful drug trials, statistical analysis and an understanding of terminology
- Have a practical knowledge of the value of various information sources. In particular they must be familiar with basic computer skills
- Have the ability to present written information in an acceptable format with the correct use of references

These skills are also relevant to the production of the Pharmacy Bulletin and other publications.

4.4 Intravenous Admixtures Services

This role requires the traditional knowledge and practical skills of asceptic dispensing techniques. It also requires a knowledge of drug stability and intravenous drug incompatibilities. This requires an understanding of basic scientific principles, since research on drug stability and compatibility remains important.

The Code of Good Manufacturing Practice has placed a greater emphasis on equipment and material monitoring, end product quality control, detailed records, cleanliness procedures, personnel training and a knowledge of in-process statistical quality control monitoring. Strict compliance with these requirements is required to avoid accidental microbiological contamination of intravenous fluids, which also emphasises the need for this service to be provided rather than having the intravenous admixtures prepared in the unsterile ward environment.

The rapid increase in the use of cytotoxic drugs has also brought the requirement for additional knowledge on the development of safe handling procedures. A knowledge on the safe disposal of cytotoxic drugs and staff health monitoring procedures is now required.

4.5 Parenteral Nutrition Services

The knowledge and skills outlined in the Intravenous Admixture Service section are required. However, pharmacists are also an integral component of hospital multidisciplinary Total Parenteral Nutrition (TPN) teams.

The pharmacist must have a knowledge of nutritional requirements (especially in illness and stress), formulation, stability of drugs and knowledge of the clinical aspects of parenteral nutrition.

Pharmacists not only prepare the solutions, but act as an advisor on th use, formulation and control of parenteral nutrition within the hospital. Pharmacists also have a role in the training of home TPN patients. This includes visits to the patient's home.

4.6 Sterile Product Manufacturing Services

The importance of this role has decreased with the greater availablility of manufactured products, rationalisation of products and economic factors.

However, pharmacists are still required to produce small batches of institution specific products, especially for clinical trials and product research. This requires a detailed knowledge of, and compliance with, the strict requirements of the Code of Good Manufacturing Practice. Therefore the traditional skills and the requirements outlined in the Intravenous Admixture Service are required, including formulation.

4.7 Manufacturing of Non Sterile Products and Packaging Services

The extemporaneous dispensing skills and other traditional roles, including formulation, continue to be important. However, the sophistication of this area of practice has also increased due to the requirements of the Code of Good Manufacturing Practice.

4.8 Clinical Drug Trials Services

Pharmacists are required to provide logistical support for many clinical dug trials. This not only involves labelling, packaging, dispensing and records, but frequently also requires the randomisation of treatments and the formulation of specific products e.g. Placebo mixtures. The pharmacist is also required to be able to provide practical advice on the structure, design, ethics and legal aspects of clinical drug trials.

Therefore, a detailed knowledge of clinical drug trial design, statistics and epidemiology is required, as was also outlined in the section on Drug Information Services. A general knowledge of drug toxicology is also required.

4.9 Influencer of Prescribing

Economic factors are causing a greater emphasis to be placed on the promotion of rational cost effective prescribing. The pharmacist is an ideal resource to assist in the achievement of this goal.

The clinical pharmacist and drug information service roles, previously outlined, are essential elements of such programmes.

However, the pharmacist also has a central and important role to play in the co-ordination and development of drug utilisation studies, adverse drug reaction incident studies and cost benefit, cost effectiveness, cost utlity analysis strategies. This role is carried out in

conjunction with the hospital's Peer Review/Quality Assurance and Therapeutics/Drug Committees, plus other personnel relevant to the particular study.

The role of pharmacist 'academic detailer' educators, clinical pharmacists and the Pharmacy Bulletins are likely to become increasingly important. Therefore pharmacists will require a knowledge of clinical epidemiology, statistical methodologies and persuasive communication techniques. The skill of presenting influential and well presented, accurate information will be a paramount requirement.

4.10 Quality Assurance

Greater emphasis on the quality of service is likely to be placed on pharmacists as the years proceed. Therefore, there is a perceived need for an understanding of the Peer Review and Quality Circles concept as well as a basic understanding of personal motivation strategies and group dynamics. This knowledge would enhance the communication skills of pharmacists as well as improving their personnel management skills.

4.11 Teaching and Research

Hospital pharmacists will continue to have a research role, not only in systems development, but in areas such as drug pharmacokinetics, bioavailability and formulation. There will also be an increasing need for pharmaco-epidemiology research.

The teaching role is also likely to become increasingly important, which emphasises the need for short post graduate courses in educational techniques.

4.12 Radiopharmacy Services

The logistical support for this type of service has been carried out for many years. It is likely this role will continue to develop, but with a greater emphasis being placed on support for research projects.

5. PROBLEMS WITH CURRENT UNDERGRADUATE TRAINING

The strong scientific component of existing undergraduate courses will need to be maintained. However, the many new roles for hospital pharmacists require changes in existing didactic content, both in terms of improved relevance and the

inclusion of new subjects. This includes the adoption of new teaching methods, the inclusion of patient contact in off campus locations and greater use of teacher practitioners.

The growing clinical role of pharmacists creates the most pressing need for change. Routine clinical ward pharmacy services were introduced into Australian hospitals in 1973. However the training of pharmacists for this role, to date, has largely fallen on the individual and the hospital pharmacy departments, although, more recently, there have been some suitable part time post graduate courses. Therefore the number of pharmacists trained in clinical skills remains relatively small.

Significant deficiencies in the clinical judgment and skills of newly graduated pharmacists has been a major problem. Therefore, the quality of these clinical pharmacy services has been largely dependent on department inservice training and self education. It is estimated that a minimum of 2 to 3 years of clinical ward pharmacy practice and training is required before the average pharmacist is able to carry out a routine clinical pharmacy role. It takes several more years of practice, self education and post graduate study before highly competent skills are achieved.

This has meant a wide variation in the standards of clinical pharmacy practice and, in many cases, has significantly inhibited the development of these services.

Major changes in pharmacy undergraduate education are therefore needed if these current deficiencies are to be corrected. To date the evolution of clinical pharmacy services has occurred in hospital pharmacy practice, however, the need for competent clinical pharmacy practitioners in community pharmacy is equally important.

6. SUGGESTED CHANGES IN DIRECTION

6.1 Skill Development

To allow future pharmacists, from all spheres, to adequately meet the changing needs of society, there is an urgent need to more fully develop the sophistication of the skills of students. Particular emphasis is placed on

- Clinical judgment skills
- Communication skills

These skills are generic in nature, although the specific application of these skills may vary according to the area of practice.

6.2 Content Changes

Changes to existing course content should include

- Greater emphasis on the therapeutic use of drugs
- Pharmacology being more oriented to the use of drugs in humans
- Pharmacokinetics having a greater emphasis on practical applications e.g. Therapeutic Drug Monitoring and Dosage Advice
- Verbal and written communication skills receiving greater emphasis, especially in practical training
- Medical terminology and a general knowledge of disease states and the use of laboratory reports
- Pharmaco-epidemiology, including Adverse Drug Reaction monitoring, together with a knowledge of cost benefit, cost effectiveness and cost utility analysis
- Human behaviour and quality assurance, including motivation and group dynamics
- the evaluation of the information, including clinical drug trial design and statistics
- The principles of nutrition, especially in disease states
- Computer skills
- The pharmaceutical application of recombinant DNA technology and monoclonad antibodies

6.3 Teaching Method Changes

It is suggested that closer links be established between pharmacy colleges and hospital pharmacy departments. Particular emphasis is placed on the need for considerable numbers of practitioner/educators to participate in tutorials (or lectures) on and off campus.

Most important is the need for students to have direct patient contact. This implies the need for some off campus training e.g. hospital wards or specialist outpatient/community settings.

There is a need for existing laboratory practical training to be reviewed with the emphasis on the relevance of the training. There should be greater use of small group tutorials where students are actively challenged and required to lead discussions i.e. they should be actively involved in the teaching process.

This approach will be needed to develop the generic skills of effective communication and clinical judgment. The development of clinical judgment skills being relevant to all pharmacists, viz to ensure they are able to accurately interpret and assess relevant information, data and patient parameters in order to make well balanced and well based decisions in choosing a course of action.

6.4 Length of Course

These changes in training require greater input and interaction from students including discussion, challenge and the development of judgment and communication skills.

This approach requires more time than traditional didactic lecturing, although the latter will obviously continue to be extremely important. In fact the current didactic content, changed though it may be, will still largely continue to be required.

This points to the need for a lengthening of the pharmacy undergraduate course from 3 years to 4 years. This obviously increases the cost of training pharmacists. However, the improved training of pharmacists will provide many benefits to the community.

7. BENEFITS TO THE COMMUNITY

Hospital pharmacists are already making a substantial contribution to the health care industry. However, the value of this contribution would be greatly enhance by improving the quality and scope of the training for undergraduate pharmacists. Importantly, not only will it further improve current services, but it will even out variations in quality.

The benefits to the general community are outlined below. A number of points have already been covered but they are repeated in order to illustrate the relevance of the point.

7.1 Documentation of Adverse Drug Reactions

Adverse Drug Reactions (ADR's) are a major cause of mortality and morbidity in the community and are a significant cause of hospital admission. (1 to 17).

Apart from the suffering caused to patients, ADR's have a major impact on health care costs and the loss of productivity. Despite the rigorous evaluation of new drugs, pre-marketing trials are not able to detect all types of ADR's, nor their incidence.

This deficiency is due to

- Limited patient numbers
- The exclusion of certain patient groups
- The low incidence of certain ADR's and
- The long lead time for certain ADR's to appear

Therefore there is an essential need for ongoing post-marketing ADR surveillance programmes. The information obtained is important because it enables:

- The risk benefit ratio for particular drugs to be estimated
- The incidence of specific ADR's to particular drugs to be estimated
- The documentation of ADR symptoms and thus assists early detection
- Risk factors to be identified

Pharmacists, during the normal practice of their profession, are ideally placed to play a major role in the documentation of ADR's. Furthermore, the well trained clinical pharmacist has an important role in assisting the early detection of ADR's and thus enable the adverse consequences of the reaction to be minimised.

The routine screening of relevant patient parameters by pharmacists can assist this process. (18 to 25)

This role can be carried out by pharmacists practicing in the wards and outpatient clinics in conjunction with hospital medical staff. In particular, the surveying of hospital admissions may provide a cost effective, post-marketing surveillance programme for the identification of serious ADR's. (1 to 6, 18)

It is important to emphasise that joint hospital and community pharmacist programmes can also be developed to establish a valuable epidemiology data base on the use and safety of medication.

7.2 Avoidance of Drug Induced Toxicity and Optimising Drug Therapy

The clinical pharmacist has a vital part to play in the avoidance of drug induced toxicity and the optimising of drug therapy. The importance of the clinical pharmacist's role was also endorsed by the Nuffield Enquiry (UK) (104).

7.2.1 Interventions by Pharmacists

Pharmacists have always had a traditional responsibility to check the safety of drug dosage.

However, the increasing complexity of treatment and the ever expanding range of therapeutic agents requires a more detailed and sophisticated approach. The complicating factors that must be considered by clinical pharmacists are:

(i) Monitoring patient medication orders for:

- Drug interactions
- Contraindications
- Incorrect dosage regime, especially for cytotoxic drugs
- The influence on renal, hepatic and cardiac dysfunction on dosage and drug choice

(ii) The selection of the specific patient parameters to be monitored. That is selecting the patients considered to be at greatest risk and monitoring for early warning signs of drug induced toxicity. This includes indications of drug

interactions and the need for dosage adjustment e.g. due to deteriorating renal function.

These parameters include biochemistry, haematology and microbiology reports.

(iii) Communication with Patients

The pharmacist interviews the patients to evaluate their understanding of medication, and to establish past drug therapy, including episodes of drug hypersensitivity.

This also assists in determining the individual need for patient medication education and the identification of risk factors. This role also enables the detection of drug order omissions or the ordering of incorrect medication or dosage.

This interventionist role and its benefits has been well documented. (26 to 30)

Unfortunately it is difficult to put an economic value on the hypothetical outcomes that are avoided by the intervention of pharmacists. Never the less there have been a number of studies that have established the cost effectiveness of the clinical pharmacist's role. (31 to 45, 96 to 101, 105 to 111)

This includes a number of studies on the benefit of having a pharmacist closely involved in parenteral nutrition therapy. (46 to 48) This role not only includes the preparation of these solutions, but also entails a formulating and general advisory role as well as patient monitoring and education. This includes home parenteral nutrition programmes.

In recent years the issue of quality assurance with respect to clinical pharmacy services has started to be addressed in Australian hospitals. (49 to 51)

The potential for clinical pharmacists to facilitate reductions in ward drug stock levels and subsequent savings, should not be underestimated. (52)

7.2.2 Therapeutic Drug Monitoring and Pharmacokinetic Dosage Advice

There are a number of drugs in which the value of monitoring serum drug levels has been established.

The pharmacist has an important role in Therapeutic Drug Monitoring and Pharmacokinetic Dosage Advisory Services in assisting the optimising of therapy while minimising avoidable drug toxicity. This includes:

- Interpretation of serum drug levels in relation to confounding factors e.g. drug interactions, patient characteristics, compliance and sampling

- Advise on dosage prediction or adjustments based on pharmacokinetic principles. In particular, the evaluation of computerised pharmacokinetic programmes may lead to a decreased requirement in the number of serum drug level readings required

The value and cost effectiveness of this role of the pharmacist has been documented in a number of studies. (53 to 68)

The pharmacist also has a valuable role in providing advice on when serum drug samples should be taken. For instance, ensuring measurements are only taken when the changed dosage or new drug will have reached "steady state" (or stabilised). This role can eliminate unnecessary drug serum assays and their associated cost. (65, 67)

7.2.3 Pharmacist as a Drug Information Advisor

The pharmacist has an important role as a provider of drug information and associated advice. This role includes the provision of detailed information on pharmacology, toxicity, dosage, pharmacokinetics, indications, contraindications, therapeutics, drug interactions, formulation, intravenous incompatibilities, drug stability and methods of drug administration. More importantly it involves the exertion of clinical judgment on the accuracy and relevance of information. There is also a need for the pharmacist to accurately ascertain the needs of the enquirer and to provide the relevant response.

This role may be carried out by pharmacists in a specialised drug information and/or poisons information centre. However, it is also carried out by hospital pharmacists working in the wards and outpatient clinics, including during their participation in ward rounds and meetings. (74, 75). This role assists in preventing inappropriate drug use and avoidable drug induced toxicity. A number of studies has illustrated the acceptance of this role by medical staff. (31, 69 to 75)

7.2.4 Clinical Drug Trials

Hospital pharmacists play a vital role in providing logistic support for clinical drug trials. However, pharmacists are also becoming increasingly involved in an advisory role.

The pharmacist's broad range of skills can be employed in assisting in this evaluation of the design, safety and ethics of clinical drug trials, thus providing another view point to blend with those of medical staff and lay personnel.

7.3 Education of Hospital Staff and Patients

7.3.1 The Need for Drug Education

Studies on the characteristics of patients most likely to experience an ADR highlight factors such as old age, previous drug hypersensitivity, renal/hepatic dysfunction and patients taking large numbers of concurrent medication.

The relevance of the number of concurrent medications probably relates to problems of patient compliance and the potential for drug interactions. (25) A recent Australian study found 28% of ADR's associated with hospital admission were related, at least in part, to drug interactions. (14) This further highlights the need for improved education of medical staff on drug interactions and the need to avoid unnecessary polypharmacy, especially in the elderly.

The hospital pharmacist is in an ideal position to take part in this education, especially in hospital intern training programmes.

Hospital pharmacists also, of course, have an extremely important role in the training of pharmacy undergraduates and the provision for inservice training of post graduate staff.

7.3.2 Patient Medication Counselling and Education

The pharmacist has routine contact with patients during the dispensing of medication and thus are ideally placed to provide a counselling and educational role for patients.

Patient non compliance, either deliberately or involuntarily, is a well established problem. The consequences of non compliance may be adverse drug reactions, treatment failure or the waste of resources.

The value of the pharmacist in this role has been established in a number of studies, including those where the pharmacist works in a hospital outpatient clinic. (76 to 89) A number of these studies have established that the needs of patients vary considerably and that the mere provision of additional information, although useful, is likely to only partly solve the problem.

Autonomous medication compliance can be assisted by increasing the patient's understanding of the need for their medication and the symptoms of common side effects and their relevance.

Involuntary non compliance can be addressed by the training of patients in simple routines and by the use of other aids. Training in the use of specialised dosage administration e.g. inhalers, also has obvious advantages.

This emphasises the need for pharmacists to be equipped with effective communication skills. Pharmacists must also be able to identify the patients at greatest risk in order to achieve a rational use of resources and to meet the needs of the individual patient. It is likely that pharmacists will be involved in group patient training activities as well as on a one to one basis.

The patient medication counselling role has also been found to be effective in detecting prescribing errors e.g. omission of needed

drugs, dosage errors, incorrect drug prescribed or accidental duplication of drugs. This has particular value when patients are sent home from hospital. (67, 81) It is also particularly important when patients are receiving medication from several sources, including over the counter drugs or those obtained from supermarkets.

The role of pharmacists in home patient care is likely to develop in the next decade. (86, 90, 91) Pharmacists are also likely to be increasingly involved in medication education programmes for the general public e.g. sun protection and the safe storage of medication.

7.4 The Pharmacist as an Influencer of Prescribing

The influence of the role of the clinical pharmacist as a drug information advisor and reviewer of prescribing has already been covered.

However, in the current climate of limited resources, governments and administrators are increasingly demanding the cost effective use of medication. The pharmacist, along with medical staff and other relevant health professional groups, will play an increasingly active role in the promotion of cost effective prescribing.

This will require pharmacists to be actively involved with drug utilisation review studies to identify target areas. They are also likely to be closely involved in the formulation of policies or protocols, and the development and implementation of educational programmes. In particular, they will be required to play a role as an influencer of prescribing opinion and attitudes.

Soumeria & Avorn (92) have established that the pharmacist as an academic detailer is a critical component of such education programmes. The effectiveness and importance of the clinical and educational role of ward pharmacist has also been established in a number of other studies. (44, 45, 93 to 103, 105 to 111)

The Pharmacy Bulletins, produced by Hospital Pharmacy Departments, are also likely to be an important avenue for the communication of drug protocols and for the provision of feedback on drug utilisation reviews conducted locally. Unfortunately there have been few

studies conducted to evaluate the effectiveness of pharmacy bulletins, but there is limited evidence of their potential benefit. (72, 98, 112)

If the community is to gain the cost benefits of this process it is essential for pharmacists to be educated to a level where they are able to gain and earn recognition from prescribers and thus become effective influencers of prescribing.

7.5 Summary of Benefits

In summary the perceived benefits to the community are:

(i) The development of useful data bases on the use and safety of medication.

(ii) Decreasing the incidence of avoidable drug induced toxicity.

(iii) The education of patients, and others, to avoid medication problems and improve compliance.

(iv) The promotion of rational, cost effective prescribing, including appropriate Therapeutic Drug Monitoring programmes.