Understanding the Impact and Management of Body Weight in Duchenne muscular dystrophy.

Natassja Billich

BNutDiet(Hons)

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Doctor of Philosophy

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List of Abbreviations

△	Change
β	Beta coefficient
r	Correlation coefficient
%Pred6MWD	Percent predicted 6-minute walk distance
6MWD	6-minute walk distance
A	Ambulatory
ACE	Angiotensin-converting enzyme
AI	Adequate Intake
AMDR	Acceptable Macronutrient Distribution Range
APD	Accredited Practising Dietitian
BA	Before and after comparison
BIA	Bioelectrical impedance analysis
BMI	Body mass index (kg/m2)
BMI%	Body mass index percentile
BP	Blood pressure
BW	Body weight
CC	Case control
CDC	Centre for Chronic Disease and Prevention
CNS	Central nervous system
CS	Cross sectional
DFZ	Deflazacort
DLW	Doubly labelled water
DMD	Duchenne muscular dystrophy
DXA	Dual energy x-ray absorptiometry
EAR	Estimated Average Requirements
F	Female
FM	Fat mass
FM%	Fat mass percentage
FVC	Forced vital capacity
HbA1c	Glycated haemoglobin A1c
HDL	High density lipoprotein cholesterol
HOMA-IR	Homeostasis model assessment insulin resistance
Ht%	Height percentile
HW	Healthy weight
IQR	Interquartile range
kcal	Kilocalories
kg	Kilogram
kJ	Kilojoule
LDL	Low density lipoprotein cholesterol

LM	Lean mass (kg)
LM%	Lean mass percentage
LoE	Level of Evidence
M	Male
MDT	Multidisciplinary team
Mo	Month
N	No
NA	Non-ambulatory
NHMRC	National Health and Medical Research
NMC	Neuromuscular clinic
NRV	Nutrient Reference Values
NSAA	North Star Ambulatory Assessment
OB	Obesity
OCD	Obsessive-compulsive disorder
ODD	Oppositional defiance disorder
OSA	Obstructive sleep apnoea
OW	Overweight
P:E	Protein to energy ratio
PAL	Physical activity level
PCS	Prospective cohort study
PNL	Prednisolone
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PUL	Performance of the Upper Limb
RCH	the Royal Children's Hospital
RCS	Retrospective cohort study
RCT	Randomised controlled trial
REE	Resting energy expenditure
REM	Rapid eye movement
SD	Standard deviation
SDS	Standard deviation score
SNAP-NMD	Supporting Nutrition And Physical activity in NeuroMuscular Disease
SNOW-P	Supporting Nutrition and Optimising Wellbeing Program
TDF	Theoretical Domains Framework
TEE	Total energy expenditure
UK	United Kingdom
USA	United States of America
UW	Underweight
Wk	Week
Wt	Weight
Wt%	Weight percentile
Y	Yes

Abstract

Background:

Duchenne muscular dystrophy (DMD) is a severe, incurable, X-linked neuromuscular disorder. Corticosteroids are the best practice therapy for DMD which increase strength and function, but also cause side effects such as weight gain and fractures. Young people with DMD are more susceptible to weight gain than unaffected individuals. There is a lack of evidence regarding the impact of weight on disease progression and effective weight management strategies for DMD.

Aims:

In young people with DMD, this thesis aims include to: describe growth and body mass index (BMI) status and explore the impact of BMI on clinical milestones; explore the role of diet in weight gain and barriers and enablers to healthy eating; and co-design an evidence-based weight management program and assess its feasibility and acceptability.

Methods:

In a retrospective clinical audit anthropometry and clinical characteristics were collected from medical records. Cox proportional hazards models explored the impact of BMI status on time to clinical milestones including time to loss of ambulation, first fracture and obstructive sleep apnoea (OSA) diagnosis.

A cross-sectional analysis of energy, macro- and micro-nutrient and food group intake for boys aged 5-13 years was conducted to explore the role of diet in weight gain.

A systematic literature review was completed to identify existing weight management program for children with complex health care needs. Following this, a survey a survey of caregivers of young people with DMD explored barriers and enablers to healthy eating. Caregivers were asked to co-design a weight management program. The feasibility and

acceptability of the program was tested and weight and waist circumference were measured. Healthcare professionals provided feedback on the program design.

Results:

In the retrospective clinical audit, 158 (90% steroid-treated) young people with DMD were analysed (n=2456 BMI measures). Obesity (BMI z-score >1.645) prevalence increased during childhood until age 11 years (51%). Compared to those without overweight or obesity, boys with obesity at six and nine years and six to nine years sustained a fracture and were diagnosed with OSA earlier, respectively. Obesity did not significantly impact physical function.

In the dietary analysis (n=37), energy intake was high amongst younger boys within a healthy weight range. Intake of core food groups was low and discretionary foods high.

From 27 caregivers surveyed, barriers to healthy eating included fussy eating, time constraints, increased appetite and lack of nutrition knowledge. Enablers included perceived benefits of healthy eating and ability to prepare healthy foods. The survey and discussions with healthcare professionals informed a co-designed, six week, intensive, lifestyle weight management program delivered via telehealth. Preliminary analysis of seven participants demonstrated the program was feasible, acceptable and led to weight or waist circumference stabilisation.

Conclusions:

Up to half of young people with DMD have obesity which significantly impacts health outcomes, including earlier fractures and OSA. Diet-related contributors to weight gain include higher energy intakes in younger boys, increased appetite, fussy eating and time constraints felt by caregivers. Preliminary analysis suggests a lifestyle weight management program has the potential to effectively manage weight in boys with DMD.

Declaration

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.

Signature:

Print Name: Natassja Billich

Date: 4/8/2021

Publications During Enrolment

Billich N, Maugeri I, Calligaro L, Truby H, Davidson ZE. Weight management interventions that include dietary components for young people with chronic health-care needs: A systematic review. *Nutr Diet*. In press 2021

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This research was supported by an Australian Government Research Training Program (RTP) Scholarship.

Preface

Duchenne muscular dystrophy (DMD) is an incurable and life-limiting, severe neuromuscular disorder characterised by relentless muscle wasting. This X-linked condition, which therefore almost exclusively affects males, is characterised by progressive loss of muscle strength and function and resulting in complete loss of independent ambulation by approximately 13 years. (1) Adolescence and adulthood are fraught with complex health issues related to declines in upper limb strength and function, respiratory and cardiac function and issues with bone health. Young people with DMD and their families also experience significant psychological stress that is associated with living with a severe and incurable disease. (2,3)

As well as these physical manifestations and the psychosocial impact of DMD, these boys and adolescent men ("young people") are disproportionately affected by obesity (Figure 1). The significance of obesity in DMD is not only about the number on the scales or physical appearance; it is significant because of the impact on overall physical and psychological health. It is recognised by several international bodies, including the World Health Organization, that obesity is a chronic disease in itself which causes considerable adverse health outcomes. (4)

a. Boys aged 10 years with DMD **b. Typically developing boys aged 10 years**

Figure 1

Rate of Obesity Amongst Australian Typically Developing and Boys with DMD Aged 10 Years (5,6)

Fortunately, DMD is no longer just a disease of childhood and adolescence. Advances in the medical management of DMD with corticosteroids ("steroids") and ventilatory support have extended life expectancy. (7) In the 1960s young men with DMD were typically dying before their 20th birthday while currently life expectancy is between 30-40 years. (7) There is also hope that disease-modifying therapies may transform the course of the DMD. Gene therapy is one promising option and one agent (PF-06939926, Pfizer) has recently commenced a Phase 3 trial. (8) The development and approval of the life-extending drug nusinersen as well as zolgensma gene therapy for spinal muscular atrophy, a neuromuscular disorder with a life expectancy of less than two years in its most severe form, is a contemporary example of the possible medical advancements that can be made. (9,10)

With an aging cohort of males living with DMD, obesity-related health problems pose significant set-backs for individuals and with DMD and their families. This thesis will explore the causes and impact of body weight on DMD and advance the evidence base for family-centred weight management strategies for these young men and their families. Internationally, this will be the first comprehensive body of work to specifically address obesity in DMD.

Aims of Thesis

The aims of this PhD thesis and the corresponding chapter can be found in Table 1.

Table 1

Aims of PhD Thesis and Respective Chapter

The aims of this PhD thesis are to:	**Chapter**
1. Synthesise the literature regarding growth and body weight in DMD.	Chapter 1
2. Describe growth, body mass index (BMI) status and body composition in the Victorian paediatric DMD population.	Chapter 2
3. Explore the impact of a higher BMI on clinically meaningful milestones.	Chapter 2
4. Explore the role of diet in the development of a higher body weight in boys with DMD in Australia.	Chapter 3
5. Identify available literature for weight management in other populations of young people with chronic healthcare needs to guide management in DMD.	Chapter 4
6. Explore potential barriers and enablers to healthy eating and weight management in DMD.	Chapter 5
7. Co-design with caregivers of a young person with DMD and neuromuscular and nutrition experts a lifestyle weight management program for young people with DMD.	Chapter 5
8. Assess the feasibility and acceptability of a co-designed lifestyle weight management program for DMD.	Chapter 6

Chapter 1.

Growth and Body Weight in Duchenne muscular dystrophy

Peer-reviewed journal article:

Title: Growth and Body Weight in Duchenne muscular dystrophy: A Narrative Review

Authors: Natassja Billich, Paula Bray, Helen Truby, Maureen Evans, Monique Ryan, Zoe Davidson

In preparation for *Journal of Neuromuscular Diseases*

1.1 Background

Duchenne muscular dystrophy (DMD) is one of the most common paediatric neuromuscular disorders which is estimated to affect approximately between 15.9 and 19.6 out of 100,000 live male births. (11-14) DMD is an X-linked disorder caused by a mutation in the *DMD* gene. As such, the disease almost exclusively affects males as they are without a second "back up" copy of the X chromosome. The *DMD* gene is responsible for production of the protein dystrophin. Under normal circumstances, the dystrophin-associated protein complex forms lattice-like structures which are responsible for muscle integrity during contraction. (15) In DMD, the absence of dystrophin results in these structures not being formed so muscles are easily damaged during contraction. (16) Over time, damaged muscles become weak and are replaced with fatty and fibrotic tissue leading to a cascade of events related to declining physical function, declining respiratory and cardiac function and premature death. (16,17) A timeline of the typical progression of DMD treated with steroids with contemporary best-practice management is shown in in Figure 2.

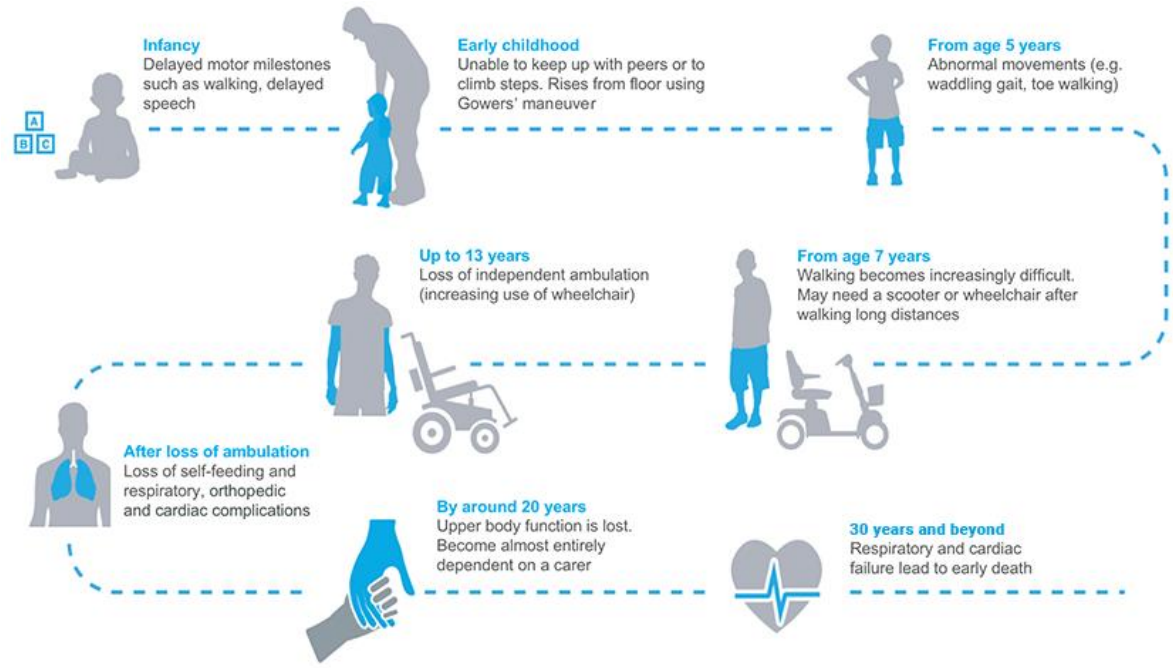

Figure 2

Typical Progression of DMD, Image Source: Duchenne and You (PTC Therapeutics Website) (18) Adapted From Birnkrant et al.; Bushby et al.; Goemans et al. and; Sussman et al. (19-22)

1.2 An Ageing DMD Population: Advances in Standard Care Management and Emerging Therapies

In the past two decades, there have been several advances in standard care management for DMD which have improved life expectancy, physical function and quality of life. (19,20,23-25) In the 1960s young men rarely survived beyond the age of 19 years, however they are now living into their 30s and 40s. (7,26) First-in-Class disease-modifying therapies are also emerging with the potential to transform the disease course. Recent advances in standard care management and emerging therapies are described in the next sections.

1.2.1 Multidiscplinary Care

It is now standard care for involvement of a multidisciplinary team (MDT) to contribute to the management of the child with DMD and the consequential impact on multiple body systems. The MDT typically includes a: neurologist, neuromuscular nurse, physiotherapist, occupational therapist, cardiologist, respiratory physician, endocrinologist, dietitian, mental health clinician and speech therapist. (20,24) Two international standard care guidelines encompassing medical and allied management of DMD have been published, one in 2010 and an update in 2018. (19,20,23-25) These guidelines characterise DMD according to the stages of disease progression from the pre-symptomatic stage to the late non-ambulatory phase. A summary of these stages and the multidisciplinary care considerations for DMD are shown in Figure 3. The aims of multidisciplinary management are to slow functional decline, manage comorbidities (e.g. contractures or OSA), maintain independence and optimise quality of life for individuals with DMD.

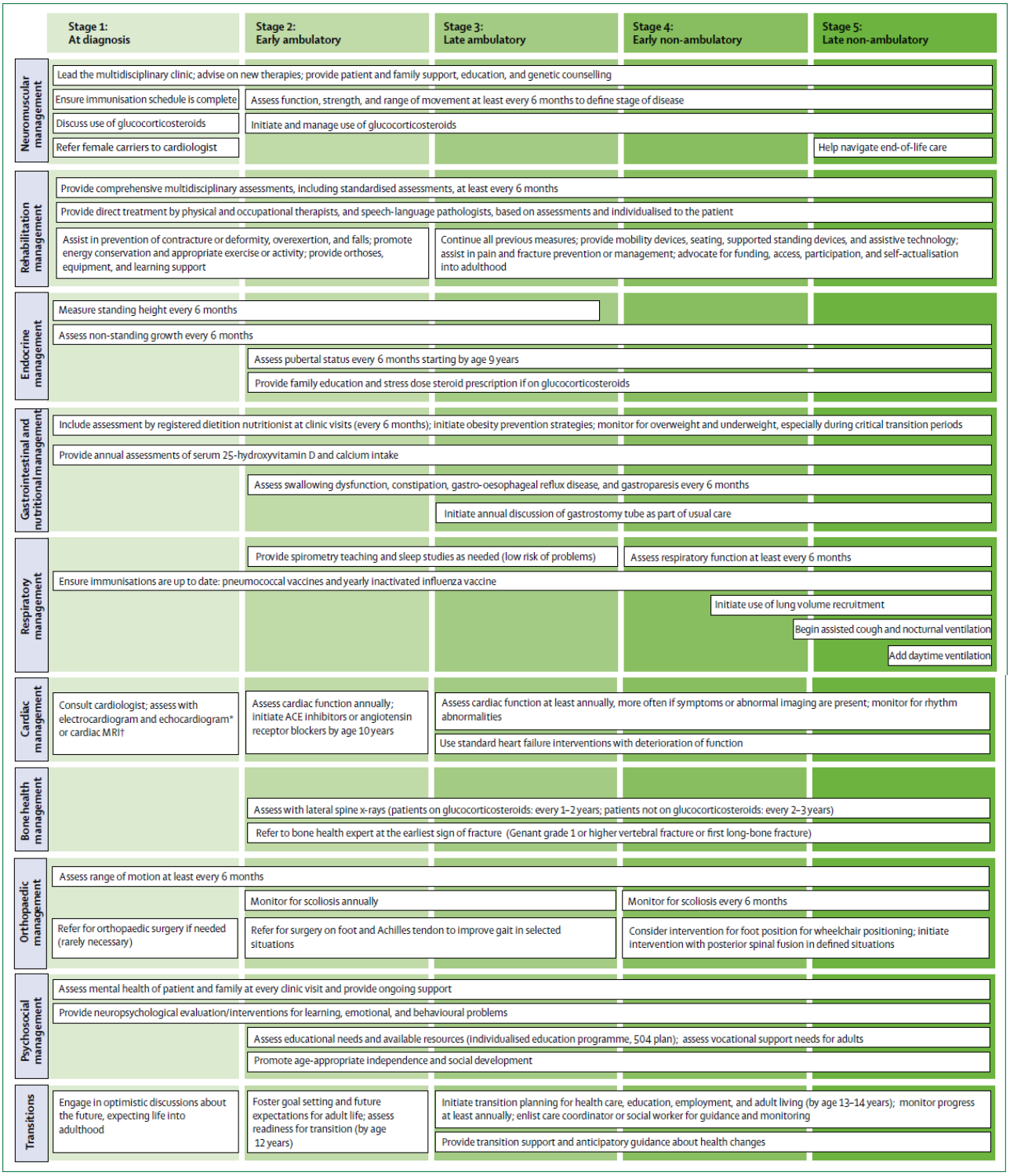

Figure 3

Stages of DMD Disease Progression and Care Considerations, Image Source: Birnkrant et al. (24)

Additionally, allied health guidelines for Australia and New Zealand have recently been released in 2021 that provide more specific advice for allied health members of the MDT, including dietitians. (27) A summary of nutrition and weight management recommendations from the Australia and New Zealand (27) and international (24) guidelines can be found in Table 2. All recommendations are based on consensus or low level of evidence, highlighting the need for further nutrition and weight management research for DMD. The role of the dietitian in the management of individuals with DMD includes monitoring of growth, assessing and managing under- and over-nutrition, assessment and management of calcium and vitamin D sufficiency and potential management of feeding via gastrostomy tube in the later stages of the disease. (24,27)

Table 2

Nutrition and Weight Management Guidance for DMD

Recommendations	Type of Recommendation
Australia and New Zealand Allied Health Guidelines [1] (27)	
Nutritional Assessment and Management	
The nutrition assessment should include an assessment of calcium and vitamin D intake in the diet as well as supplement sources across all stages of DMD.	Consensus based
We suggest dietary counselling (food or supplements) to increase the intake of calcium to the age appropriate Recommended Dietary Intake.	Evidence based ⊕
The dietitian should support the medical team in the monitoring and management of vitamin D status at least annually.	Consensus based
The nutrition assessment should include an assessment of supplements used by the individual to assist with strength.	Consensus based
We suggest nutritional supplements may be used to assist strength in ambulatory boys.	Evidence based ⊕
Weight Assessment and Management (Over- and Under-nutrition)	
We suggest skinfold measures not be used to estimate body composition.	Evidence based ?
From age 2-18 years, height and weight should be measured and assessed at least six monthly and tracked using the Centers for Disease Control and Prevention (CDC) 2000 growth charts to identify at risk patterns of growth.	Consensus based
Over 18 years of age, weight changes should be monitored at least six monthly to identify at risk nutritional status.	Consensus based
When an individual can no longer stand for an accurate measure of height, ulnar length or knee height (in the absence of contractures) may be used to estimate height.	Consensus based
The dietitian should meet the family to conduct an initial nutrition assessment within 6 months of diagnosis.	Consensus based
The dietitian should conduct a full nutrition assessment at yearly intervals or sooner if indicated in the following situations: • When a boy commences corticosteroid therapy • When deviations in growth pattern are identified • When parents voice concerns about dietary intake or swallowing • To assess the nutritional adequacy of enteral feeds.	Consensus based

Table 2

Nutrition and Weight Management Guidance for DMD

Recommendations	Type of Recommendation
There is some evidence to suggest that bioelectrical impedance analysis (BIA) may provide a reasonable estimate of body composition. (criterion validity: +). More research is needed to understand the clinical utility of BIA for measuring and monitoring body composition.	Research recommendation
We suggest that the Schofield weight equation (28) may be used to estimate resting energy requirements.	Evidence based ⊕
We suggest that gastrostomy feeding -where indicated- may be effective in improving nutritional status in DMD.	Evidence based ⊕
To determine total energy expenditure, an activity factor of 1.3-1.4 for ambulatory boys and 1.0-1.1 for non-ambulatory boys may be applied. Intake, weight and activity levels should be monitored to adjust energy prescription as required.	Consensus based
Anticipatory counselling aimed at preventing excessive weight gain should commence at or soon after diagnosis and be reiterated when a boy commences corticosteroid therapy.	Consensus based
In the absence of any evidence supporting DMD specific approaches, the Clinical practice guidelines for the management of overweight and obesity in adults, adolescents and children in Australia may be used to guide weight management approaches. (29)	Consensus based
When dysphagia is present, the dietitian should work together with the speech pathologist to ensure oral intake is both texturally and nutritionally appropriate and provide adequate hydration.	Consensus based
The dietitian can assist the decision for gastrostomy placement by providing a full nutrition assessment including weight history, nutritional intake and previous dietetic intervention.	Consensus based
Following gastrostomy placement, the dietitian can manage the enteral feeding regime.	Consensus based
International Care Considerations (24)	
Nutritional Assessment and Management	
At every visit, assessment by a registered dietitian nutritionist (Accredited Practising Dietitian, APD is the Australian equivalent) and monitoring of weight and height or an alternative height estimate for non-ambulatory patients.	Consensus based
Every six months questions about dysphagia, constipation, gastro-oesophageal reflux, and gastroparesis.	

Table 2

Nutrition and Weight Management Guidance for DMD

Recommendations	Type of Recommendation
Annual assessment of serum 25-hydroxyvitamin D and calcium intake.	
Weight Assessment and Management (Over- and Under-nutrition)	
Maintaining healthy weight (diet) At the time of glucocorticoid initiation, the nutritionist should address an individual's diet by emphasizing family-centred health eating.	Consensus based and general weight management
At the time of glucocorticoid initiation, the nutritionist should create a general nutritional plan based on the total energy expenditure (TEE) that includes specific recommendations for calorie, protein and fluid intake.	
At the time of glucocorticoid initiation, the physical therapist should emphasize family-centred physical activity (adapted in terms of amount/duration/frequency as necessary and as recommended by care team to meet the needs of the individual with Duchenne as his ambulation declines).	

[1] Not included in table are guidelines for nutritional supplements, swallow or physical therapy
Research recommendation: A recommendation for further research in areas where the assessment or management strategy of interest was identified through the systematic literature review but is also of significant cost, or not currently accepted in current clinical practice.
GRADE rating legend: Evidence based ⊕, very low
COSMIN rating legend: ?, unknown level of evidence; +, limited level of evidence

1.2.2 Corticosteroids

Oral corticosteroid therapy ("steroids") is part of best-practice medical management. International care considerations recommend that steroids are commenced when functional ability plateaus and before function significantly declines and only after a nutrition consultation. (24) Two steroid types have been approved for use in DMD; prednisolone and deflazacort. In Australia, prednisolone is prescribed as first line therapy while deflazacort can be accessed via the Special Access Scheme if significant side effects occur with prednisolone. Both steroid types are typically given daily (0.75mg/kg/day for prednisolone and 0.9 mg/kg/day for deflazacort), however weekend-end only dosing and intermittent dosing (e.g. 10 days on, 10 days off) are emerging as equally effective treatment regimens with fewer side effects. (30,31) There are clear benefits of steroids for boys with DMD including prolonging the ability to walk independently from 10 years in steroid-naïve boys to 13 years in treated boys, see Figure 4. (1)

Using pooled data from 12 studies (667 participants), a 2016-updated Cochrane systematic review and meta-analysis demonstrated steroid treatment resulted in statistically significant improvements in muscle strength, ability to lift weights, time to rise from the floor to a standing position, nine metre walking time, four stair climbing time, leg function, lung function measured by forced vital capacity (FVC) and quality of life. (32) Despite the benefits of steroid treatment, there are several adverse side effects of long-term steroid use with the most common being weight gain, impaired linear growth and Cushingoid features. (33) Other adverse effects include increased appetite, hyperglycaemia, hypertension, behaviour difficulties and emotional dysregulation, osteoporosis and fracture risk and increased risk of infection due to their immunosuppressant effects. (32,33) Vamorolone is an emerging First-in-Class steroid for DMD which has shown to improve physical function but with lower rates of Cushingoid features, weight gain, hirsutism, and behaviour change compared to prednisone and deflazacort. (34) A Phase 2b RCT for vamorolone is currently underway. (35)

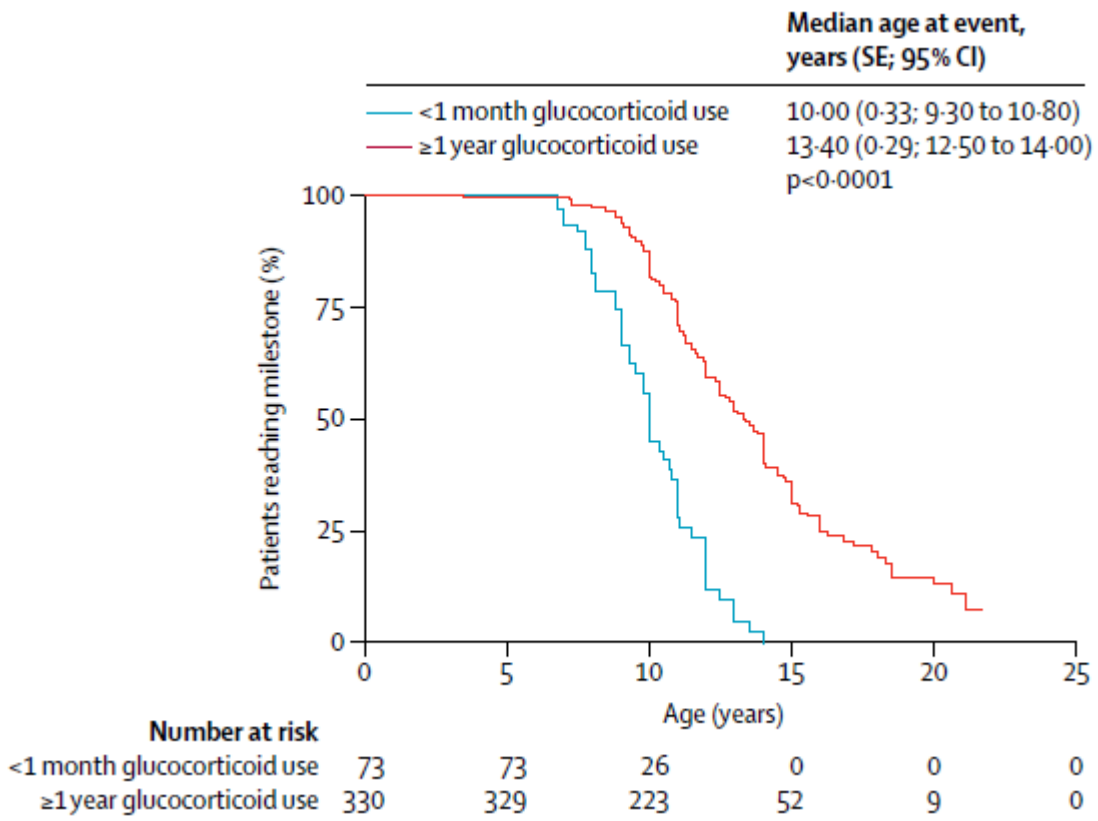

Figure 4

Kaplan-Meier Analyses Comparing Cumulative Glucocorticoid use (<1 Month or Never Treated vs ⩾1 Year) for Loss of Ambulation, Image Source: McDonald et al. (1)

1.2.3 Respiratory Support

Lung function is routinely monitored in DMD with annual measurements of FVC for ambulant boys and biannual measurements for non-ambulant boys recommended. (23) Sleep studies are conducted when clinically indicated to monitor for obstructive sleep apnoea and nocturnal hypoventilation. (23) Timely use of nocturnal non-invasive ventilation, typically in the non-ambulant period, and subsequent daytime non-invasive ventilation are highly recommended. (23) Invasive ventilation via tracheostomy may also be used in the late non-ambulatory phase depending on individual preferences and healthcare access. (23) Even in steroid-naïve cohorts, the introduction of routine non-invasive ventilation increased life expectancy considerably from approximately 19 to 25 years. (26)

1.2.4 Emerging Treatments

Steroids in the form of prednisolone and deflazacort are the only approved therapies for DMD in Australia. Advanced therapeutics are emerging as promising treatment and some, such as exon-skipping antisense oligonucleotides and ataluren, have been approved for use overseas. (36-38) Gene therapy is a promising disease-modifying treatment option; recruitment for a Phase 3 clinical trial of gene therapy across multiple sites internationally is currently underway. (8,39)

1.3 A Closer Look at Growth in DMD

Even before routine steroid use (in the early 2000s), growth in children with DMD was observed to differ from typically developing children. In 1995, using a prospective cohort design, McDonald and colleagues provided the first comprehensive description of growth in DMD (n=162) which included a comparison to typically developing, age-matched controls (n=22). (42) To date, this is still the largest prospective study of growth in DMD. (42) The study found that boys with DMD were shorter than typically developing children and after 10 years of age short stature was further exacerbated. (42) Weight measurements in DMD were more varied than the typically developing cohort and from age 9 to 13 years 44% were above the 90th percentile using typically developing growth data. (42) When using the DMD-specific Griffiths & Edwards charts (see Box 1 for a description of growth charts), which accounts for progressive loss of muscle mass, by age 17 years 64-73% of those with DMD were above the ideal weight (weight >90th percentile). (41,42) Analysis of longitudinal growth showed that over time younger boys with DMD gained more weight than their typically developing peers while those who were older (17-21 years) lost weight. (42)

Box 1.

A Note on Growth Charts

The growth charts produced by the Centers for Disease Control and Prevention (CDC) are considered in Australia as best practice for assessing growth in populations aged two to 20 years. (40) DMD-specific growth charts exist (41) that consider reduced muscle mass and these have been utilised within some studies. However, these DMD-specific growth charts that were developed in 1988 are now outdated because they were based on a steroid-naïve cohort without the benefit of best practice management. Most studies use the CDC growth charts cohort as a reference population which allows for comparison of growth in DMD to typical growth and allows comparison across DMD cohorts (e.g. steroid-naïve vs. steroid-treated cohorts).

There have been a number of contemporary analyses of growth for steroid-naïve, steroid-treated, ambulatory and non-ambulatory individuals with DMD. (5,43-47) These analyses use retrospective datasets ranging from sample sizes of n=144 to n=513, which are relatively large considering the rare prevalence of DMD. There are limitations to using retrospective data such as relying on the accuracy of measurements obtained through clinical settings and being unable to systematically screen for factors that influence growth (such as commencing steroid therapy). However consistent themes have emerged across these international cohorts: individuals with DMD experience short stature, excessive weight gain in childhood and adolescence and underweight in adulthood. Table 3 provides a summary of contemporary (approximately the past 20 years) studies that have observed growth in DMD.

1.3.1 Height

At birth, length, weight and head circumference for boys with DMD (n=263) are comparable to typically developing populations. (46) However, retrospective and prospective data demonstrates from as early as two years old both steroid-treated and steroid-naïve boys with DMD exhibit short stature and this persists into adulthood. (5,42-46) Factors that have been suggested to have a role in the aetiology of short stature in steroid-naïve boys with DMD include hypogonadism which reduces or delays growth spurts, potential functional adaptation as shorter height is associated with improve function, reduced bone mineralisation and biomechanical load on the bone due to muscle weakness and genetic factors. (48-50) In the only Australian analysis of growth in DMD which used retrospective data (n=144) height z-scores declined with increasing age and by 17 years, the height of young men treated with steroids were two to three standard deviations below typically developing populations. (5) Two large retrospective analysis of boys within the United States of America (USA, n=324, ambulatory) and the United Kingdom (UK, n=322, ambulatory and non-ambulatory) demonstrated steroids exacerbate impaired linear growth and earlier age at steroid commencement, at least daily dosing (compared to less than daily e.g. weekend-only), longer duration and greater dose are associated with shorter stature. (44,47)

1.3.2 Weight

An analysis of a large retrospective dataset from the USA (n=513) demonstrated steroid-naïve ambulatory boys with DMD were more likely to be at the extreme ends of the weight growth curves compared to typically developing children (10th and 90th percentiles). (45) Boys with DMD also had an increase in weight gain velocity at approximately seven to 10 years. (45) This data was then compared to a second dataset of steroid-treated individuals with DMD in the USA (n=324). This comparison demonstrated steroids exacerbated weight gain and compared to those who are steroid-naïve, ambulatory steroid-treated boys had a significantly higher median (50th percentile) weight. (44) However, compared to those who were steroid-naïve there were fewer steroid-treated boys with extreme weights at the 10th and 90th percentiles. (44) In non-ambulatory individuals with DMD in the USA (n=392) who are either steroid-naïve or steroid-treated, weight-for-age decreases with increasing age but steroids are protective against extreme lower weights. (43)

Table 3

Summary of Studies Exploring Growth in Duchenne muscular dystrophy, Sorted by Steroid Treatment Status [1]

Study design	Study ID country (n)	Steroid status: Ambulant or non-ambulant: Age range	Reference population	Measure	Key findings
Steroid-treated cohorts					
RCS	Crabtree 2019 (51) UK (50)	Treated: A + NA: mean age (years) daily 8.1 ± 2.3 and intermittent steroids 8.5 ± 2.7	Cole *et al.* (52)	Height SDS	During the follow-up period (2.5 ± 0.9 years): • Height SDS decreased significantly in the boys receiving daily steroids but remained constant for those on intermittent regimens.
				Weight SDS	• Weight SDS increased significantly for daily and intermittent regimens.
				BMI SDS	• BMI SDS increased at the same rate for both regimens.
RCS	Chew 2016 (53) Aus. (34)	Treated: A + NA: 8-19	CDC	BMI z-score	• BMI z-score increased by 0.55 ± 0.86 per year.
RCS	Davidson 2014 (5) Aus. (144)	72% treated: A + NA: 2-17	CDC	BMI z-score	• BMI z-score was +1.0 from 2-12 years and declined to -1.3 at 17 years • Obesity peaked at 10 years (50%) and declined to 0% at 17 years.
				Height z-score	• Height z-score was between -0.5 to -1.2 at 2-13 years and declined to -1.2 at 14 years and -2.7 at 17 years.

Table 3

Summary of Studies Exploring Growth in Duchenne muscular dystrophy, Sorted by Steroid Treatment Status [1]

Study design	Study ID country (n)	Steroid status: Ambulant or non-ambulant: Age range	Reference population	Measure	Key findings
RCS	Lamb 2016 (44) USA (324)	Treated: A: 2-12	Steroid-naïve DMD (45)	BMI%	• At all percentiles BMI was higher in steroid-treated compared to steroid-naïve until 12 years. • > 12 years 75th & 90th percentiles were comparable for steroid-treated & steroid-naïve.
				Weight%	• At the 50th percentile weight for steroid-treated were higher than steroid-naïve. • Less extreme weights at 10th and 90th percentiles for steroid-treated.
				Height%	• Height was lower for steroid-treated at the 50th percentile than steroid-naïve • Later age at steroid initiation was associated with taller height. • Daily dosing, longer duration, greater dose dosage was associated with shorter height.
RCS	Lamb 2018 (43) USA (392)	Treated & naïve (comparison): NA: 7-29 years	CDC	BMI%	• In steroid-naïve males, BMI-for-age was lower compared to CDC. • In steroid-treated males, BMI-for-age was higher than CDC.
				Weight%	• Steroid-naïve males had lower weight-for-age compared with steroid-treated males with DMD and CDC males. • At younger ages, weight-for-age in DMD (steroid-naïve and steroid-treated) was greater than CDC • With increasing age, weight-for-age decreased compared with CDC.

Table 3

Summary of Studies Exploring Growth in Duchenne muscular dystrophy, Sorted by Steroid Treatment Status [1]

Study design	Study ID country (n)	Steroid status: Ambulant or non-ambulant: Age range	Reference population	Measure	Key findings
RCS	Joseph 2019 (47) UK (322)	83% treated: A + NA: median 6.9 (baseline) to 10.9 (follow-up)	Cole *et al.* (52)	Height SDS	• Median height SDS at baseline were: daily prednisolone −1.2 (IQR −1.9, −0.5); intermittent prednisolone −0.9 (IQR −1.3, −0.4); daily deflazacort −1.4 (IQR −2.9, −0.6); intermittent deflazacort −1.0 (IQR −1.9, −0.4); steroid-naïve −0.8 (IQR, −1.7 to −0.4). • Change from baseline to the end of follow-up for height SDS was lower only in the daily deflazacort compared with steroid-naive group. • Steroid dose was negatively associated with change in height SDS.
				BMI SDS	• Median BMI SDS at baseline were: daily prednisolone 1.1 (IQR 0.3, 1.8); intermittent prednisolone 1.7 (IQR 0.9, 2.0); daily deflazacort 1.8 (IQR 1.2, 2.9); intermittent deflazacort 1.2 (IQR 0.4, 1.7); steroid-naïve 1.1 (IQR 0.3, 1.5). • Change from baseline to the end of follow-up for BMI SDS was higher only for the daily prednisolone compared with steroid-naive group, no change was observed for deflazacort. • Steroid dose was not associated with change in BMI SDS.
PCS	Vuillerot 2014 (54) France (29)	72% treated: A + NA: 5-15	Within-participant	BMI	• At baseline the steroid-naïve group had a higher BMI compared to steroid-treated. • After two years the steroid-treated group had a higher BMI compared to baseline, no change for steroid naïve.
Steroid-naïve cohorts					
RCS	Martigne 2011 (55) France (70)	Naïve: A + NA: 13-26	Griffith & Edwards (DMD) (41)	Weight%	• Obesity prevalence was 73% at 13 years and 47% at 15-26 years • 61% of those with obesity at 13 years were obese at 15-26 years • 34% were underweight at 15-26 years

Table 3

Summary of Studies Exploring Growth in Duchenne muscular dystrophy, Sorted by Steroid Treatment Status [1]

Study design	Study ID country (n)	Steroid status: Ambulant or non-ambulant: Age range	Reference population	Measure	Key findings
RCS	West 2013 (45) USA (513)	Naïve: A: 2-12	CDC	Height%	• DMD males were shorter across all ages. • DMD boys aged two to 12 years were 4.3 cm shorter than CDC.
				BMI%	• DMD has greater BMI at 90th but DMD & CDC were similar at the 10th percentile. • At nine to 10 years DMD curves rapidly increase compared to steady increase for CDC.
				Weight%	• Greater percentage of DMD patients at the extreme ends of the growth curves (10th and 90th percentiles). • Increase in weight gain velocity observed at 7-10 years.
RCS	Sarrazin 2014 (46) Germany (263)	89% naïve: A + NA: 2-17	German growth charts (56-58)	BMI%	• 68% of DMD cohort had a BMI > 50th percentile, underweight was more prevalent in older participants.
				Weight%	• At birth, weight was normally distributed.
				Height%	• At birth length was normally distributed but was shorter than the reference population at two to five years and 30% had short stature.

[1] Age is in years

Abbreviations: A, ambulant; BMI, body mass index; BMI%, BMI percentile; CDC, Centre for Disease Control and Prevention growth charts; CS, cross sectional study; Height%, height percentile; IQR, interquartile range; NA, non-ambulant; PCS, prospective cohort study; RCS, retrospective cohort study; SDS, standard deviation score; Weight%, weight percentile

1.3.3 BMI

Throughout childhood, retrospective analyses from Australia (n=144), the USA (n=324 to 513), UK (n=322), France (n=70) and Germany (n=263) demonstrate BMI (weight in kg/height in m^2) is persistently higher in steroid-treated, steroid-naïve ambulatory and non-ambulatory DMD cohorts compared to typically developing children. (5,43-47,55) One study by Davidson *et al.* (n=144) has explored longitudinal BMI patterns in an Australian context. (5) In this steroid-treated cohort, BMI is approximately one standard deviation above the CDC mean from three to 12 years. (5) During adolescence, BMI steadily declined to below one standard deviation below the CDC mean at 17 years. (5) The prevalence of obesity peaked at 10 years of age, when 48% of boys had obesity. (5) While steroids can cause weight gain, even in steroid-naïve cohorts the rate of obesity has been reported to be up to 70% (42,55,59) In the late non-ambulatory phase, young men with DMD are at risk of underweight. (5) Factors contributing to underweight includes dysphagia and feeding difficulties, progressive muscle wasting with age and a potential hypermetabolic resting energy expenditure (see section 1.5.5). (23)

It is difficult to compare rates of obesity and other BMI status categories across cohorts as studies use a range of different cut-off values, report data based on wide age ranges, combine BMI categories (e.g. combined overweight/obese category) or steroid status (treated or naïve) is unable to be determined. The CDC cut-off BMI z-score values (Box 2) are typically used in Australia for all children and adolescents. Internationally, either the CDC or country-specific growth charts are used to classify BMI status, while some older studies use the DMD Griffith & Edwards weight charts. (41) A summary of Australian and international studies that describe the prevalence of BMI or weight status and reference values used are described in Table 4. In Chapter 2 of this thesis, an updated description of growth and BMI status from an Australian cohort of young people with DMD is provided.

Box 2
CDC BMI z-score Cut-Off Values to Classify BMI Status
Underweight: z-score ≤ -1.645
Healthy weight: > -1.645 and < 1.036
Overweight: ≥ 1.036 and <1.645
Obesity: ≥ 1.645

1.3.4 Strengths and Limitations in Using BMI

There is some contention around the use of BMI in DMD as it does not capture altered body composition (higher fat and lower lean mass) and short stature results in a higher BMI calculation. BMI also relies on accurate height measures which may be complicated in DMD by an inability to stand with flat feet, ankle contractures, scoliosis, and in non-ambulatory individuals height must be estimated (e.g. from ulnar length). (24) BMI may underestimate true obesity in DMD and therefore it has been suggested that FM% may be a more accurate indicator. (60,61) However, height and weight (which enable BMI calculation) are routinely measured in clinical settings and equipment to conduct these measurements are usually accessible. BMI can also be easily interpreted on standard growth charts and is described in large normative and DMD datasets. (62) As discussed in section 1.6, there are associations between BMI and clinical outcomes. Measuring BMI, however blunt an instrument it is, can therefore provide some insight into the broader health of young people with DMD.

Table 4

Summary of Studies That Report on the Prevalence of BMI or Weight Status in DMD, Sorted by Steroid Treatment Status [1]

Study design	Study ID country (n)	Steroid status: A/NA: Age range (years)	BMI status cut-off	UW	HW	OW	OB
RCS	Davidson 2014 (5) Aus. (144)	72% treated: A + NA: 2-17 years	CDC - Box 2	2-27%	26-53%	6-36%	13-48%
RCS	Joseph 2019 (47) UK (322)	Treated: A + NA: median 6.9 (baseline) to 10.9 years (follow-up)	CDC >2.5 z-score				<5 years 6% 5-7.9 years 13% 8-10.9 years 29% 11-13.9 years 26% ≥14 years 26%
RCS	McKane 2017 (63) USA (85)	73% treated: A + NA: 4-38	CDC - Box 2	9%	37%	54%	
CS	Saure 2018 (61) Argentina (63)	83% treated: A + NA: 5-19	Argentinian growth charts (64)	6%	44%	22%	28%
RCS	Martigne 2011 France (55) (70)	Naïve: A + NA: 13-26 years	Griffith & Edwards weight percentiles (41)	<10th 13: 4% 15-26: 34%	10-90th 13: 23 %	-	>90th 13: 73% 15-26: 47%
CS	Mok 2006 France (65) (11)	Unclear: Unclear: mean 10.0 ± 2.5	Cole *et al.* (66) obesity BMI > 30	-	-	-	18%
CS	Mok 2010 France (67) (26)	Unclear: A: 3-11	Cole *et al.* (66) obesity BMI > 30	-	-	0%	0%
CS	Shimizu-Fujiwara 2012 Japan (68) (77)	Unclear: NA: 10-37 years	Japanese growth charts (69)	<80% 10-14: 14% 15-17: 44% <18.5 kg/m^2 18-37: 68%	10-14: 29% 15-17: 38% 18-37: 23%	-	>120% 10-14: 57% 15-17: 19% >25 kg/m^2 18-37: 9%

[1] Abbreviations: UW, underweight; HW, healthy weight; OW, overweight; OB, obesity; CS, cross-sectional; RCS, retrospective cohort study

1.4 Body Composition

DMD is characterised by lower proportion of lean mass (LM) and higher fat mass (FM) as atrophied muscles are replaced with adipose tissue with disease progression, see Table 5. Across international cohorts FM percentage (FM%) as measured by dual energy x-ray absorptiometry (DXA) in DMD ranges from approximately 20% (French boys aged 3 to 11 years) (67) to 52% (Greek pubertal adolescents). (70) In younger age groups FM% is comparable to typically developing cohorts, however as boys with DMD age FM increases beyond that of general populations. (71) Lean tissue mass is relatively consistent across published body composition data with averages ranging from approximately 14kg (Mexican steroid-naïve boys aged 2 to <6 years (60)) to 22kg (Greek pubertal steroid-treated boys observed in a case-control study, age not specified (70)), which is considerably lower than typically developing 8 to 15 year old males who have approximately 26 to 43kg of lean mass. (71) In majority of case-control studies which compare body composition data for boys with DMD (n=15 to n=499) to typically developing boys, LM is lower and FM higher in the DMD cohorts. (72-74) In an Australian context only one cross sectional study using a small sample size (n=10) has explored body composition using gold standard methods (doubly labelled water) who reported a mean FM% of 34% in boys aged approximately nine years. This PhD thesis will extend our understanding by providing the largest Australian description of body composition in young people with DMD (see Chapter 2).

Table 5

Body Composition Measured with Dual Energy X-Ray Absorptiometry or Doubly Labelled Water for Typically Developing and DMD Males [1]

Study design	Study ID Country: Body composition measure [2]	Steroid status: Age range in years (n)	FM%	LM (kg)	Comparison to controls
		Typically developing			
CS	Borrud 2010 (71) (NHANES)	8-11 (1067)	28.0 *SE* 0.4	25.9 *SE* 0.2	-
		12-15 (1726)	25.2 *SE* 0.3	42.8 *SE* 0.4	-
		DMD			
RCS	Canapari 2015 (75) Canada/USA	68% treated: 6-19 (44)	41.4 ± 14.2	-	No control
CC	Doulgeraki 2016 (70) Greece	Treated: Median 10 range 12			LM significantly lower
		Pre-pubertal (31)	Median 29 (range 15)	Median 15.8 (range 5)	
		Pubertal (11)	Median 52 (range 9)	Median 22.0 (range 8.2)	
CS	Elliot 2015 (76) Aus: DLW	Treated: mean 9.0 ± 2.3 (10)	34.2 ± 11.6	-	No control
CC	Söderpalm 2007 (72) Sweden	67% treated: 2–20 (24)	37 ± 17	21 ± 4.5	FM% significantly higher and LM lower
RCS	Summer 2020 (73) USA	Treated: 5-23 (499)	Median 37.9 (range 14.0-67.5)	Median 20.6 (range 10.4-47.2)	FM% higher & LM lower (statistical testing not performed)
PCS	Vuillerot 2014 (54) France	Treated & naïve: 5-15 (29)	Treated: 33.0 ± 13.0 Naïve: 62 ± 10	Treated: 20.0 ± 5.2 Naïve: 14.6 ± 3.5	Steroid-naïve significantly higher FM% and lower LM than steroid-treated

CS	Bernabe-García 2019 (60) Mexico	Naïve: 2-<6 (20) 6-<12 (64) 12-<18 (17)	 2-<6: Median 13.5 (range 7.6-54.8) 6-<12: Median 28.8 (range 8.5-7.2 [3]) 12-<18: Median 51.1 (range 12.7-60.0)	 2-<6: Median 13.0 (range 10.1-16.2) 6-<12: Median 16.9 (range 11.2-28.2) 12-<18: Median 25.0 (range 10.7-36.6)	No control
CS	Cruz-Guzmán 2015 (77) Mexico	Naïve: 4-18 (66)	28.1 ± 14.2	18.3 ± 5.2	No control
CC	McDonald 2005 (74) USA	Naïve: 6-13 (15)	30.4 SE 3.1	19.2 SE 1.1	FM% and LM significantly lower than obese controls
CS	Mok 2006 (65) France: DLW	Unclear: mean 10.0 ± 2.5 (11)	40.1 ± 17.1	-	No control
CS	Mok 2010 (67) France	Unclear: 3-11 (26)	19.8 ± 8.6	-	No control

[1] Data presented as mean unless otherwise specified
[2] Method is DXA unless otherwise specified
[3] Error in reported data range
Abbreviations: CC, case control; CS, cross-sectional; DLW, doubly labelled water; FM%, fat mass percentage; LM, lean tissue mass (kg); PCS, prospective cohort study; RCS, retrospective cohort study

1.5 Factors Contributing to a Higher Body Weight in DMD

Excessive weight gain is caused by an energy intake that exceeds the total energy that is required for living and physical activity. However, the drivers behind this basic concept are complex and multifactorial relating to an individuals' environment, genetic predisposition, biological and psychosocial factors. (78) It is likely that these complex factors also contribute to obesity in DMD in addition to unique characteristics specific to the disease itself. Several potential factors that contribute to obesity in DMD include dietary intake, steroids, physical activity, sleep and fatigue, resting energy expenditure and genotype.

1.5.1 Dietary Intake

Little is known about the role of dietary intake and its impact on weight in DMD. In one cross-sectional study of steroid-naïve Mexican children and adolescents, preschool- (2 to < 6 years, n=20) and school-aged boys (6 to < 12 years, n=64) had higher total energy intakes compared to estimated recommended intakes. (60) For adolescents (12 to 18 years, n=17) energy intake was comparable to recommendations. (60) Energy intake varied widely across the cohort; the highest energy intakes from preschool-age and school-age groups were over twice the recommended amount. (60) Males who were able to independently ambulate had higher energy intakes compared to males who could not, which may be due to the reduced energy expenditure in those who were non-ambulatory resulting in a lower appetite. (60) Based on current literature, little is known about consumption of core food groups, discretionary food and drinks or micronutrients by boys with DMD and how this compares to recommended intakes. These aspects of dietary intake and their relationship to weight are investigated in Chapter 3.

The broader influences on dietary intake (e.g. emotional, environmental) had not been explored in DMD. Of particular relevance is how a young person's diagnosis of DMD may impact parental food provision. For example, whether parents find it difficult to set boundaries due to their son's diagnosis or perhaps parents are more focussed on nutritious foods for their son to prevent excessive weight gain. There may also be differences in the division of responsibility compared to typically developing young people. That is, parental provision of food may extend beyond that of typically developing children due to limitations in physical function. It has been observed in DMD that the time of transition to a powered

wheelchair was associated with increased parent care requirements. (3) These care requirements may also include food provision as boys may not be able to access food autonomously.

1.5.2 Steroids

Systematic review evidence demonstrates that increased appetite and weight gain are one of the most common side effects of long-term steroid treatment in children, including those with DMD. (32,33) Steroids may cause weight gain due to their known effects on increased appetite, hyperglycaemia and hyperinsulinemia which leads to increased FM. (79) In DMD, there is evidence from retrospective data (n=322) and from a meta-analysis (n=43) of very low quality RCTs that there is less weight gain with deflazacort than with prednisolone. (32,47) In the Australian clinical setting, changing from prednisolone to deflazacort is considered by treating neurologists for patients who have had significant weight gain or experience behavioural issues.

1.5.3 Physical Activity

Data from case-control studies demonstrates physical activity is limited amongst ambulatory and non-ambulatory individuals with DMD. One study demonstrated ambulatory, predominantly steroid-treated boys with DMD (n=70) took 63% of the daily steps recorded by unaffected boys (n=10). (80) A decline in daily step count with increasing age was also noted. (80) Non-ambulatory individuals with DMD (n=13) spend more time in sedentary behaviours and less time participating in low intensity or moderate-vigorous physical activity compared to both unaffected (n=11) and ambulatory boys with DMD (n=31). (81)

1.5.4 Sleep and Fatigue

There is a well-established link between poor sleep and an increased risk of overweight and obesity in typically developing children. (82) In DMD, obstructive sleep apnoea (OSA) occurs in approximately 31-65% of individuals and nocturnal hypoventilation in 17-32%. (83,84) Issues with initiating and maintaining sleep, sleep–wake transition disorders and disorders of excessive somnolence are also common in DMD. (85) Sleep disturbance is associated with fatigue and young people with DMD experienced greater fatigue compared with their typically developing peers. (86) Sleep disorders are associated with lower parent-reported and self-reported psychosocial subscales on quality of life tools. (85) Greater fatigue is also associated with depressive symptoms according to self- and parent-reports for young people with DMD. (86) It can be hypothesised that sleep disturbance, fatigue, daytime somnolence, low mood and lower perceived quality of life in DMD may lower motivation, make participating in physical activities challenging and reduce the cognitive ability to make healthier daily food choices. Obesity and sleep disturbances have a bidirectional relationship; while sleep disturbance may inhibit healthy weight behaviours, obesity also causes sleep disorders such as OSA.

1.5.5 Reduced Energy Expenditure

Muscle is a metabolically active tissue, therefore in individuals with a muscle wasting disease - such as DMD - resting energy expenditure (REE) may be lower than unaffected individuals. Several studies have described REE in steroid-treated (n=9 to n=63) and steroid-naïve (n=5 to n=310) individuals with DMD, see Table 6. The evidence for whether REE is lowered in DMD compared to unaffected controls or reference equations is mixed. For steroid-treated populations some studies report agreements between measured REE and some reference equations (87), while others report significantly lower REE compared to controls (61). In ambulant, steroid-treated boys the Schofield equation for estimating REE (imputing weight rather than both weight and height) was found to have the least bias compared to measured REE. (87) In a cross-sectional Argentinian study with the largest available sample of young people with DMD and obesity who were predominantly steroid-treated (n=18) measured REE was 4448 ± 1049 kJ/day and was significantly lower than unaffected controls with obesity (controls REE 7194 ± 1960 kJ/day). (61) These comparisons are based on kJ per day, when REE is adjusted for body composition and

expressed as kJ/kg FM/day there may be no differences between boys with DMD and unaffected controls or obese and non-obese boys with DMD. (88,89)

Total energy expenditure (TEE) in DMD has been measured in only one, small (n=14), cross-sectional study without a control comparison. (90) In this cohort of Australian, ambulant, steroid-treated boys with DMD TEE was 7432 ± 1087 kJ/day with 37% of total energy expenditure derived from physical activity level. (90) The small sample size of this study did not allow for stratification by BMI status, therefore the TEE of those with DMD and obesity remains unknown. However, the mean BMI z-score of this cohort was 1.54 z-scores within the overweight range. (90)

One study published in 1992 describes hypermetabolism in the advanced stages of DMD in Japanese steroid-naïve males aged 17-29 years. (91) In those aged 17 years and above, energy intakes were 110-115% of estimated requirements despite majority being underweight. (91) To achieve nitrogen equilibrium (a negative nitrogen balance can lead to malnutrition), it was estimated that those with DMD required a protein intake 68% higher (equalling approximately 1.3g/kg/day) than those without DMD. This has not been specifically explored in steroid-treated individuals. This study is now outdated as the young men were not receiving steroids, ventilation or multidisciplinary care. A contemporary replication of this study that compared REE compares and energy intake in the advanced stages of the disease is required to further understand hypermetabolism in DMD.

Table 6

Studies Reporting Measured Resting Energy Expenditure Using Indirect Calorimetry or Total Energy Expenditure Using Doubly Labelled Water in Young People with DMD

Study design	Study ID country (n)	Steroid status: Ambulant (A) or non-ambulant (NA), age (years) [1]	BMI z-score	Resting energy expenditure kJ/day (kJ/kg/day) [2]	Other key findings related to energy expenditure
Studies including children or adolescents only					
CS	Elliot 2012 (87) Aus (9)	Treated: A, 8.8 ± 2.5	1.52 ± 0.85	5400 ± 400	• Harris-Benedict equation over-estimated REE. Schofield height and weight, Schofield weight only, Muller and Henry equations did not differ from measured REE. • Schofield weight only equation had the least bias.
CS	Elliot 2015 (90) Aus (14)	Treated: A, 8.4 ± 1.9	1.54 ± 0.89	5447 ± 418 (180 ± 38)	• TEE=7432 ± 1087 kJ/day (242 ± 59 kJ/kg/day) PAL=37%
Pre-post intervention (L-arginine)	Hafner 2016 (92) Switzerland (5)	4/5 naïve: A, 7.9 ± 0.75	-	4229 ± 567	-
CC	Hankard 1996 (88) France (13)	Naïve: A (2) & NA (11), No ob: 9.9 SE 0.6 Ob: 10.6 SE 0.5	-	No ob: 4765 SE 200 Ob: 5136 SE 310	• REE was 13% lower in no obesity group compared to controls. • REE was not different between obesity group and both no obesity and control groups.

Table 6

Studies Reporting Measured Resting Energy Expenditure Using Indirect Calorimetry or Total Energy Expenditure Using Doubly Labelled Water in Young People with DMD

Study design	Study ID country (n)	Steroid status: Ambulant (A) or non-ambulant (NA), age (years) [1]	BMI z-score	Resting energy expenditure kJ/day (kJ/kg/day) [2]	Other key findings related to energy expenditure
CC	Hankard 1998 (93) France (13)	Naïve: Not reported, 9-13	-	Data presented as graph only	• REE was lower than controls.
CS	Saure 2018 (61) Argentina (63)	83% treated: 54% ambulant, median 11.4 (range: 5.4-18.7)	Median 1.03 (range: -3.39-3.28)	Median 4435 (range: 2094-7332)	• % predicted REE (Schofield equation) = median 89 (range: 38-143) • Subgroup with obesity (n=18) REE= 4448 ± 1049, significantly lower REE than controls with obesity (control REE=7194 ± 1960)
CS	Zanardi 2003 (89) Italy (9)	Not reported: NA (3/9), 9 ± 3	-	1. No ob (184 ± 10) 2. Ob (113 ± 22)	• REE in obesity group significantly lower than no obesity.
Studies including adults					
CC	Gonzalez-Barmejo 2005 (94) France (20)	Naïve: NA, 25.0 ± 4.0, all ventilated (nocturnal NIV n=9, n=7 nocturnal tracheostomy, n=7 continuous tracheostomy)	BMI: 17.0 ± 6.0	4559 ± 853	• Significantly lower than controls. • REE for those on continuous ventilation significantly lower than those on nocturnal-only ventilation.

Table 6

Studies Reporting Measured Resting Energy Expenditure Using Indirect Calorimetry or Total Energy Expenditure Using Doubly Labelled Water in Young People with DMD

Study design	Study ID country (n)	Steroid status: Ambulant (A) or non-ambulant (NA), age (years) [1]	BMI z-score	Resting energy expenditure kJ/day (kJ/kg/day) [2]	Other key findings related to energy expenditure
CS	Okada 1992 (91) Japan (310)	Naïve: 1. 11 years (n=12) 2. 12 (n=14) 3. 13 (n=15) 4. 14 (n=13) 5. 15 (n=13) 6. 16 (n=10) 7. 17 (n=8) 8. 18 (n=11) 9. 19 (n=5) 10. 20-29 (n=49)	-	1. 3223 ± 560 (140 ± 35) 2. 3382 ± 360 (143 ± 22) 3. 3549 ± 355 (135 ± 25) 4. 3574 ± 435 (133 ± 19) 5. 3649 ± 347 (130 ± 14) 6. 3628 ± 414 (123 ± 16) 7. 3892 ± 619 (134 ± 21) 8. 4025 ± 510 (139 ± 28) 9. 3875 ± 238 (116 ± 15) 10. 3896 ± 460 (124 ± 21)	• The minimum requirement to maintain nitrogen equilibrium (prevent catabolism) was estimated to be 1.3g/kg/day • For those aged 11-16 years resting energy expenditure was 96-111% of predicted, for those aged 17-29 this increased to between 110-130% predicted
CS	Shimizu-Fujiwara 2012 (68) Japan (30)	1. Obesity: 10-14 2. Normal weight: 10-14 3. Underweight: 10-14 4. Obesity: 15-17 5. Normal weight: 15-17 years 6. Underweight: 15-17 Steroids not reported	-	1. 4870 ± 773 2. 5409 ± 510 3. 4151 ± 0 4. 5559 ± 192 5. 4686 ± 907 6. 4966 ± 966	REE lower compared to controls

[1] Steroid-treated indicates ≥50% steroid treated, steroid-naïve indicates ≥50% steroid-naïve
[2] If REE reported in kilocalories, values were converted to kilojoules using the conversion 1 kilocalorie=4.18 kilojoules
Abbreviations: CC, case control; CS, cross-sectional; NIV, non-invasive ventilation; ob, obesity; REE, resting energy expenditure; TEE, total energy expenditure

1.5.6 Genotype

The *DMD* gene is one of the largest genes in the human body which is responsible for producing several dystrophin isoforms that are expressed in various body tissues. (95) The main role of the longest isoform is expression in skeletal muscle to maintain sarcolemma integrity. (95) However shorter dystrophin isoforms are expressed in the retina, brain, kidney tissue, adult peripheral nerves, liver, lung and cardiac tissue. (95) The location of the *DMD* mutation dictates which isoforms are maintained in expression of the protein.

Whether or not the site of the mutation is associated with a higher body weight in DMD is unknown. A small number of studies have suggested this but much larger sample sizes are likely required to detect meaningful results. One cross sectional study (n=66) observed those with deletions in exon 45 or exon 50 had a higher likelihood of insulin resistance (96) however, these form part of the most commonly mutated region of *DMD.* (95) Another retrospective cohort study (n=263) found no relationship between the deletion site and BMI. (46)

1.6 Impact of a Higher Body Weight on Clinical Outcomes

Individuals with DMD with a higher BMI or adiposity (higher FM) have poorer physical and respiratory function and metabolic health, see Table 7. (48,53,61,75,83,96-99) For physical function, one study explored the impact of BMI (in kg/m^2) on the annualised change in time to climb four stairs in three steroid-treated cohorts (total n=92) of which two were prospective and one retrospective. (97) Of these cohorts, BMI was associated with a clinically and statistically significant increase in time in one cohort (1.2 seconds, prospective cohort), a statically but not clinically significant increase in a second cohort (0.3 seconds, retrospective cohort) and in one cohort (Leuven, prospective) there was no effect. (97) In a separate analysis of the prospective Leuven cohort study (n=54), a higher BMI was associated with a reduced distance walked in six minutes over a one-year period. (48) These two studies both by Goemans *et al.* are unique in that they analyse prospective and longitudinal data. In one small cross-sectional analysis of a steroid-naïve cohort (n=26), a higher adiposity and lower lean mass measured using bioelectrical impedance analysis was correlated with reduced mobility measured with the Gross Motor Function Classification System (GMFCS) and Expanded Hammersmith Functional Motor Scale. (100) The relationship between BMI and upper limb function and strength is inconclusive. (101,102) One cross sectional study (n=213) identified a higher BMI was associated with significantly reduced (indicating better arm function) score on the Brooke's scale of upper limb function however the coefficient was small (β -0.03) and unlikely to be of clinical significance. (102) No studies have explored whether BMI affects age at loss of ambulation.

A number of studies have explored the effect of BMI and body composition on respiratory function. Retrospective data from Australia, the US and Canada (n=34 to n=144) suggests an increased BMI (in kg/m^2 or z-score) may be protective against worsening lung function as it is associated with a higher FVC. (5,53,75) However, higher adiposity (higher total and truncal FM) is associated with a lower FVC. (53,75) One hypothesis for this is that FVC increases as BMI increases from the underweight to healthy weight range but there may then become a point where excess adipose tissue hinders lung function and thus a declining FVC is observed. A higher BMI has been shown to increase the prevalence and severity of obstructive sleep apnoea (OSA). (83)

Metabolic risk factors such as insulin resistance are prevalent in DMD. In one cross sectional study of an Argentinian steroid-treated boys (n=63) dyslipidaemia was present in 40% and insulin resistance in 29% of individuals. (61) Steroids contribute to metabolic risk factors, however one cross sectional study (n=66) suggests even in steroid-naïve cohorts 21%, 18% and 37% have one, two or three features of metabolic syndrome, respectively. (98) Young people with DMD with a higher BMI status are further at risk of insulin resistance. (96) A higher waist circumference may also be an indicator for insulin resistance and other features of metabolic syndrome. (61,98) Acanthosis nigricans is associated with insulin resistance in DMD, which may be a quick and practical way of identifying young people at risk of metabolic complications in the clinical setting. (61) The prevalence of hypertension amongst steroid-treated individuals DMD aged 4 to 16 years (n=67) has been documented to be 22-39% in one retrospective analysis from the Netherlands. (99) In this analysis, an increasing BMI was associated with increase systolic and diastolic blood pressure. (99) There is limited guidance available for the monitoring and management of metabolic complications in DMD. (24) Best practice management guidelines outline the role of the endocrinologist in the assessment and management of delayed growth and puberty, however not specifically metabolic complications related to excessive weight gain. (24) However, for those on testosterone therapy for delayed puberty, guidelines states consideration should be given to some metabolic markers such as assessment of lipids and blood glucose. (24)

There has been little exploration of the impact of obesity on patient- or parent-reported health-related quality of life. One cross-sectional study conducted in young (4 to 7 years, n=196), steroid-naïve boys found no significant relationship between BMI and health-related quality of life. This analysis was limited by the young age of the boys who may not be experiencing the degree of disease morbidity or obesity as experienced by older boys and adolescents.

Table 7

Studies Exploring Anthropometry or Body Composition and Clinical Outcomes in DMD

Design	Study ID: Participant characteristics	Anthropometry & body composition variables	Clinical outcome variables	Relationship between anthropometry/body composition and clinical outcome variables
Physical function and strength				
CS	Bayram 2013 (100): age 3-17 years (n=26): Steroid status not reported	Measured using BIA: Fat %	Gross motor function classification system (GMFCS) and Expanded Hammersmith Functional Motor Scale [1]	Strong positive correlation with GMFCS (r=0.785, p<0.001) and strong negative correlation with Hammersmith (r = -0.779) [2]
		Body FM index		Strong positive correlation with GMFCS (r=0.719, p<0.001) and moderate negative correlation with Hammersmith (r=-0.698)
		Fat free mass index		Moderate negative correlation with GMFSC (r=-0.401, p=0.042) and positive correlation with Hammersmith (r not reported)
		Triceps skinfolds		Moderate positive correlation with GMFSC (r= 0.643, p<0.001) and moderate negative correlation with Hammersmith (r=-0.618)
		Scapular skinfolds		Strong positive correlation with GMFSC (r= 0.712, p<0.001) and moderate negative correlation with Hammersmith (r=-0.683)
Tadalafil PCS, *Leuven* PCS, *CCHMC* RCS	Goemans 2020 (97): ages *Tadalafil* 9.4 ± 1.8 *Leuven* 9.1 ± 2.7 *CCHMC* 8.8 ± 2.7 (total n=92): Steroid-treated [3]	BMI (kg/m^2)	Annualised Δ four stair climb time [4]	*Tadalafil*: 1 kg/m^2 increase in BMI was associated with an increased (slower) time of 1.2 seconds *Leuven*: no relationship *CCHMC*: 1 kg/m^2 increase in BMI was associated with an increased (slower) time of 0.3 seconds

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Studies Exploring Anthropometry or Body Composition and Clinical Outcomes in DMD

Design	Study ID: Participant characteristics	Anthropometry & body composition variables	Clinical outcome variables	Relationship between anthropometry/body composition and clinical outcome variables
PCS	Goemans 2016 (48): *Leuven* age 9.4 ± 2.4 years at baseline (n=54): Steroid-treated	BMI (kg/m^2)	Annualised Δ 6-minute walk distance [5]	1 kg/m^2 increase in BMI was associated with a reduced 6-minute walk distance by 17 metres
CS	Jacques 2018 (101) age 24.2 ± 6.1 years (n=15): Steroid status not reported	Measured using BIA: Lean mass	Hand grip strength	No significant relationship
CS	Janssen 2016 (102) age 1–35 years (n=213):	BMI	Brooke scale [6]	A higher BMI associated with small decrease in Brooke scale β -0.03 (95% CI -0.05; -0.01)
			Lung function	
RCS	Canapari 2015 (75): age 12.0 years ± 3.4 (n=44): Steroid treated	Truncal FM %	FVC% predicted	1% increase was associated with a 1.2% decrease in FVC% predicted
			Apnoea–hypopnea index	No significant relationship
			Cough peak flow	No significant relationship
		BMI (kg/m^2)	FVC% predicted	1 kg/m^2 increase in BMI was associated with a 2.3% increase in FVC% predicted
			Apnoea–hypopnea index	No significant relationship
			Cough peak flow	No significant relationship

Table 7

Studies Exploring Anthropometry or Body Composition and Clinical Outcomes in DMD

Design	Study ID: Participant characteristics	Anthropometry & body composition variables	Clinical outcome variables	Relationship between anthropometry/body composition and clinical outcome variables
RCS	Chew 2016 (53): age 13.7 years ± 3.6 (n=34): Steroid treated	BMI z-score	FVC % predicted	1 unit increase in BMI z-score associated with a 7.4% increase in FVC% predicted
			FEV1	1 unit increase in BMI z-score associated with a 7.2% increase in FEV1
		FM %	FVC% predicted	1% FM increase associated with a 1.5% reduction in FVC% predicted (n=12)
			△ Cough peak flow (sit to lying)	1% FM increase associated with a 1.5% △ cough peak flow (greater postural reductions)
RCS	Davidson 2014 (5): age 11.9 years ± 4.0 (n=144): Steroid treated	BMI z-score	FVC % predicted	1 unit increase in BMI z-score associated with 0.4% increase in FCV % predicted
RCS	Martigne 2011 (55): age at baseline 13 years, max follow up 15-26 (n=70): Steroid naïve	BMI status	Spinal surgery	No significant relationship
			Respiratory support	Fewer patients with obesity required respiratory support
RCS	Sawnani (83) 2015: age 5-18 years (n=111): Steroid-treated	BMI (kg/m^2 and z-score)	Obstructive index (obstructive events per hour)	Positive correlation with rapid eye movement (REM) obstructive index (BMI r=0.22, p=0.04; BMI z-score r=0.22, p=0.04)
			OSA	No difference in BMI between those with (22.8 ± 7.8 kg/m^2) and without OSA (20.4 ± 5.0 kg/m2, p=0.09).
			Central sleep apnoea	BMI was greater in those with central sleep apnoea group (24.7 ± 9.5 kg/m^2) compared to those without (20.4 ± 5.0 kg/m^2, p=0.03).
			Hypoventilation	BMI was greater in those with hypoventilation group (22.3 ± 6.4 kg/m^2) compared to those without (20.4 ± 5.0 kg/m^2, p=0.4).

Table 7

Studies Exploring Anthropometry or Body Composition and Clinical Outcomes in DMD

Design	Study ID: Participant characteristics	Anthropometry & body composition variables	Clinical outcome variables	Relationship between anthropometry/body composition and clinical outcome variables
		Cardiac function		
RCS	McKane 2017 (63): age 14.9 years (range 3.5-37.5) (n=85): Steroid treated	BMI status	Cardiomyopathy diagnosis or age at onset	No significant relationship
		BMI z-score	% change of left ventricular fractional shortening	
			Left ventricle dimension in diastole	
RCS	van de Velde 2019 (99): (n=67): Steroid treated	BMI (kg/m^2)	Systolic blood pressure	Systolic blood pressure z-score increased with a higher BMI (β 0.07 95% CI 0.03-0.11)
			Diastolic blood pressure z-score	Diastolic blood pressure z-score increased with a higher BMI (β 0.05 95% CI 0.03-0.08)
			Peak systolic global longitudinal strain	Reduced peak systolic global longitudinal strain (representing left ventricle deformation) was associated with increased BMI (β 0.348 95% CI 0.123 to 0.573) in patients <11 years
		Renal function		
CS	Braat 2015 (103): age 5-22 years (n=20): 80% steroid-treated	BMI	Glomerular filtration rate, hypertension or non-dipping blood pressure	No significant relationship

Table 7

Studies Exploring Anthropometry or Body Composition and Clinical Outcomes in DMD

Design	Study ID: Participant characteristics	Anthropometry & body composition variables	Clinical outcome variables	Relationship between anthropometry/body composition and clinical outcome variables
		Metabolic health		
CS	Bostock 2018 (104): age 24.6 ± 4.3 years: 40% steroid treated	BMI (kg/m^2)	Blood glucose level on oral glucose tolerance test	No correlation between anthropometric/body composition measures and blood glucose 120-minute post glucose ingestion or glucose area under the curve
		FM %		
		Fat free mass (kg)		
CS	Cruz-Guzmán 2015 (77): age 9.4 years ± 3.1 (n=66): Steroid naïve	BMI status	Proinflammatory cytokines	No significant trend
			Leptin	Leptin levels increased significantly in overweight/obese boys compared to those who were a healthy weight
			Adiponectin	No significant trend
CS	Rodríguez-Cruz 2015 (96) DMD and BMD: age median 8.96 years range: 4.61, 17.75 (n=66): Steroid naïve	BMI status	Glucose	Higher levels of glucose in overweight/obese compared to normal weight
			Insulin	Higher levels of insulin in overweight/obese compared to normal weight
			HOMA-IR	Higher HOMA-IR in overweight/obese compared to normal weight
		FM %	HOMA-IR	Positive: 1 unit increase in FM associated with 0.6 unit increase in HOMA-IR [7]

Table 7

Studies Exploring Anthropometry or Body Composition and Clinical Outcomes in DMD

Design	Study ID: Participant characteristics	Anthropometry & body composition variables	Clinical outcome variables	Relationship between anthropometry/body composition and clinical outcome variables
CS	Rodríguez-Cruz 2016 (98) DMD and BMD: ages <6 years, 6 to <16 years and ≥ 16 years: Steroid naïve	Waist circumference	Metabolic syndrome	• Those with three or more components of metabolic syndrome had a significantly higher waist circumference (median 77 range: 49-112) and were significantly older (16.6 ± 10.2) than those with two or less components. • For those with three of more components: insulin resistance 100%, obesity (using waist circumference [8]) 24.1%, hyperglycaemia 41.4%, hyperinsulinaemia 100%, hypertriglyceridemia 75.9%, low HDL 24.1%
CS	Saure 2018 (61)age median 11.4 (range 5.4-18.7) (n=63): Steroid treated	Obesity (64)	Insulin resistance	Positive correlation between obesity and insulin resistance [9]
		Pathological waist circumference (105)	Insulin resistance	Positive correlation between pathological waist circumference and insulin resistance
Health-related quality of life				
CS	Campbell 2021 (106) age 4-7 years (n=196): Steroid-naïve	BMI	Peds QL Generic and Neuromuscular modules	No significant relationship

Table 7

Studies Exploring Anthropometry or Body Composition and Clinical Outcomes in DMD

Design	Study ID: Participant characteristics	Anthropometry & body composition variables	Clinical outcome variables	Relationship between anthropometry/body composition and clinical outcome variables
		Survival		
RCS	Cheeran 2017 (107): age median 24 (range 21–27) years (n=43): 56% steroid treated	BMI status (on arrival to the clinic)	Survival (within the follow-up period)	The non-surviving group had significantly lower BMI (n=8, median 17.3 IQR 14.8–19.3) compared to the surviving group (n=35, 25.8 IQR 20.8–29.1), a higher proportion of the non-surviving cohort were underweight compared to the surviving (75% vs. 11%).

[1] GMFCS levels 1-5, lower level indicates greater independent mobility, Hammersmith 0-33, higher score indicates better function
[2] P-values for Hammersmith not reported
[3] *Tadalafil DMD Trial*, ambulatory, steroid-treated boys in the placebo arm of a RCT (Phase 3) of tadalafil; *Leuven*, data from the paediatric neurology clinic at Universitaire Ziekenhuizen in Leuven, Belgium; *CCHMC*, natural history data of patients receiving care at Cincinnati Children's Hospital Medical Center
[4] Annualised Δ four stair climb = (four stair climb time at outcome visit – four stair climb time at baseline visit)/ time in years, > 0 indicates worsened performance
[5] Annualised Δ 6-minute walk distance = (distance at outcome visit – distance at baseline visit)/ time in years corresponding number of elapsed years, > 0 indicates worsened performance
[6] Discrete categories 1-6, lower score indicates better arm function
[7] HOMA-IR = [fasting insulin, μU/mL] x [fasting glucose, mmol/L])/22.5. Values of HOMA-IR > 3.16 were indicated insulin resistance
[8] Obesity was refined as WC ≥90th percentile according to age and sex for children 6 to <16 years and 90 cm for boys >16 years
[9] Regression coefficients not reported
Abbreviations: Δ, change; β, beta coefficient; CS, cross sectional study; HDL, high density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment insulin resistance; PCS, prospective cohort study; *r*, correlation coefficient; RCS, retrospective cohort study

1.7 Weight Management

1.7.1 Specific Guidance for DMD

Due to paucity of evidence, all recommendations for obesity management in DMD are based on consensus expert opinion or recommendations for general paediatric populations (see Table 2 for recommendations). (24,27,108) Only two case studies have investigated weight management strategies in DMD. The first, published in 1984 implemented a protein-sparing very low energy diet (2621kJ/day) in one non-ambulatory individual with DMD aged 14.8 years. (109) The participant lost 38kg over 12 months. (109) The authors report analysis of total body water demonstrated the patient's lean body mass was maintained, however as no further studies have been conducted using a very low energy diet it is unknown whether this is amount of weight loss safely maintains muscle mass. (109) In contemporary times, this level of energy restriction which is approximately 40% of typical resting energy required for a 14 year old male (110) raises concern. The second case study, published in 2010, included three non-ambulatory participants (one was steroid-treated) and used a six-month family-based intervention that used behavioural techniques and the Traffic Light Diet. (111) Weight decreased, remained stable and increased across the three participants. (111) One other noteworthy study is that by McPherson *et al.* who assessed the feasibility and acceptability of a solution-focused coaching intervention for setting physical activity and nutrition goals for boys with DMD (n=5). (112) Although weight outcomes were not measured, the intervention used motivational interviewing techniques to help children identify goals and develop solutions to help achieve their preferred future, which may be an acceptable and promising approach for promoting physical activity and a healthy diet in males with DMD. (112)

There have been two reports on drug therapy for weight management in DMD. Carter *et al.* reported a case study of two adolescents with DMD (15 and 13 years) who lost weight when given topiramate, an antiepileptic and appetite suppressant. (113) The case study reports topiramate was prescribed following failure of dietary weight management, it is unclear whether the two participants had epilepsy. (113) The two individuals were also prescribed a very low energy diet of 3344kJ/day and lost 26% and 41% of their initial body weight, respectively. (113) The authors did not report on changes in body composition. Casteels *et al.* investigated metformin in an RCT including young people with spina bifida (n=42), DMD (n=13, n=12 were treated with deflazacort) and other unspecified neuromuscular diseases

(n=7). (114) Participants were randomised to either metformin or placebo and standard advice on diet and exercise were provided to all participants. (114) Those receiving metformin had a significantly lower weight, BMI and visceral fat following six months of treatment. (114) The analysis was not stratified by diagnosis type nor was LM reported. (114)

These studies are a starting point in understanding how to manage weight in DMD. However, there has been no empirical research studies that have employed best-practice, first-line lifestyle weight management interventions. There is a clear gap in the literature on whether lifestyle weight management strategies can be successful in DMD and what effect they have on health and disease outcomes.

1.7.2 Guidance for Typically Developing Young People

In light of the lack of evidence regarding obesity management in DMD, advice for weight management in general paediatric populations must be considered. Obesity management in typically developing young people has been comprehensively investigated and several systematic reviews (115-123) and clinical practice guidelines (124,125) exist. There is currently no local Australia guidance available as the National Health and Medical Research (NHMRC) *Clinical Practice Guidelines for the management of overweight and obesity in adults, adolescents and children in Australia* have been rescinded. (29) A summary of these and guidelines from the Academy of Nutrition and Dietetics (USA) (124) and National Institute for Health and Care Excellence (UK) (125) are summarised in Supplementary Table 1. Importantly, an umbrella review of 14 systematic reviews found that lifestyle weight management interventions for children and young people are safe and have no adverse events. (119) Consensus from international guidelines and systematic reviews is that the management of overweight and obesity in children and young people should:

- be focussed on manipulation of lifestyle as first-line therapy
- be multi-component including strategies that focus on diet, physical activity, reducing sedentary behaviour and screen time and behaviour change
- include the whole family (or household) including parents, children and young people and other household dependants
- include goal-setting for behaviour change
- be developed and/or delivered by a MDT

The recently updated 2020 World Health Organization physical activity guidelines provide specific guidelines for individuals with disabilities. (126) The guidelines suggest that young people living with disability:

- should do at least an average of 60 minutes per day of moderate-to-vigorous intensity, mostly aerobic, physical activity, across the week.
- should incorporate vigorous-intensity aerobic activities, as well as those that strengthen muscle and bone, at least 3 days a week.
- should limit the amount of time spent being sedentary, particularly the amount of recreational screen time.

It is clear that evidence for obesity management in DMD is lacking. However, it is unclear what evidence is available weight management in young people with other disabilities and chronic healthcare needs. This will be investigated in Chapter 4.

1.7.3 Consumer Perspectives Regarding Weight Management in DMD

There is no comprehensive body of work that has explored the perspectives of consumers regarding weight management in DMD. However, there are some reports of consultation regarding nutrition (including obesity) with individuals with DMD, their families, healthcare professionals and patient advocacy groups which provide rationale for developing weight management strategies specific to DMD.

In 2018, 26 representatives from academia, clinics, patient organisations and industry from eight countries attended the workshop on *Nutrition in Duchenne muscular dystrophy* organised by the Duchenne Parent Project the Netherlands. (127) During the workshop one 27-year old adult with DMD commented “he has always been aware of the necessity of maintaining a healthy weight, but regrets that information is missing about what aspects in his diet require specific attention.”. (127) The overall outcomes of the workshop were a number of priority areas which included: a budget to support nutritional research and improvement of information in DMD; and increased awareness of the importance of nutrition. (127)

A survey of physicians, nurses, physiotherapists, social workers, dietitians, psychologists and respiratory therapists (n=37) published in 2020 identified that healthcare professionals working in neuromuscular disorders lack the confidence in addressing weight management. (128) Better management options and guidelines, obesity-specific training of those working within the neuromuscular field and more patient engagement on the topic of weight management have been identified as potential strategies to improve neuromuscular healthcare professional's confidence in weight management. (128)

Using an online modified-Delphi approach, (129) Denger *et al.* assessed the weight management guidelines from the 2018 DMD Care Considerations (Table 2) (24) for patient-centredness with 27 adults with DMD and 95 caregivers. (108) Participants confirmed that all diet- and activity-related weight management recommendations were important and acceptable and participants highlighted the issues of both overweight during younger ages and feeding difficulties and weight loss later in life. (108)

1.8 Summary

Growth in DMD is altered compared to typically developing populations. Boys with DMD experience short stature, higher weight gain and different body composition to typically developing children. As with typically developing children, obesity is caused by a complex range of factors that lead to an imbalance between energy consumption and energy expenditure. These factors are accentuated in DMD by the degree of disability and therefore limitations on physical activity, use of long-term steroids, potentially reduced resting energy expenditure, sleep disturbance and fatigue. There is a small body of predominantly retrospective research that suggests obesity may have negative implications on metabolic risk factors, respiratory function (including obstructive sleep apnoea) and physical function. There is limited guidance for physicians available for weight management in DMD. There is some insight from individuals with DMD, parents, neuromuscular experts and healthcare professionals that weight management strategies are important, but purposively designed strategies for DMD are not sufficiently available or accessible. It is now timely to comprehensively assess the impact of obesity on disease outcomes and develop evidence-based, family-centred, lifestyle weight management strategies for DMD. While the DMD community eagerly awaits disease-modifying therapies, it is essential that we advance our understanding of weight management to prevent complications related to a higher body weight as life expectancy increases.

Chapter 2.

Growth, BMI Status and the Implications of a Higher BMI on Clinical Outcomes in Boys with DMD

Ethics Reference: LNR/18/RCHM/233

Peer-Reviewed Journal Article:

Title: Body Mass Index Status During Childhood and Its Impact on Time to Milestones of Disease Progression in Duchenne Muscular Dystrophy

Authors: Natassja Billich, Justine Adams, Kate Carroll, Helen Truby, Maureen Evans, Monique Ryan, Zoe Davidson

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2.1 Preamble

Short stature, susceptibility to both over- and underweight, decreased muscle mass and increased FM are well documented anthropometric characteristics of DMD (see sections 1.3 and 1.4). In an Australian context, only one study has comprehensively described linear growth in DMD which analysed anthropometric measurements taken from clinical care between 1997 and 2009. (5) This chapter builds on and extends that previous work and provides an update on growth and BMI status amongst Australian males with DMD. One feature of this chapter is a descriptive comparison of 'old era' data from 1997 to 2009 (5) with 'new era' data from 2010 to 2018 (collected for this PhD thesis).

There is evidence to suggest that a higher BMI is associated with a slower time to climb four stairs, a reduced 6-minute walk distance, cardiac and metabolic risk factors in DMD (see section 1.6). (48,61,96,97,99) However, it is unclear whether BMI status effects the age in which diagnosis of comorbidities occurs or boys reach significant milestones related to physical function (e.g. age at loss of ambulation). This study will be the first to explore the effect of BMI status on clinically meaningful milestones such as age at loss of ambulation, fractures and OSA. The identified knowledge gaps regarding growth, body composition and the impact of BMI status on clinical outcomes are summarised in Box 3.

Box 3

Identified Knowledge Gaps (Chapter 2)

In young people with DMD...

- Up-to-date understanding of the contemporary growth pattern and BMI status in Victoria, Australia
- Description of body composition in an Australian context
- Clinical factors that predict obesity
- The impact of BMI status on clinical outcomes including physical function, fractures and sleep
- The impact of BMI status on time to clinically meaningful milestones e.g. time to loss of ambulation

This chapter has two main aims with individual objectives corresponding to distinct statistical analyses. The methodology and outcome measures for the two aims is described together. Results for each aim are then presented separately. The chapter concludes with a combined discussion and conclusion for Aim 1 and Aim 2.

2.2 Aims and Objectives

2.2.1 Aim 1

To explore anthropometric and body composition measures over time in young people with DMD.

In young people with DMD attending the Neuromuscular clinic at the Royal Children's Hospital (RCH), the objectives for Aim 1 are to:

i. Describe anthropometry and body composition measures over time.

ii. Determine the prevalence of underweight, healthy weight, overweight, obesity and obesity severity categories (moderate obesity, severe obesity, severe obesity class 1, severe obesity class 2).

iii. Determine the impact of ambulatory status on BMI z-score, fat and lean mass.

iv. Compare the BMI status of old vs. new era young people with DMD.

v. Identify predictors of having obesity.

vi. Identify predictors of FM and lean mass.

2.2.2 Aim 2

To investigate the impact of BMI status on clinical outcomes in boys with DMD.

In young people with DMD attending the Neuromuscular clinic at RCH, the objectives of Aim 2 are to:

i. Determine the impact of BMI status at the first available measure of BMI on time to reaching clinical milestones.

ii. Determine the impact of BMI status at age five to nine years, respectively, on time to reaching clinical milestones.

2.3 Methods

2.3.1 Study Design

This was a retrospective, clinical audit of patients attending the Neuromuscular Clinic at RCH in Melbourne.

2.3.2 Setting

The Neuromuscular Clinic at RCH is a multi-disciplinary clinic specialising in the management of paediatric patients with a range of neuromuscular conditions, including DMD. The neuromuscular clinic team includes neurologists, respiratory physicians, nurse, physiotherapists, occupational therapist and dietitian. In addition to the neuromuscular team, young people with DMD may also be referred to other specialists within the hospital including cardiologists and endocrinologists. Young people with DMD are typically seen in the clinic from the age of diagnosis until 18 years of age or until the completion of high school when they transition to adult services. RCH hosts the largest neuromuscular clinic in Australia and the only paediatric neuromuscular service in Victoria. The clinic also provides a service to young people in Tasmania. The data collected for this study therefore represents the Victorian and Tasmanian paediatric DMD cohort.

2.3.3 Patients

Eligible medical records were identified from central clinic patient lists. Medical records were reviewed if the patient had a diagnosis of DMD and attended the neuromuscular clinic at RCH between January 2011 and March 2018. Diagnosis could be made by either genetic testing or muscle biopsy confirming DMD or a clinical diagnosis by a neurologist in patients with elevated creatine kinase where other conditions have been excluded. The cut-off date (2011) reflects the period where scanned and electronic medical records were introduced in the hospital. The electronic medical record system at RCH contains all progress notes, investigations, pathology results, scans, growth data and correspondence for each patient. Having anthropometric data available in medical records was not an eligibility criterion, however if anthropometry and majority of clinical information was missing the patient was excluded e.g. if a patient attended one appointment but then moved to another state. Patients

were excluded if they had a diagnosis of Becker muscular dystrophy. There were no age limits set for patients. As data was collected from a paediatric clinic, the majority of patients were ≤ 18 years at maximum follow up, however there were some older patients with the highest age at maximum follow-up being 21 years.

2.3.4 Procedures

Ethical approval was granted for this retrospective clinical audit by the Royal Children's Hospital Research Governance Office (LNR/18/RCHM/233). As this was a clinical audit, this study was exempt from obtaining consent from patients. Data from medical records were collected retrospectively and managed using REDCap (Research Electronic Data Capture) (130). REDCap is a secure, web-based software platform designed to support data capture for research studies. The REDCap database was built and piloted amongst three investigators (NB, KC, ZD). The database functionality and data collection accuracy were piloted by two investigators extracting test data from the electronic medical record of one patient. The investigators then compared data and developed guidelines around data collection to ensure consistency. To optimise data accuracy, fixed database responses (e.g. multiple choice) and number limits (e.g. only numbers could be entered for anthropometric measures) were used where possible. Individual medical records were reviewed and data collected by one researcher (NB, JA or KC). When there was uncertainty about the interpretation of data within a record, this was resolved by consensus among the researchers. For eligible patients, data were collected from the first neurologist appointment or date of diagnosis, whichever came first. The last data point was the 31st July 2018 corresponding to the date data collection commenced or earlier if the patient was non-active in the clinic. Patients were recorded as non-active because they had: transitioned to adult services, were lost to follow-up, moved, attended an alternative clinic or died.

2.3.5 Patient Characteristics

Demographic and clinical characteristics collected from medical records included: age at first neurologist appointment, length of follow up, diagnostic information (method of diagnosis, type of mutation and dystrophin isoform maintained), steroid medication (age of commencement, type of steroid), other medications and supplements (e.g. vitamin D and calcium supplementation, angiotensin-converting enzyme or ACE inhibitor including age of

commencement) and diagnosis of co-morbidities (neurodevelopmental disabilities, mental health conditions or respiratory compications). Steroid-treated was defined as any period of steroids (prednisolone, deflazacort or vamorolone). Length of follow up was defined as the time from initial appointment with the neurologist until the last data point prior to July 2018 or until the patient was non-active in the clinic (whichever came first). Information was also collected for the involvement of a dietitian in the nutritional management of each patient. Whether or not the patient saw a dietitian outside of the hospital was not available.

Date of diagnosis was recorded as the date of genetic confirmation of DMD diagnosis or date of muscle biopsy confirming DMD. If confirmation by genetic testing or muscle biopsy was not available, the date of neurologist opinion of clinical findings with interpretation of an elevated creatine kinase was recorded. Genetic mutation was categorised based on type of mutation (deletion, duplication or duplication/triplication) and the dystrophin isoforms maintained based on the location of the mutation (Table 8).

Table 8

Categorisation of Dystrophin Isoforms [1]

Dystrophin isoform	**Key areas of protein expression (95)**	**Mutation location criteria (category number)**				
		Before intron 29 (category 1)	**Before intron 44 (category 2)**	**Before intron 55 (category 3)**	**Before intron 62 (category 4)**	**After intron 62 (category 5)**
Dp260	Retina	✓	×	×	×	×
Dp140	CNS & kidney	✓	✓	×	×	×
Dp116	Schwann cells	✓	✓	✓	×	×
Dp71	Brain, liver, & cardiac muscle	✓	✓	✓	✓	×

[1] ✓ denotes isoform maintained, × denotes isoform not maintained
Abbreviations: CNS, central nervous system

2.3.6 Anthropometry and Body Composition Measures

Data for height and weight were collected from various sources within medical records including: clinic notes, lung function test reports, echocardiogram reports and DXA scan reports. The method of measuring weight (e.g. chair scales or wheelchair scales) and method of measuring or estimating height (e.g. stadiometer or estimation from ulnar length) were recorded if available.

Anthropometric data were analysed from two years of age onwards. Anthropometric data from infants aged 0-2 years were excluded as only a limited number of patients had this data available. Height and weight measures were used to calculate BMI (body mass index, weight kg/height m^2) and height, weight and BMI z-scores were calculated using Cole's LMS method. (131) BMI z-scores were used to classify patients into BMI status categories based on the CDC reference values (Box 2).

Body composition measures were also collected from DXA scan reports which included: total FM%, truncal FM percentage and LM (kg).

2.3.7 Clinical Outcome Measures

Clinical outcomes measures included in Aim 1 and 2 of the analyis are described in Table 9. For timed function tests (10m walk/run, supine-to-stand and four stair climb), North Star Ambulatory Assessment (NSAA), 6 minute walk distance (6MWD) and FVC only assessments performed above seven years were analysed as younger boys are potentially still gaining motor skills and improving performance. (24) When exact dates were not known for events (e.g. date at loss of ambulation or first fracture) the first day of the documented month was recorded.

Clinical outcomes were explored in the form of clinical milestones. Clinical milestones refer to key events in the DMD disease progression that are clinically meaningful, for example, age at loss of independent ambulation. The age at which these clinical milestones occurred was used within models for both Aim 1 and 2. Most clinical milestones were selected *a priori* from the literature (see Table 9 for sources). One exception to this was the clinical milestone of a supine-to-stand time of >7 seconds. This milestone was included after observing few patients (n=4) who had reached a >30 second supine-to-stand, a milestone

which is indicative of loss of ambulation in the proceeding months. (24,132) This clinical milestone was not available for many patients as the assessment is likely to be skipped for patients with the degree of weakness that occurs in the months preceeding loss of ambulation. Furthermore, a 10m walk/run completed in 7-10 seconds was included as an exploratory outcome. Based on clinical observation, this milestone typically indicates a period of rapid functional decline.

Table 9

Clinical Outcome Measures Used in Modelling for Aim 1 and Aim 2 [1]

Outcome measure (observations n)	Clinical milestone	Source of information	Aim 1	Aim 2
Physical function and mobility				
Loss of ambulation (77)	Time to first documentation of loss of ambulation	Clinic notes or correspondence	✓	✓
Timed 10m walk/run (528)	Time to first >10 second time for a 10m walk/run (24,132)	NMC physiotherapy assessments	×	✓
	Time to first 7-10 second time for a 10m walk/run		✓	✓
Timed supine-to-stand (420)	Time to first >30 second time to stand from supine (24,132)	NMC physiotherapy assessments	×	✓
	Time to first >7 second time to stand from supine			
Timed stair climb (470)	Time to first >8 second time for a 4 stair climb (24,132)	NMC physiotherapy assessments	×	✓
NSAA (468)	Time to NSAA score ≤ 9 (133)	NMC physiotherapy assessments	×	✓
6MWD (83)	Time to first 6MWD <325m (24,132)	NMC physiotherapy assessments	×	✓

Table 9

Clinical Outcome Measures Used in Modelling for Aim 1 and Aim 2 [1]

Outcome measure (observations n)	Clinical milestone	Source of information	Aim 1	Aim 2
Strength				
Hand grip strength (left 219, right 220)	-	NMC physiotherapy or occupational therapy assessments	×	✓
Respiratory function and sleep				
FVC (1002)	Time to first FVC < 1L (134)	Pulonary function test reports	×	✓
OSA diagnosis (71)	Time to polysomnography-confirmed OSA diagnosis	Polysomnography reports	×	✓
Nocturnal hypoventilation diagnosis (25)	Time to polysomnography-confirmed nocturnal hypoventilation diagnosis	Polysomnography reports	×	✓
CPAP commencement (26)	Time to CPAP initiation	Polysomnography reports or clinic notes	×	✓
Bi-level commencement (22)	Time to bi-level initiation	Polysomnography reports or clinic notes	×	✓
Bone and skeletal health				
Scoliosis diagnosis (48)	Time to first documentation of xray-confirmed scoliosis	Spinal xray reports	×	✓
Scoliosis surgery (15)	Time to scoliosis corrective surgery	Inpatient admission notes	✓	×
First fracture (crush or other) (71)	Time to first fracture	Clinic or inpatient notes	✓	✓

[1] Abbreviations: 6MWD; 6 minute walk distance; CPAP; continuous positive airway pressure, FVC; forced vital capacity, NSAA; North Star Ambulatory Assessment; OSA; obstructive sleep apnoea; NMC, neuromuscular clinic

2.3.8 Data Cleaning

During the data cleaning process, the expertise of each researcher was utilised to assist with validation of the data. Individual weight, height and BMI plots were reviewed for each individual by two Accredited Practising Dietitians (APD; NB, ZD). After review of the plots, implausible and duplicate values were identified and removed by consensus by the two investigators. Examples of implausible anthropometric values included data points where decreases in height were recorded or a change of 20kg over two months. For physical function and mobility outcome measures, these were reviewed and implausible values identified by consensus by two physiotherapists (JA, KC).

2.3.9 Statistical Analysis

Data analysis was performed using SPSS statistical software (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). Normality of data was determined by visual inspection of histograms. In descriptive analyses, continuous parametric data is reported as mean and standard deviation (SD), continuous non-parametric data is reported as median and interquartile range (IQR) and categorical data is reported is n (N%). Missing descriptive data are also reported in tables. For all analyses, a p-value of <0.05 was considered statistically significant. Statistical analysis procedures are reported according with the objectives of the study.

Objective I - to describe anthropometry and body composition measures over time:

Descriptive data for anthropometric and body composition measures were collected for all patients and stratified by age group (ages 2-21). Anthropometric measures were: height, height z-score, weight, weight z-score, BMI, BMI z-score and change in BMI z-score. Body composition measures analysed were: FM (kg), FM%, truncal FM (kg), truncal FM%, LM (kg) and LM%. Absolute values for height, weight and BMI were presented graphically and overlaid with CDC smoothed percentile data. (135)

For anthropometric data stratified by age group, only one measure per patient per age group was included. Measures were included if both height and weight measures were available (to enable calculation of BMI/BMI z-score) and it was the closest measure to the patient's

birthday. Change in BMI z-score across age groups was determined by calculating the difference in z-score between the first and last measure available within each year of age. If there was only 1 BMI z-score measure for any given age, the change in BMI z-score was recorded as missing. Only four patients had more than one DXA scan within a given year, so only one set of body composition measures per patient per year was included in all analyses. For these four patients for the purposes of analysis, measures taken closest to their birthday was selected for the four patients with multiple yearly measures.

Objective ii - to determine the prevalence of underweight, healthy weight, overweight, obesity and obesity severity categories:

To determine the prevalence of underweight, healthy weight, overweight and obesity BMI z-score was categorised into BMI status categories using the CDC reference values (see Box 2). Proportions of each categories were presented graphically across age groups. Those with obesity were then further categorised into obesity severity based on the percentage greater than the 95th BMI percentile (BMI%95) using methods which have been previously described (136). To determine BMI%95, the BMI (in kg/m^2) for each patient with obesity was divided by the reference BMI at the 95th BMI percentile from CDC data and then multiplied by 100. For example, a BMI of 32.0 kg/m^2 for a male aged 220.5 months would be 109% of the reference BMI at the 95th percentile which is 29.2 kg/m^2 (32.0/29.2x100=109%). BMI%95 was categorised according to following cut offs: moderate obesity 100-120%, severe obesity class 1 120-140% and severe obesity class 2 >140%.

Objective iii - to determine the impact of ambulatory status on BMI z-score, fat and lean mass percentage:

To determine the impact of ambulatory status on BMI z-score, FM and LM, measures were stratified according to whether patients were ambulant or non-ambulant at each age group. To test for differences across ambulatory status, a Mann-Whitney U test for non-parametric data was used.

Objective iv - compare the BMI status of old vs. new era young people with DMD:

To compare old vs. new era patients with DMD, a subgroup of BMI status observations was analysed. New era patients were those from the current study with a BMI measure after October 2009. Data from a prior study were used to describe old era patients with BMI measured before October 2009 (5).

Objective v - identify what predicts the risk of having obesity:

To identify what demographic or clinical factors predict the risk of obesity, generalized estimating equation (GEE) was used to account for within-patient repeated measures. The GEE was computed using an unstructured correlation matrix with a binary logistic distribution.

The dependant (outcome) variable was obesity (yes/no) and the independent (predictor) variables were: age, length of follow-up, age at diagnosis, ambulation status (ambulant/non-ambulant), >7 second 10m walk/run (yes/no), ≥ 1 fracture (yes/no), ≥ 1 dietitian visit (yes/no), scoliosis surgery (yes/no), steroid treatment (naïve/prednisolone/deflazacort/other), dystrophin isoform maintained (see Table 8 for categories) and neurodevelopmental disability diagnosis (yes/no). Steroid treatment was defined as taking steroid at the time of anthropometry measurement. For other time-dependant predictor variables (ambulation status, >7 second 10m walk/run, ≥ 1 fracture, ≥ 1 dietitian visit, scoliosis surgery) each BMI value was coded based on whether these events occurred prior to the measurement. For this analysis, odds ratio (OR) and 95% confidence intervals (CI) are reported.

Objective vi - Identify the predictors of FM% and LM%

A GEE was also used to determine what demographic and clinical factors predict fat and lean mass. For these two models an unstructured correlation matrix and a scale linear distribution was used to predict FM% and LM% (dependant variables in two separate models). The independent (predictor) variables for both of these models were: age, age at diagnosis and ambulation status (ambulant/non-ambulant). For both models the beta coefficient and standard errors are reported.

For the three GEE models (dependant variables; obesity, FM% and LM%), unique patient record IDs were entered as the subject identifier and age at measure (BMI status or body

composition measure) was entered as the within-subject identifier. Independent variables for the model were chosen *a priori*.

Objective vii and viii - To determine the impact of BMI status at the first available measure of BMI and ages five to nine years on clinical milestones

Time-to-event analysis was conducted to determine the impact of BMI status on time to clinical milestones (see Table 9). For this analysis Cox proportional hazards models were fitted and data were presented graphically using Kaplan-Meier curves with number at risk tables. Patients with the clinical milestone documented within medical records were coded as 'event' and the age at the milestone occurring was imputed as the time variable. When the clinical milestone did not occur, patients were coded as 'censored' and the age at last follow-up was imputed as the time variable. For censored patients, the age at last follow-up was July 2018 (the time of commencing data collection) or the age at last neuromuscular clinic appointment for those who had transitioned to adult services, died, moved or were lost to follow-up. Patients were coded as missing if BMI measures prior to the event or clinical milestone data was not available.

For each clinical milestone the time-to-event analysis was stratified by BMI status at the first available measure of BMI and BMI status at age five, six, seven, eight and nine years, respectively. Separate models were fitted for each age groups to explore the impact of BMI status on clinical milestones at different ages. BMI status categories were 'no overweight or obesity' or 'overweight' or 'obesity'. Patients who were underweight were classified as 'no overweight or obesity' alongside patients who were a healthy weight due to the low numbers in the underweight category. For all analyses, 'no overweight or obesity' was the reference category.

Some analyses were adjusted for covariates which were selected *a priori*: time to first fracture was adjusted for zoledronic acid treatment prior to the fracture, time to scoliosis diagnosis was adjusted for ambulatory status and time function tests (10m walk/run, supine-to-stand and four stair climb) were adjusted for involvement in a drug trial. Some patients within the RCH neuromuscular clinic received prophylactic zoledronic acid treatment prior to their first fracture as part of a clinical trial. (137) Due to the low number of steroid-naive patients across the sample (n=16), analyses were not adjusted for steroid status. For Cox

proportional hazard models, hazard ratios and 95% CI are reported. As there are no clinically meaningful milestones for hand grip strength, this was not analysed using time-to-event analysis. Data for handgrip were analysed descriptively. Age groups used were: four to five years; six to seven years; eight to nine years; 10-11 years; 12-14 years; 15-16 years and; 17-20 years.

2.4 Results - Aim 1

2.4.1 Patient Characteristics

There were 158 male patients with DMD that met the eligibility criteria and were included in analyses. Of eligible patients from clinic lists, three were excluded as there was insufficient data available in medical records: one moved overseas, one was managed at an alternative hospital and one was lost to follow up. The date of diagnosis was known for 157 (99.4%) patients, for the remaining one patient the date of diagnosis was unclear as the patient was diagnosed overseas and initial the genetics report was not available. Majority were steroid-treated (n=142, 89.9%), see Table 10.

Across the sample 118 (74.7%) saw a dietitian at least once during the follow up period. The mean number of visits with the dietitian was 4 ± 3 and ranged from one to 14.

Table 10

Patient Characteristics (n=158) [1]

Age at diagnosis (years) *(n=157)* [2]	4.2 ± 2.1
Method of diagnosis, n (N%)	
Genetics	141 (89.2)
Muscle biopsy	7 (4.4)
Elevated creatine kinase with neurologist opinion	10 (6.3)
DMD mutation type, n (N%)	
Deletion	93 (58.9)
Duplication or duplication/triplication	18 (11.4)
Point mutation	29 (18.4)
Genetic testing conducted but mutation not identified	5 (3.2)
Report not found	13 (8.2)
Dystrophin isoforms maintained, n (N%)	
Dp260, Dp140, Dp116 and Dp71 maintained (Category 1)	36 (22.8)
Dp140, Dp116 and Dp71 maintained (Category 2)	21 (13.3)
Dp116 and Dp71 maintained (Category 3)	70 (44.3)
Dp71 maintained (Category 4)	5 (3.2)
Nothing maintained (Category 5)	8 (5.1)
Exons affected not available	18 (12.7)

Table 10

Patient Characteristics (n=158) [1]

Clinic information	
Age (years) at first neurologist appointment	4.5 ± 2.5 [3]
Length of follow-up (years) [4]	8.7 ± 4.7
Steroid treatment, n (N%) [5]	
Steroid-treated	142 (89.9)
Age (years) at steroid commencement *(n=139)*	6.6 ± 2.3
Prednisolone only	81 (51.3)
Prednisolone then deflazacort	58 (36.7)
Other	3 (1.9)
Steroid-naïve	16 (10.1)
Other medications, n (N%)	
Zoledronic acid	56 (35.4)
Metformin	9 (5.7)
Angiotensin-converting enzyme (ACE) inhibitors	111 (70.3)
Beta blockers	7 (4.4)
Testosterone	33 (20.9)
Psychotropic medications	19 (12.0)
Anti-hypertensive medications	4 (2.5)
Total no. of other medications types[6]	2 ± 1
Physical function, n (N%)	
Ambulant at the end of the follow-up period	76 (48.1)
Non-ambulant at the end of the follow-up period	82 (51.9)
Age at loss of ambulation *(n=77)*,	11.1 ± 2.6
Respiratory diagnosis, n (N%)	
Obstructive sleep apnoea	72 (45.6)
Nocturnal hypoventilation	27 (17.1)
Continuous positive airway pressure (CPAP) initiated	24 (15.2)
Bi-level initiated	20 (12.7)
Both CPAP & Bi-level initiated	2 (1.3)
Co-morbidities, n (N%)	
Any neurodevelopmental disability diagnosis[7]	39 (24.7)
Autism spectrum disorder	22 (13.9)

Table 10	
Patient Characteristics (n=158) [1]	
Intellectual disability	13 (8.2)
Attention deficit hyperactivity disorder	5 (3.2)
Other developmental/language/speech/hearing disorders	5 (3.2)
Any mental health diagnosis[8]	22 (13.9)
Depression/anxiety	13 (8.2)
Obsessive-compulsive disorder	5 (3.2)
Other mental health diagnosis	8 (5.1)
Fractures, n (N%)	
≥ 1 fracture during follow-up period	71 (44.9)
Age at first fracture *(n=71)*	11.2 ± 3.2
Deaths	
Deaths during follow-up period	10 (6.3)
Age at death *(n=10)*	15.7 ± 3.0

[1] Categorical values are reported as n (N%), continuous variables are reported in years and as mean ± SD
[2] Missing data is as follows: age of diagnosis (n=1), mutation type (n=1, genetic testing performed but mutation type not available), steroid commencement date and age (n=3), age at loss of ambulation (n=5)
[3] Mean age at diagnosis is lower than the mean age at first neurologist appointment due to antenatal diagnoses and patients being diagnosed at external clinics (interstate or overseas) before transferring care to RCH.
[4] Length of follow-up: date of first neurologist appointment to last neurologist/neuromuscular appointment
[5] Steroid-treated: treated with steroids for any length of time during the follow-up period
[6] Total medications: oral bisphosphonates, IV zoledronic acid, metformin, ace inhibitors, beta blockers, testosterone, insulin, psychotropic medications or anti-hypertensive
[7] Any neurodevelopmental disability diagnosis: autism spectrum disorder, intellectual disabilities, attention deficit hyperactivity disorder or other developmental disorders
[8] Any mental health diagnosis: depression/anxiety, obsessive-compulsive disorder or other mental health diagnosis

2.4.2 Descriptive Data for Anthropometric and Body Composition Measures

Of the 158 patients in the cohort, 156 had anthropometric measures available. The two patients without anthropometric measures were both young (3.7 years and 5.2 years), were actively attending clinic (ie. had not moved away) and had diagnostic and medication data available and were therefore included in analysis of patient characteristics. During the data cleaning process, 379 height and 348 weight measures across 121 patients were deemed implausible and were removed. The total number of observations included were: 2480 height, 2902 weight and 2456 BMI measures (Table 11).

For analysis of body composition analysis, 86 patients had total body DXA scans available and were included in analyses. Of the sample, 52 did not have a DXA scan during the follow-up period and 20 had analysis of bone only (e.g. hip scan).

Table 11

Descriptive Data for Anthropometric and Body Composition Measures

Measure (n observations)	**Mean ± SD [min-max]**
Height (n=132)	
Number of observations per patient across follow-up	16 ± 10
Number of observations per patient per year of follow-up	2 ± 1
z-score *(n=2480)*	-1.47 ± 1.40 [-6.06-2.97]
Weight (n=155)	
Weight observations per patient across follow-up	18 ± 11
Weight observations per patient per year of follow-up	2 ± 1
Weight z-score *(n=2902)*	0.10 ± 1.56 [-8.51-3.24]
BMI (n=131)	
BMI observations per patient over total follow-up	16 ± 10
BMI observations per patient per year of follow-up	2 ± 1
BMI z-score *(n=2456)*	1.00 ± 1.60 [-14.23-3.36]
Change in BMI z-score across follow-up *(patients n=150)*	0.23 ± 1.58 [-7.36-4.59]
Body composition (n=86)	
FM (kg) *(n=227)*	19.7 ± 12.0 [3.27-60.4]
FM % *(n=232)*	42.0 ± 11.8 [16.6-64.7]
Truncal FM (kg) *(n=227)*	9.5 ± 6.6 [1.38-32.6]
Truncal FM % *(n=232)*	41.7 ± 13.5 [13.9-68.3]
LM (kg) *(n=227)*	22.5 ± 4.9 [12.5-36.0]
LM% *(n=227)*	55.9 ± 11.5 [34.2-80.6]

Of included anthropometric values, the majority (n=1272, 43.4%) were taken during neuromuscular clinic appointments (Figure 5). There were 86 patients with DXA body composition measures available. No body composition measures were deemed implausible during the data cleaning process.

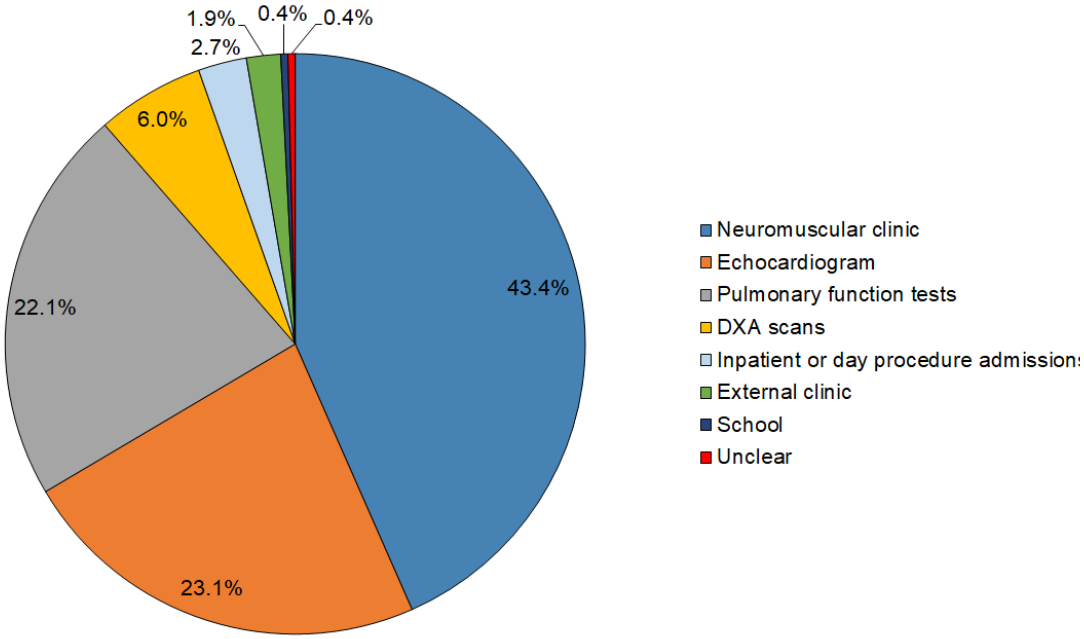


Figure 5

Sources of Anthropometry Measures, N=2480 Height, N=2902 Weight and N=2456 BMI

2.4.3 Anthropometric and Body Composition Measures Across Age Groups

All available absolute values for height, weight and BMI for DMD patients are plotted on CDC percentile charts (Figure 6-Figure 8). From visual inspection of the charts, boys with DMD exhibit slowed height growth compared to the CDC cohort. Figure 6 shows how height growth appears to slow from six years of age and by approximately 11-12 years majority of boys are below the 3rd centile for height.

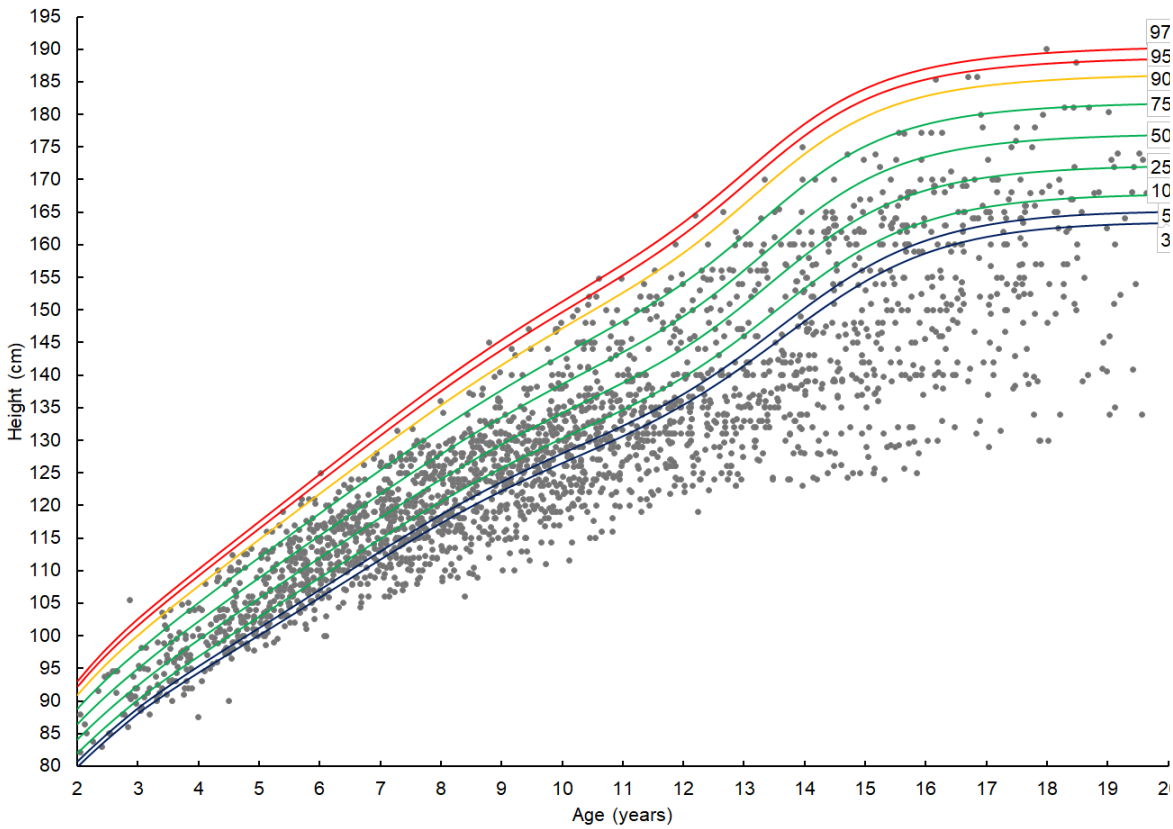


Figure 6

Measures of Height (cm) for DMD Population with DMD Height-For-Age Percentile Chart Overlaid

Until approximatley 6-7 years, the majority of weight measurements are within the limits of the percentile charts, after which the variance increases and values both over the 97th percentile and below the 3rd percentile are observed in weight (Figure 7).

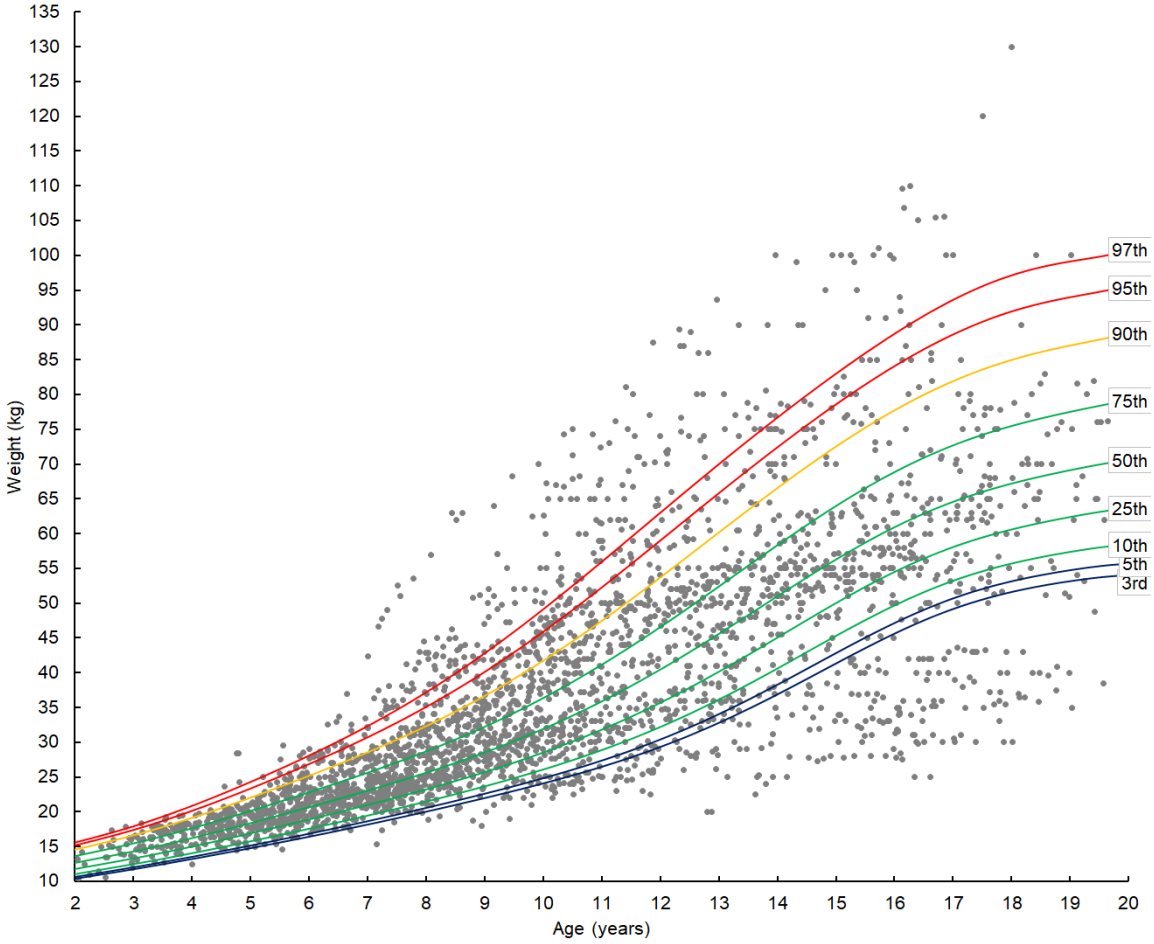


Figure 7

Measures of Weight (kg) for DMD Population with CDC Weight-For-Age Percentile Charts Overlaid

For BMI, there is a wide spread of values that fall accross the limits of the percentile charts, over the 97th percentile and below the 3rd percentile. Figure 8 provides a pictorial overlay of how the the variance in BMI increases with increasing age.

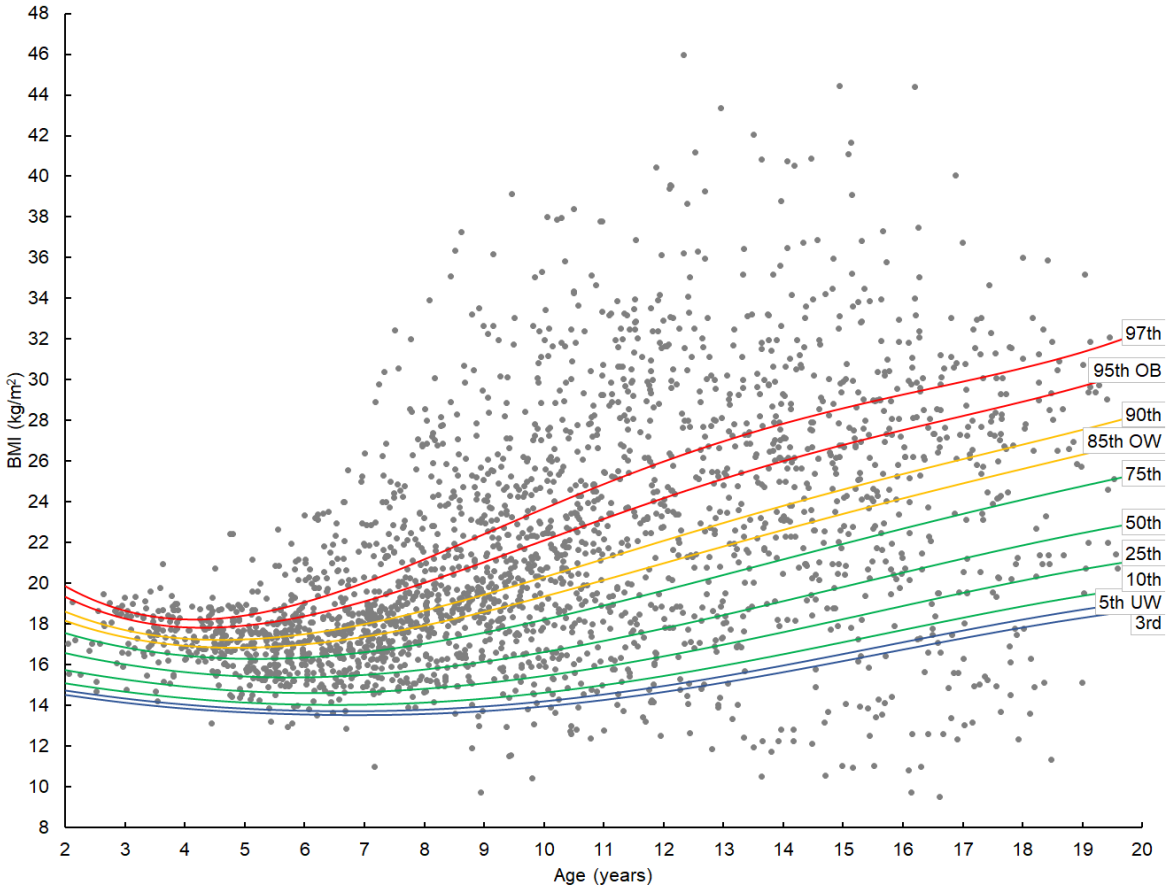


Figure 8

Measured of BMI (kg/m²) for DMD Population with CDC BMI-For-Age Charts Overlaid

Descriptive data for all the anthropometric measurements stratified by age group are shown in Figure 9-Figure 11 and in Supplementary Table 2, only one measure per patient per age group was analysed. All age groups exhibited short stature compared to CDC reference values, a trend which is exacerbated with increasing age (Figure 9). Height z-score was the lowest at age 17 years, when the median height z-score was -3.03 (IQR -4.28, -1.55).

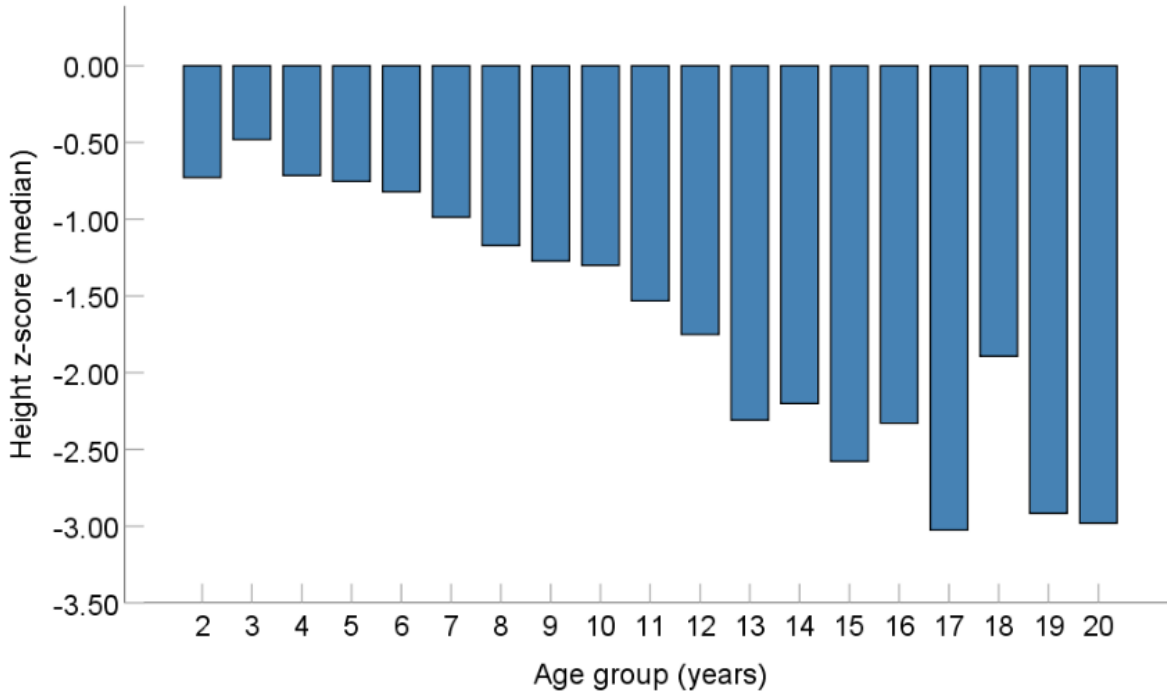


Figure 9

Median Height Z-Score Across Age Groups

Weight z-scores fluctuate between 0 and +1 from ages 2-14 after which it declines (Figure 10). Median weight z-score was highest at 3 years of age at 0.84 (IQR -0.11,1.10) and lowest at 17 years of age with a median Z score of -0.89 (-2.97,0.04).

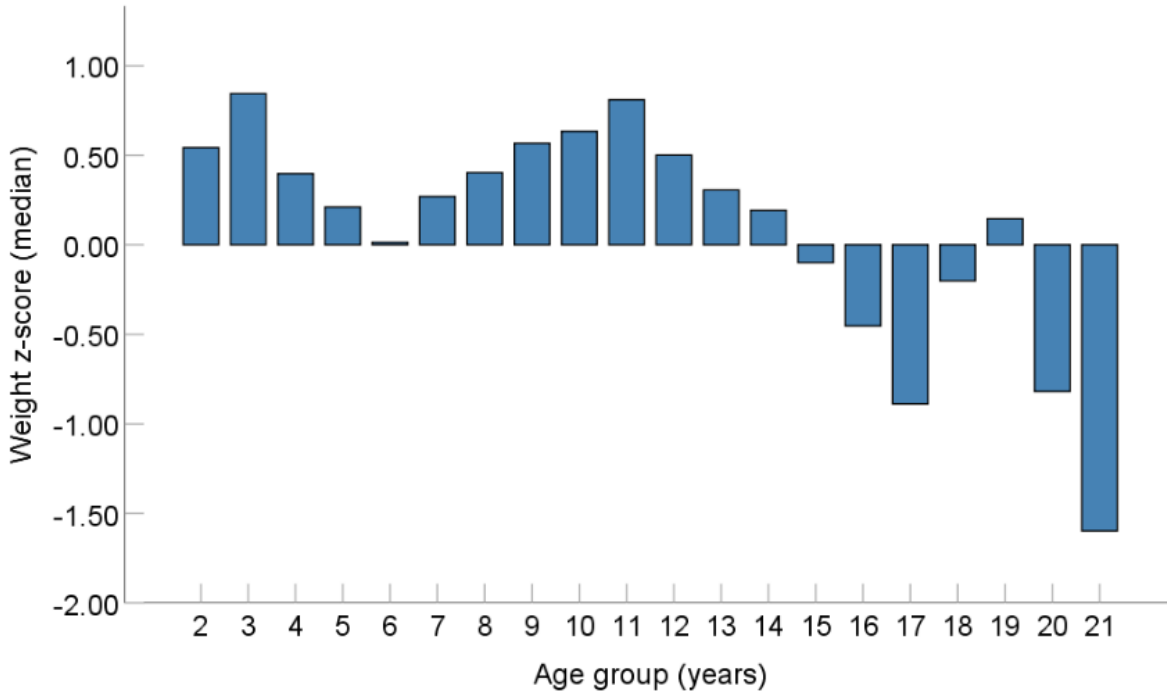


Figure 10

Median Weight Z-Score Across Age Groups

BMI z-score was consistently above +1 z-score between 3-19 years and peaked at 11 years when the median was 1.67 (IQR 0.63, 2.24), see Figure 11.

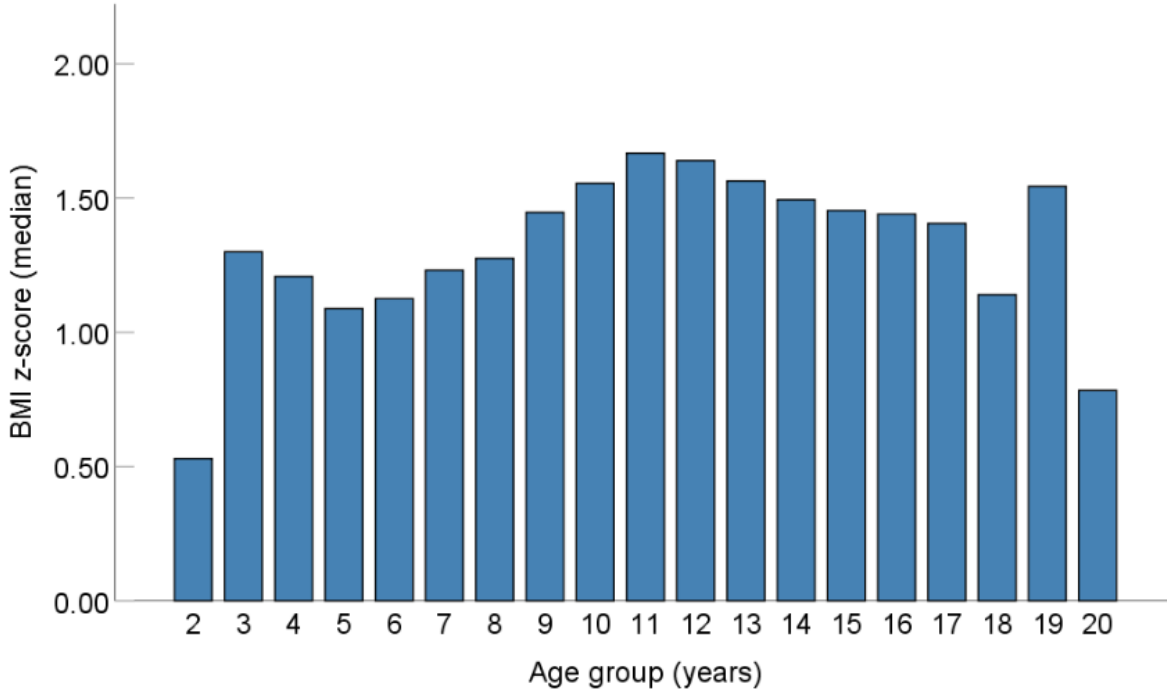


Figure 11

Median BMI Z-Score Across Age Groups

The greatest increases in BMI z-score across each age group was observed in those aged 19 years (median change 0.35 IQR -0.39, 0.41), however only 3 patients were available for this age group (Figure 12). This was followed by children aged five years (n=49), median change in BMI z-score was 0.21 (IQR -0.20,0.58). The greatest decline in BMI z-score was observed at 17 years (n=26), median BMI z-score change -0.30 (IQR -0.73, -0.05).

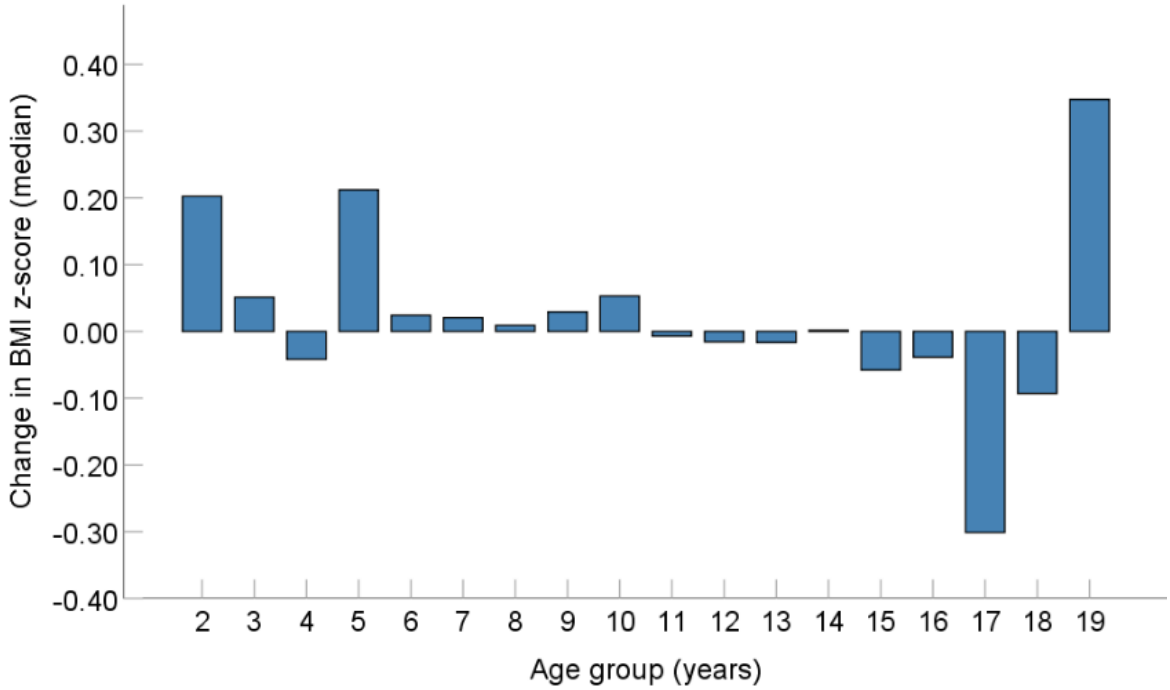


Figure 12

BMI Z-Score Change Across Age Groups [1]

[1] Note small sample size for 19 years of age (n=3)

Body composition data was available for five to 20 years. Data shows that FM% increases and LM% decreases with age (see Figure 13, Figure 14 and Supplementary Table 3). FM% peaks at age 17 (median 54.3% IQR 49.1, 55.6) while LM% peaks at age four (median 73.7% IQR 72.4, 76.9).

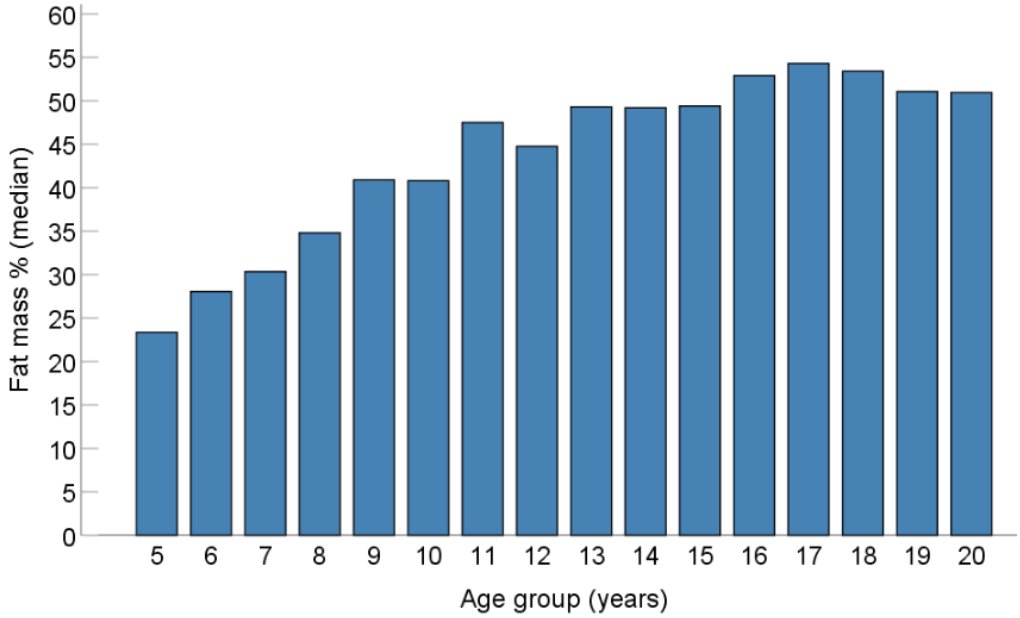


Figure 13

Median Mat Mass Percentage Across Age Groups

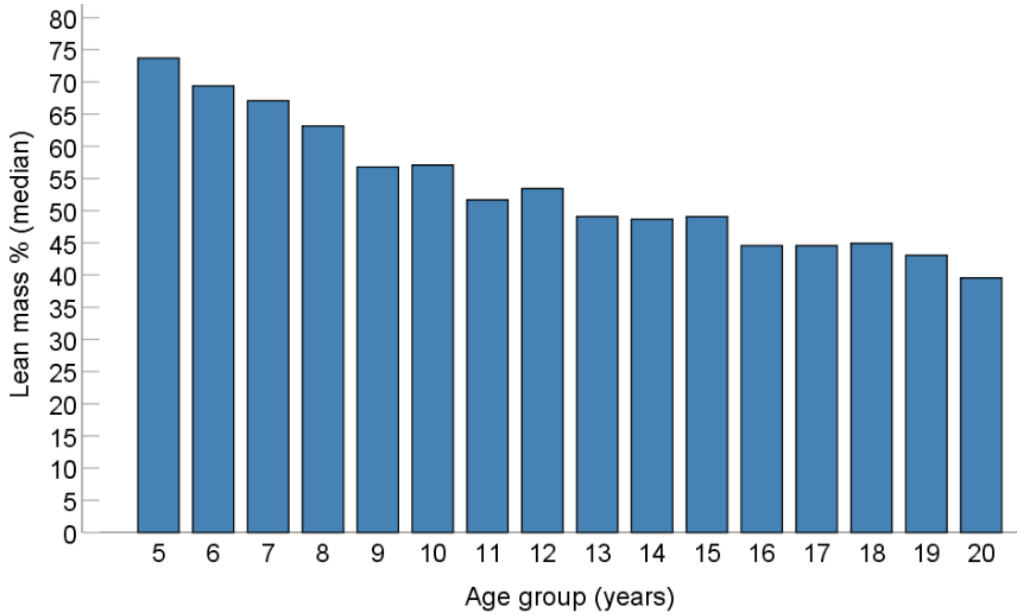


Figure 14

Median LM% Across Age Groups

2.4.4 Description Of BMI Status Across Age Groups

The distribution of BMI status across age groups are shown in Figure 15 and Supplementary Table 4. The highest prevalence of underweight was observed in 18 years olds (20.0% underweight). The highest prevalence of healthy weight was observed in 20 year olds (75.0%), however the sample size at this age was small (n=4). This was followed by 2 year olds, whom 52.9% were a healthy weight. The greatest prevalence of overweight was observed in 5 year olds (39.7%). Obesity prevalence steadily increases from 5 years (16.7%) until it peaks at 11 years (50.6%) and then declines again to 25.0% at 19 years. At 11 years 19.8% have severe obesity class 1 and 8.6% have severe obesity class 2 (Table 12). Severe obesity class 1 and 2 are most prevalent between the ages of eight and 15 years.

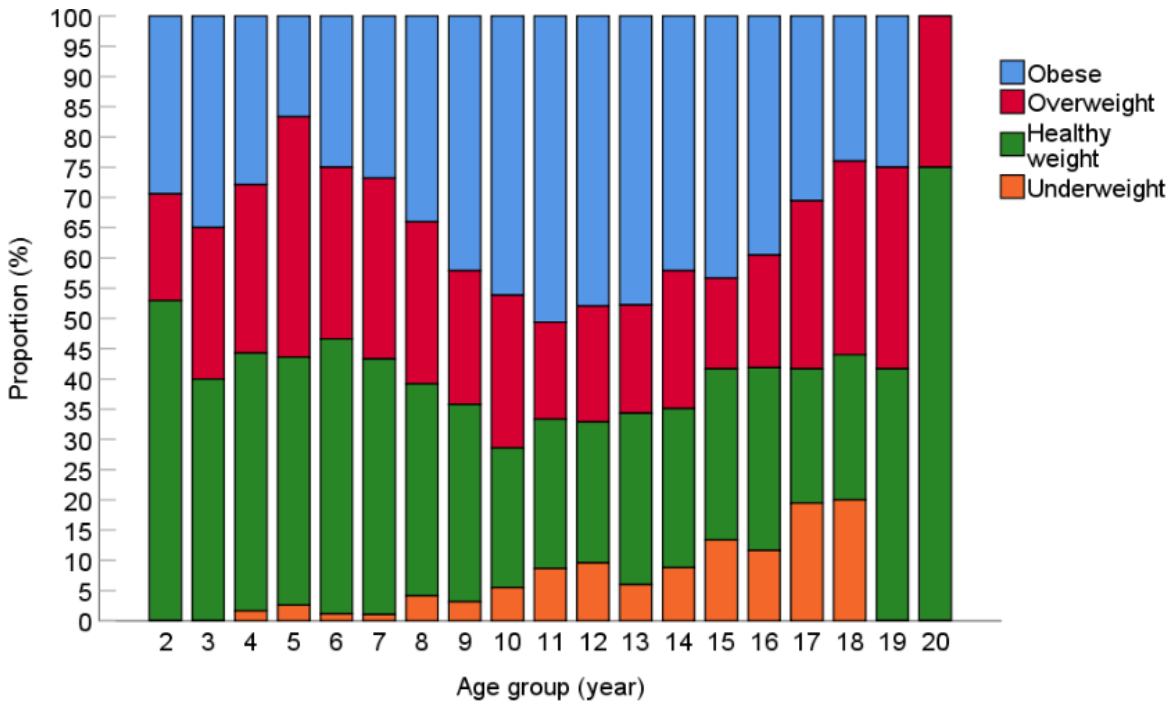


Figure 15

BMI Status Across Age Groups

Table 12

Obesity Severity Across Age Groups

Age group (year)	Moderate obesity n (%) [1]	Severe obesity class 1 n (%)	Severe obesity class 2 n (%)
2	5 (29.4)	0	0
3	14 (35.0)	0	0
4	16 (26.2)	1 (1.6)	0
5	12 (15.4)	1 (1.3)	0
6	18 (20.5)	4 (4.5)	0
7	18 (18.6)	8 (8.2)	0
8	17 (17.5)	13 (13.4)	3 (3.1)
9	22 (23.2)	12 (12.6)	6 (6.3)
10	26 (28.6)	9 (9.9)	7 (7.7)
11	18 (22.2)	16 (19.8)	7 (8.6)
12	16 (21.9)	13 (17.8)	6 (8.2)
13	19 (28.4)	10 (14.9)	3 (4.5)
14	17 (29.8)	5 (8.8)	2 (3.5)
15	18 (30.0)	5 (8.3)	3 (5.0)
16	13 (30.2)	3 (7.0)	1 (2.3)
17	10 (27.8)	1 (2.8)	0 (0.0)
18	5 (20.0)	1 (4.0)	0 (0.0)
19	3 (25.0)	0	0
20	0	0	0

[1] Moderate obesity BMI%95 100-120; severe obesity class 1 BMI%95 120-140; severe obesity class 2 BMI%95 >140

2.4.5 Anthropometric and Body Composition Stratified By Ambulatory Status

BMI z-score, FM% and LM% stratified by age group and ambulatory status are shown in (Supplementary Table 5, Supplementary Table 6 and Supplementary Table 7). There was no difference in BMI z-score, FM% and LM% between ambulant and non-ambulant groups across most age groups. Those who were ambulant at eight years had a significantly greater BMI z-score (median 1.33 IQR 0.50, 2.04) comapared to those who were non-ambulant (median 0.24 IQR -4.48, 1.10) at eight years (p=0.024). However, there were few (n=5, 5.2%) in the non-ambulant group (ambulant n=91). Those who were ambulant at 16 years old had a greater LM% (median 54.2 IQR 53.9, 54.5) than their non-ambulant peers (median 43.2 IQR 42.6, 47.5), however these sample sizes were small (n=2 ambulant, n=10 non-ambulant).

2.4.6 BMI Status: New Vs. Old Era Patients

The prevalence of each BMI status classification (underweight, healthy weight, overweight or obese) across age groups (3-16 years) for new and old era young people with DMD is shown in Figure 16 and Supplementary Table 8. The number across each BMI status category in the new era data are different to that presented in section 2.4.4 as a subset of data from 2009 onwards was analysed. Across all age groups the prevalence of underweight was lower in the new era cohort than the old era cohort. For the old era cohort, the prevalence of obesity peaks at 10 years of age at 47.9%, then BMI begins to decrease after 12 years. For the new era cohort, the prevalence of obesity peaks at age 11 years at 52.5% and remains persistently above 40% until 16 years, then begins to decrease. At ages when obesity peaks (10-12 years), the rates are similar between the old and new era cohorts. From the descriptive data it was observed that between ages 13 and 16 years the rate of obesity in the new era cohort was between 1.7 to 3.2 times that of the old era cohort.

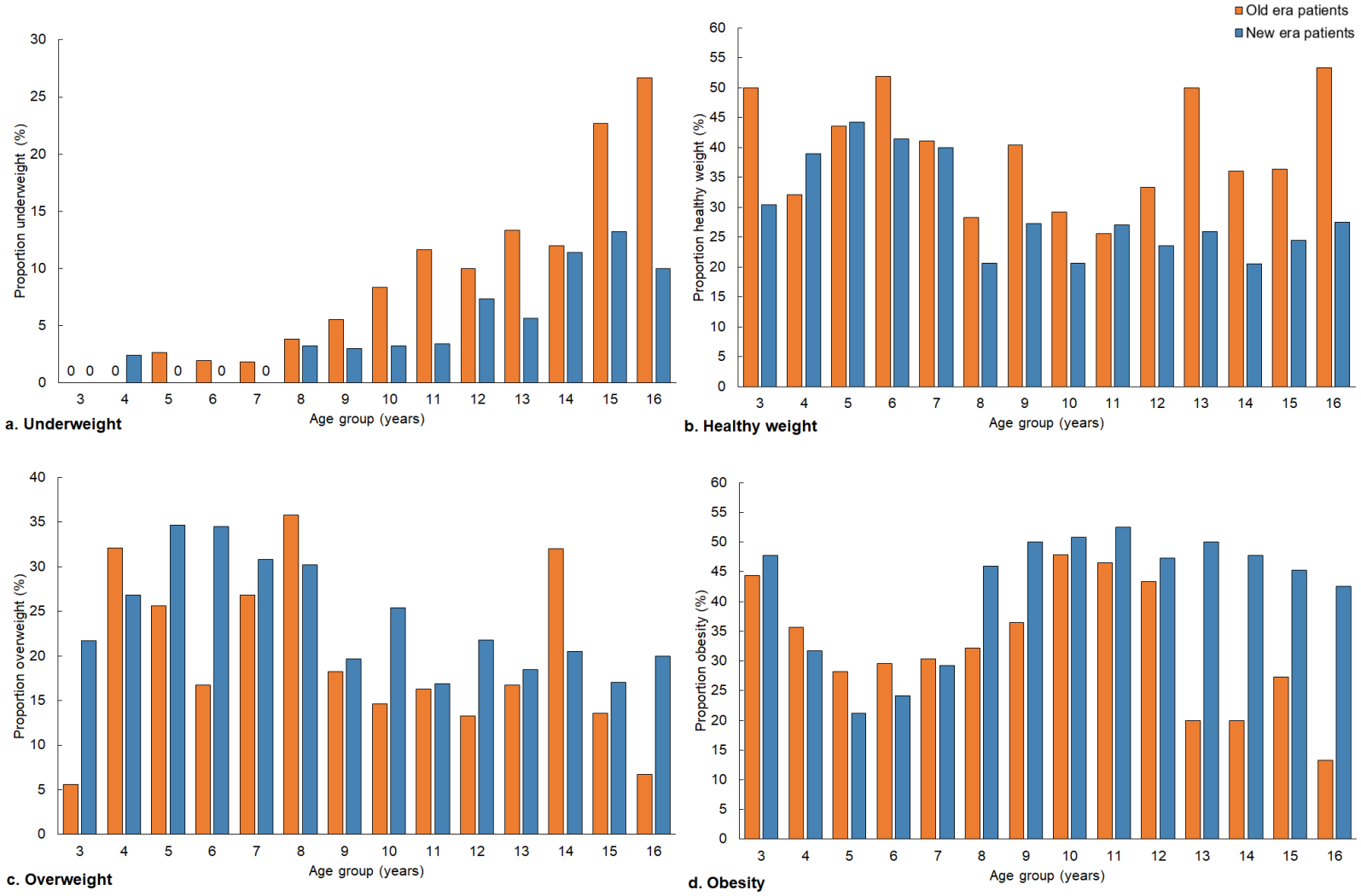

Old era patients
New era patients
Proportion underweight (%)
Age group (years)
a. Underweight
Proportion healthy weight (%)
Age group (years)
b. Healthy weight
Proportion overweight (%)
Age group (years)
c. Overweight
Proportion obesity (%)
Age group (years)
d. Obesity

Figure 16a-d

Comparing Old Vs. New Era Data for BMI Status Categories Within Each Age Group (Sample Sizes Available in Supplementary Table 8)

2.4.7 Predictors of Obesity

The results from the GEE analysis are presented in Table 13. Those who saw a dietitian were more likely to have obesity (OR 1.188 95% CI 1.064-1.327) compared to those who had not seen a dietitian. Patients who were treated with prednisolone then deflazacort were 30% more likely to have obesity (OR 1.298 95% CI 1.093-1.543) compared to patient who were steroid-naïve. Scoliosis surgery decreased the likelihood of obesity by 55% (OR 0.449 95% CI 0.351-0.574). Those diagnosed with a neurodevelopmental disability had decreased odds of obesity (OR 0.826 95% CI 0.695-0.983). Age, ambulatory status, completing a 10m walk/run in ≥7 seconds and dystrophin isoforms maintained did not predict obesity.

Table 13

Predictors of Obesity Using a Generalized Estimating Equation (N=141 Patients, N=2070 Observations)

Predictors [1]	OR	95% CI lower	95% CI upper	P-value [2]
(Intercept)	0.918	0.618	1.363	0.671
Age	0.991	0.971	1.011	0.392
Length of follow-up	0.994	0.971	1.018	0.642
Age at diagnosis	1.012	0.968	1.059	0.591
Ambulant [a]	0.921	0.806	1.054	0.231
≥7 seconds in a 10m walk/run [b]	1.132	0.933	1.375	0.209
10m walk/run data missing [b]	1.153	0.958	1.387	0.132
≥ 1 fracture [c]	1.103	0.955	1.273	0.182
≥ 1 dietitian consult [d]	1.188	1.064	1.327	**0.002**
Scoliosis surgery (yes) [e]	0.449	0.351	0.574	**<0.001**
Steroid-treated predisolone only [f]	1.090	0.978	1.215	0.120
Steroid-treated prednisolone then deflazacort [f]	1.298	1.093	1.543	**0.003**
Steroid-treated other [f]	1.297	0.445	3.774	0.634
Dystrophin isoforms maintained: Dp140, Dp116 and Dp71 (Category 2) [g]	0.776	0.577	1.043	0.093
Dystrophin isoforms maintained: Dp116 and Dp71 (category 3) [g]	0.941	0.789	1.123	0.501
Dystrophin isoforms maintained: Dp71 OR nothing maintained (Category 4 or 5) [g]	0.830	0.583	1.182	0.302
Unknown/missing genetic information [g]	0.782	0.645	0.948	**0.012**
Diagnosis of a neurodevelopmental disability [h]	0.826	0.695	0.983	**0.031**

[1] Reference categories are: [a] Non-ambulant [b] Less than 7 second [c] No fracture [d] No dietitian consult [e] No scoliosis surgery [f] Steroid-naïve [g] Dp260, Dp140, Dp116 and Dp71 maintained [h] No diagnosis of neurodevelopmental disability

[2] P-values in boldface indicate statistical significance using a p-value of <0.05

2.4.8 Predictors of Body Composition

A GEE predicted that for every yearly increase in age, FM% increased by 1.5% and LM% decreased by 1.6% (Table 14 and Table 15). Compared to non-ambulant patients, ambulant patients were predicted to have 4.9% less FM% and 5.0% more LM%. Steroid treatment or age at steroid commencement did not significantly impact lean or fat mass.

Table 14

Predictors of FM % Using a Generalized Estimating Equation (N=81 Patients, N=219 Observations)

Predictors	B	Standard Error	P-value
(Intercept)	17.31	6.864	**0.012**
Age	1.51	0.292	**<0.001**
Ambulant at measure [a]	-4.89	2.49	**0.049**
Steroid-treated [b]	2.78	2.79	0.317
Age at steroid commencement	1.06	0.64	0.094

Table 15

Predictors of LM% Using a Generalized Estimating Equation (N=79 Patients, N=214 Observations)

Predictors [1]	B	Standard Error	P-value
(Intercept)	80.02	6.724	**<0.001**
Age	-1.60	0.27	**<0.001**
Ambulant at measure [a]	4.99	2.40	**0.037**
Steroid-treated [b]	-2.90	2.52	0.251
Age at steroid commencement	-0.83	0.61	0.175

[1] Reference categories for Table 14 and Table 15 are: [a] Non-ambulant at measure [b] Steroid-naïve

2.5 Results - Aim 2

2.5.1 Available BMI Data Across Age Groups

In total, 154 patients had at least one BMI measure available for analysis. Clinical outcomes were assessed in relation to first available BMI measures. The median age at first BMI measure was 5.4 (IQR 3.7, 7.2) years and ranged from 2.0 to 16.2 years (Figure 17).

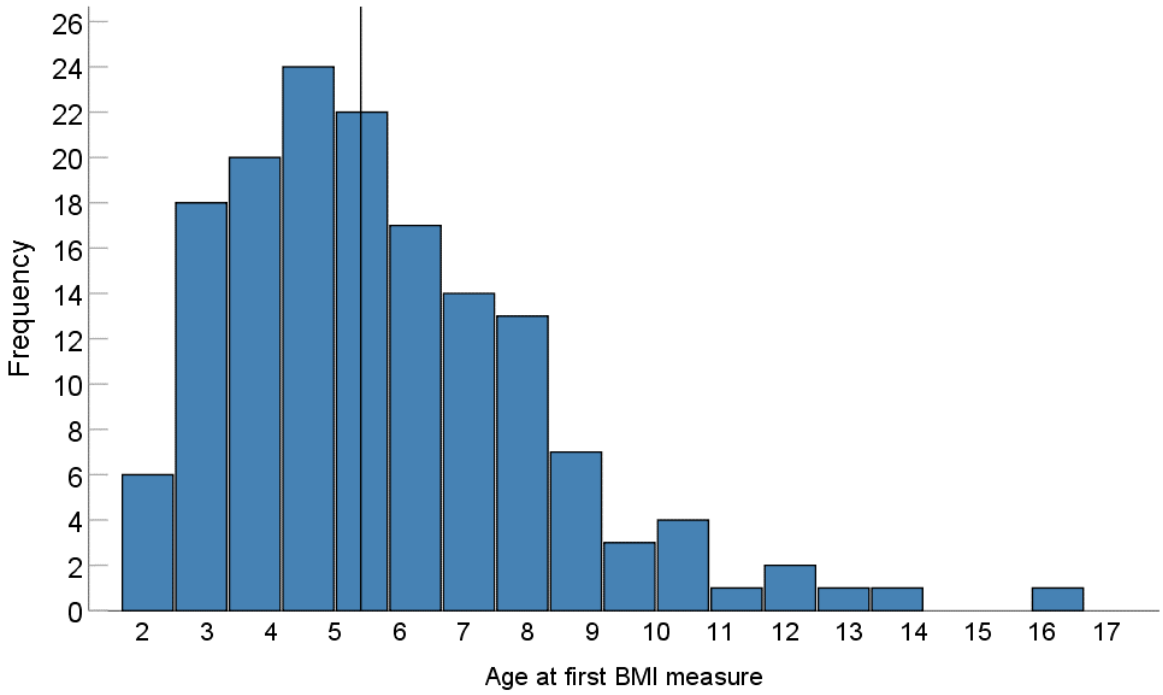


Figure 17

Histogram of Age at First BMI Measure with Median Line

Clinical outcomes in relation to BMI at different ages was also explored. Ages five to nine were analysed in individual time-to-event analysis. The number of patients with a BMI measure available for each of these age groups were: five years n=78, six years n=88, seven- and eight-years n=97 and nine years n=95. The number of underweight patients at the first available BMI measure through to nine years ranged from n=1 to n=4. These patients were categorised as “no overweight or obesity” together with those in the healthy weight category.

2.5.2 Impact of BMI Status on Time to Loss Of Ambulation

BMI status at the first available measure:

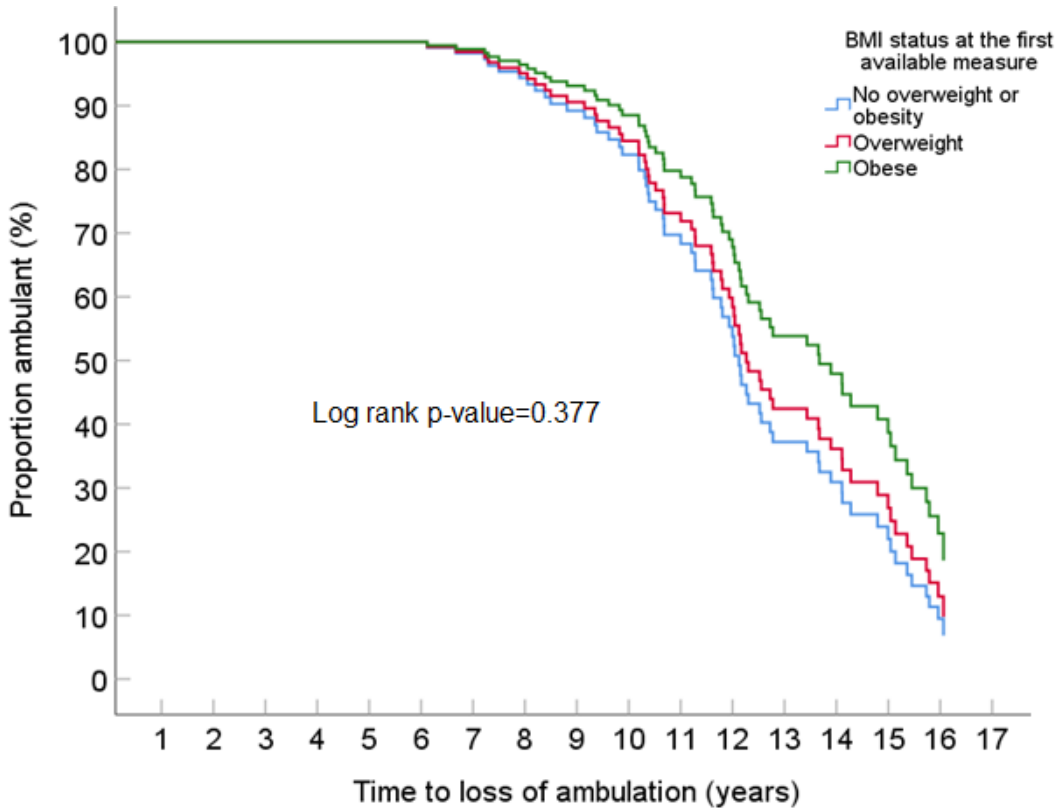
At the end of follow up period, 66 boys (41.8%) were non-ambulant (event) and 72 (45.6%) were ambulant (censored) and 20 (12.7%) were excluded due to missing data (Table 16). BMI status at the first available BMI measure did not impact time to loss of ambulation (Figure 18, Table 17).

Table 16

Description of Loss of Ambulation Across BMI Status at the First Available Measure of BMI (N=158) [1]

	Lost ambulation during follow-up period, n (N%)	**Median time to loss of ambulation (95% CI)** [2]
No overweight or obesity	34 (51.5)	12.0 (11.6-12.5)
Overweight	20 (30.3)	12.2 (9.8-14.6)
Obese	12 (18.2)	13.9 (9.8-18.0)
Total	66 (100)	12.3 (11.6-12.9)

[1] Censored n=72, missing n=20
[2] Time to loss of ambulation log rank p-value=0.377



Number at risk

No ov/ob	64	64	62	58	47	31	17	9	2	1
Ov	43	43	43	40	32	24	12	6	1	
Ob	31	31	30	25	20	16	11	6	1	

Figure 18

Kaplan-Meier Curve Time for Loss of Ambulation Stratified by BMI Status at The First Available Measure

Table 17

BMI Status at the First Available Measure as a Predictor of Time to Loss of Ambulation Using a Cox Proportional Hazards Model [1]

BMI status	Hazard Ratio	95% CI lower	95% CI upper	P-value
Overweight	0.867	0.498	1.510	0.615
Obese	0.627	0.323	1.215	0.166

[1] Event n=66, censored n=72, missing n=20
Reference category is no overweight or obesity

BMI status at ages five to nine:

BMI status at any age between five to nine years did not predict time to loss of ambulation (Supplementary Table 9).

Box 4

Summary of Findings for The Impact of BMI Status on Loss of Ambulation

There was no significant impact of BMI status on time to loss of ambulation using BMI at the first available measure or BMI at ages five to nine years.

2.5.3 Impact of BMI Status on Time Function Tests

To explore the impact of BMI status on timed function tests, the following milestones were analysed: time to a 10m walk/run completed in 7-10 seconds; 10m walk/run completed in >10 seconds; four stair climb completed in >8 seconds and; supine-to-stand completed in >7 seconds.

BMI status at the first available measure:

See Table 18 for descriptive data for timed function tests across BMI status categories at the first available measure of BMI. In both unadjusted analyses and adjusted analyses for enrolment in a drug trial, there were no differences across BMI status at the first available measure for time to time function test milestones (Figure 19, Supplementary Table 10).

Table 18

Description of Timed Function Tests Across BMI Status at the First Available Measure of BMI (N=158)

	10m walk/run completed in 7-10 seconds [1]		**10m walk/run completed in >10 seconds [2]**		**Four stair climb completed in >8 seconds [3]**		**Supine-to-stand >7 seconds [4]**	
	n (N%)	**Median time to event (95% CI) [5]**	**n (N%)**	**Median time to event (95% CI)**	**n (N%)**	**Time event (95% CI)**	**n (N%)**	**Median time to event (95% CI)**
No overweight or obesity	25 (44.6)	10.6 (9.1-12.2)	14 (40.0)	13.6 (11.3-16.0)	21 (46.6)	12.0 (10.2-13.7)	24 (42.1)	10.0 (8.9-11.2)
Overweight	20 (35.7)	10.6 (9.7-11.5)	11 (31.4)	11.8 (11.4-12.2)	16 (35.6)	11.3 (11.0-11.6)	21 (36.8)	10.2 (9.1-11.4)
Obese	11 (19.6)	10.8 (10.1-11.6)	10 (28.6)	12.4 (9.1-15.8)	8 (17.8)	11.0 (9.8-12.1)	12 (21.1)	10.5 (9.3-11.8)
Total	56 (100)	10.6 (10.1-11.2)	35 (100)	12.0 (10.6-14.5)	45 (100)	11.3 (10.4-12.1)	57 (100)	10.4 (9.7-11.0)

[1] *10m walk/run in 7-10 seconds*: Event n=56, censored n=35, missing n=66. Time to event log rank p-value=0.560.
[2] *10m walk/run in >10 seconds*: Event n=35, censored n=48, missing n=75. Time to event log rank p-value=0.915.
[3] *Four stair climb in >8 seconds:* Event n= 45, censored n=42, missing n=50. Time to event log rank p-value=0.876.
[4] *Supine-to-stand in >7 seconds:* Event n=57, censored n=34, missing n=67. Time to event log rank p-value=0.639

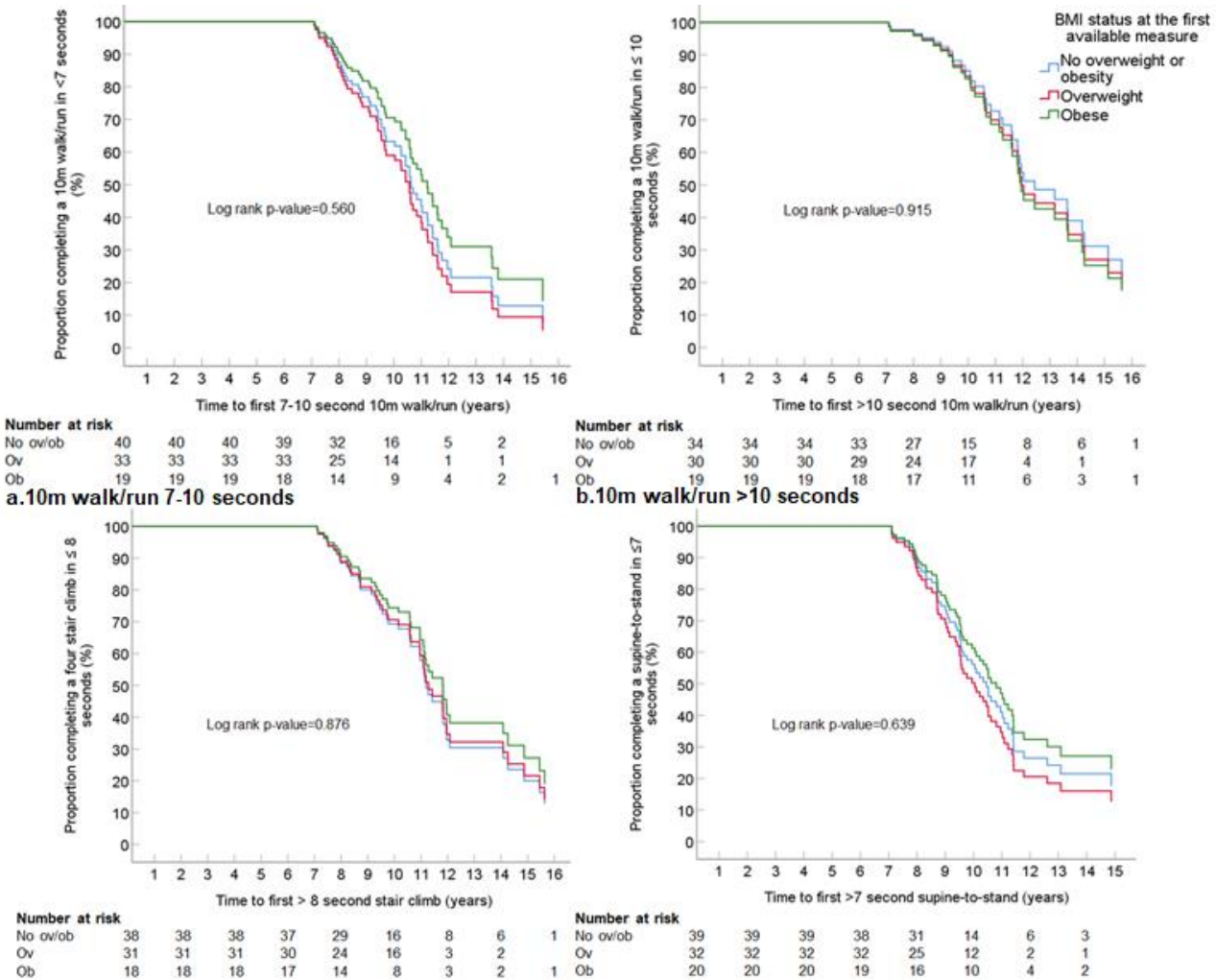
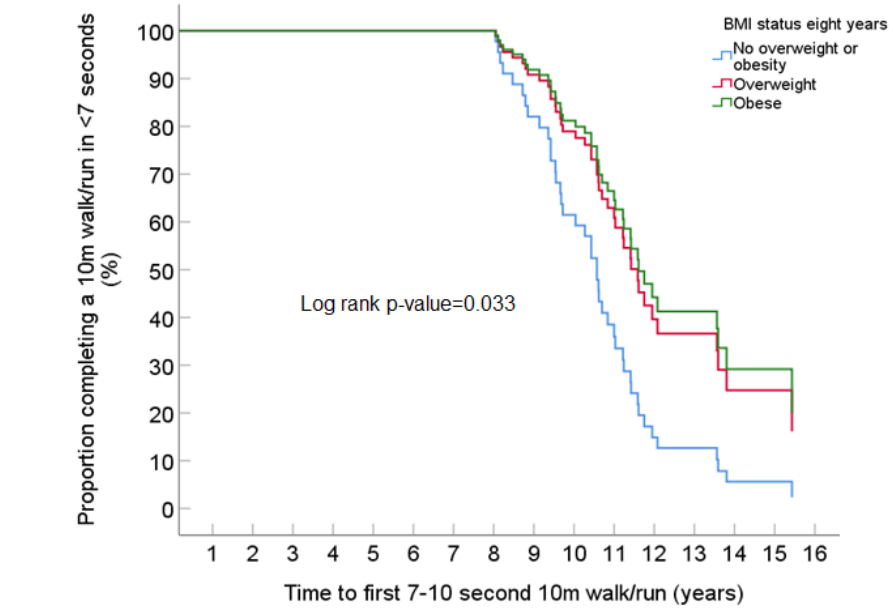


Figure 19a-d

Kaplan-Meier Curves for Time Function Tests Stratified by BMI Status at The First Available Measure

BMI status at ages five to nine:

For the 10m walk/run, boys with obesity at eight years were older when they reached the milestone of completing the assessment in 7-10 seconds compared to those with no overweight or obesity (HR 0.428 95% CI 0.207-0.887), this remained significant when adjusting for enrolment in a drug trial (see Figure 20 for the unadjusted analysis). The median time to first 10m walk/run completed in 7-10 seconds was 11.8 years (95% CI 10.9-12.6) for obesity, 12.0 years (95% CI 10.2-13.7) for overweight and 10.6 (95% CI 10.3-10.9) for those with no overweight or obesity at eight years (log rank p-value=0.033). BMI status at five, six, seven and nine years did not predict time to a 10m walk/run completed in 7-10 seconds in either unadjusted analysis or adjusted for enrolment in a drug trial (Table 19). BMI status at five to nine years did not impact time to a 10m walk/run completed in >10 seconds, a four stair climb completed in >8 seconds or a supine-to-stand completed in >7 seconds (Supplementary Table 11, Supplementary Table 12 and Supplementary Table 13).



Number at risk									
No ov/ob	23	23	23	23	23	15	4	1	
Ov	20	20	20	20	19	10	2	2	
Ob	27	27	27	27	24	12	4	2	1

Figure 20

Kaplan-Meier Curve for Time to a 10m Walk/Run Completed In 7-10 Seconds Stratified by BMI Status at Eight Years

Table 19

BMI Status at Ages Five to Nine Years as a Predictor of Time to a 10m Walk/Run Completed in 7-10 Seconds Using a Cox Proportional Hazards Model [1]

Age at BMI measure	BMI status [2]	Hazard Ratio	95% CI lower	95% CI upper	P-value
Five years	*Overweight*	0.935	0.447	1.954	0.857
	Obese	0.440	0.100	1.941	0.278
Six years	*Overweight*	0.913	0.405	2.058	0.826
	Obese	0.729	0.304	1.749	0.479
Seven years	*Overweight*	0.997	0.505	1.967	0.993
	Obese	0.702	0.330	1.493	0.359
Eight years	*Overweight*	0.486	0.220	1.075	0.075
	Obese	0.428	0.207	0.887	**0.023**
Nine years	*Overweight*	0.622	0.249	1.553	0.309
	Obese	0.585	0.275	1.241	0.162

[1] *Five years*: event n=31, censored n=28, missing n=98, censored cases before the earliest event in a stratum n=1. *Six years*: event n=34, censored n=32, missing n=92. *Seven years*: event n=45, censored n=33, missing n=80. *Eight years*: event n=42, censored n=28, missing n=88, excluded 10m walk/run completed in 7-10 seconds occurred prior to eight years n=11. *Nine years*: event n=35, censored n=21, missing n=102, excluded 10m walk/run completed in 7-10 seconds occurred prior to nine years n=20

[2] Reference category if no overweight or obesity

Box 5

Summary of Findings for the Impact of BMI Status on Time Function Tests

Those with obesity at eight years had a later time to completing a slower 7-10 second 10m walk/run compared to those without overweight or obesity. There was no impact of BMI status at other ages on time to completing a 10m walk/run in 7-10 seconds. BMI status at five to nine years did not impact time to a 10m walk/run completed in >10 seconds a four stair climb completed in >8 seconds or a supine-to-stand completed in >7 seconds.

2.5.4 Impact of BMI on Time to a NSAA Score ⩽ 9

BMI status at the first available measure:

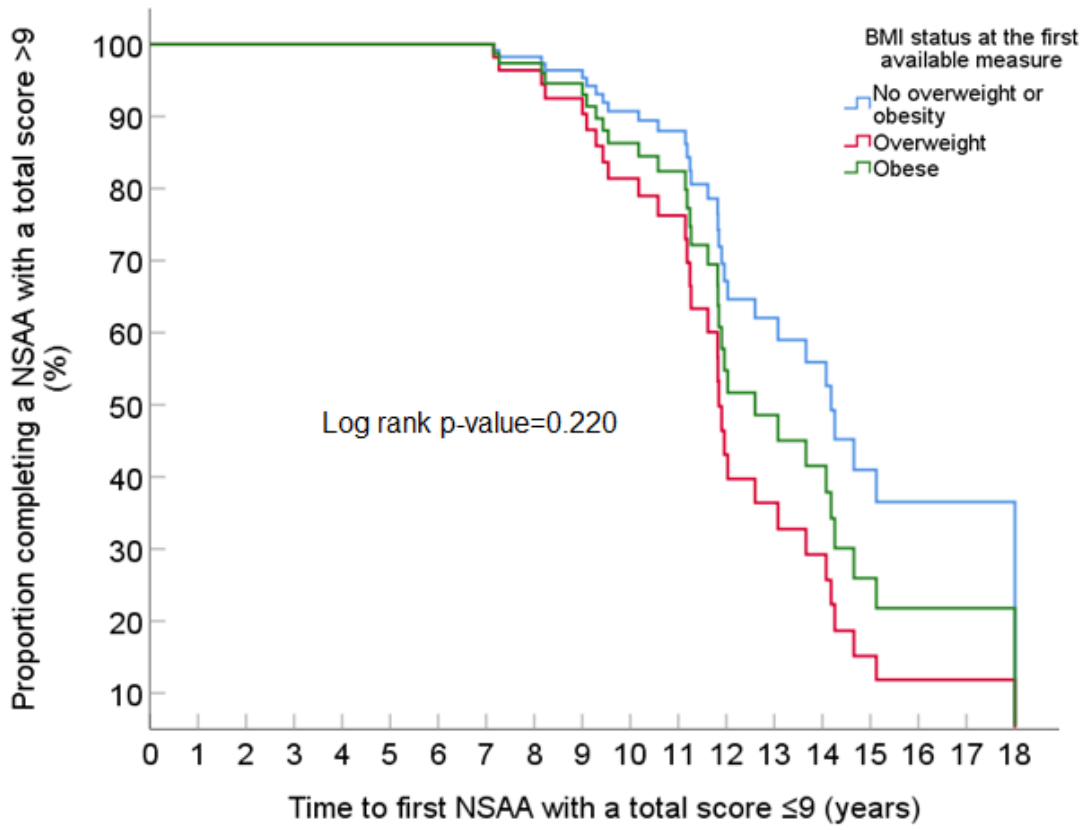
Across patients, 31 (19.6%) recorded a NSAA total score of ≤9 (event), for 44 (27.8%) all scores were >9 (censored) and 83 (52.5%) were excluded due to missing data (Table 20). BMI status at the first available measure did not impact time to a NSAA total score of ≤9 (Figure 21, Table 21).

Table 20

Description of a NSAA Score ⩽ 9 Across BMI Status at First Available Measure of BMI (N=158) [1]

	NSAA ≤ 9, n (N%)	**Median time to NSAA ≤ 9 (95% CI)** [2]
Healthy weight	10 (32.3)	14.3 (12.6-15.9)
Overweight	13 (41.9)	11.9 (10.8-12.9)
Obesity	8 (25.8)	11.9 (9.5-14.3)
Total	31 (100)	12.6 (10.5-14.7)

[1] Event n=31, censored n=46, missing n=81
[2] Time to NSAA ≤ 9 log rank p-value=0.220



Number at risk

No ov/ob	30	30	30	29	24	15	9	7	2	1
Ov	30	30	30	29	24	15	5	2		
Ob	17	17	17	16	15	10	5	3	1	

Figure 21

Kaplan-Meier Curve for Time to a NSAA Score ⩽ 9 Stratified by BMI Status at the First Available Measure

Table 21

BMI Status at the First Available Measure as a Predictor of a NSAA Score ⩽ 9 Using a Cox Proportional Hazards Model [1]

BMI status	Hazard Ratio	95% CI lower	95% CI upper	P-value
Overweight	2.116	0.896	4.996	0.087
Obesity	1.512	0.583	3.925	0.395

[1] Event n=31, censored n=45, missing n=81, censored cases before the earliest event in a stratum n=1

BMI status at ages five to nine:

At ages five to nine years, BMI status did not predict time to a NSAA total score of ≤ 9 (Supplementary Table 14).

Box 6

Summary of Findings for the Impact of BMI Status on Time to a NSAA ⩽ 9:

There was no impact of BMI status at the first available measure or at ages five to nine on time to completing a NSAA with a low total score of ≤ 9.

2.5.5 Impact of BMI on Time to Reaching < 325m 6MWD

Impact of BMI at the first available measure:

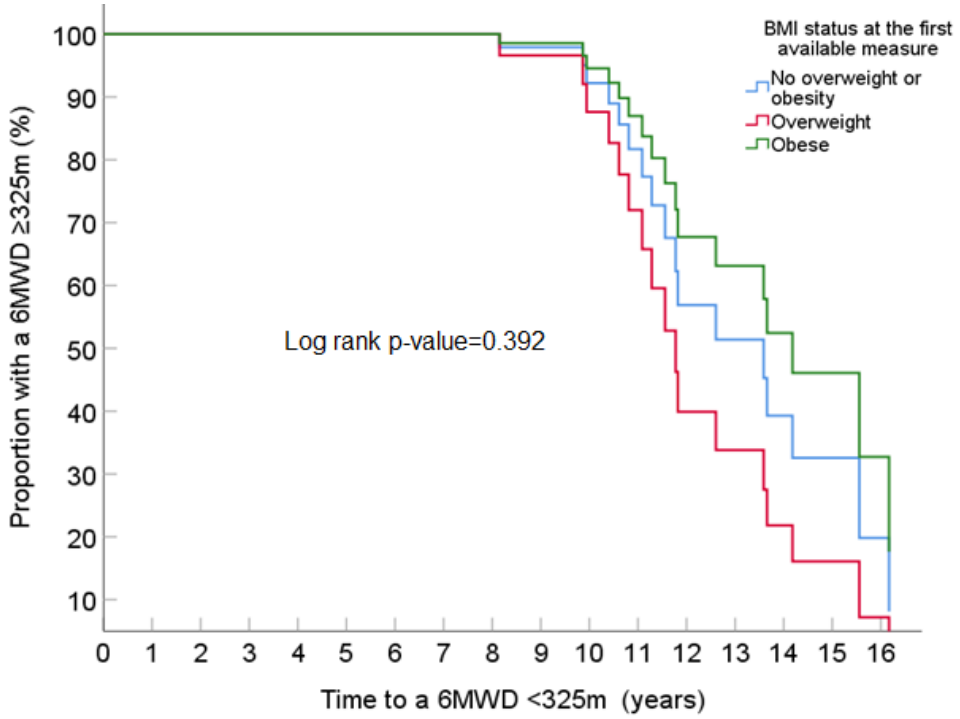
During the follow-up period, 17 (10.8%) young people had a recorded 6MWD <325m (event), for 27 (17.1%) all recorded 6MWD were ≥325m (censored) and 114 (72.2%) were excluded due to missing data (Table 22). BMI status at the first available measure did not impact time to a 6MWD <325m (Figure 22, Table 23).

Table 22

Description of a 6MWD <325m Across BMI Status at First Available Measure of BMI (N=158) [1]

	Recorded 6MWD < 325m, n (N%)	**Time to first recorded 6MWD < 325m (95% CI)** [2]
Healthy weight	6 (35.3)	13.6 (8.6-18.5)
Overweight	6 (35.3)	11.8 (11.0-12.6)
Obesity	5 (29.4)	14.2 (13.1-15.3)
Total	17 (100)	13.6 (10.0-17.1)

[1] Censored n=27, missing n=114
[2] Log rank p-value=0.392



Number at risk

No ov/ob	14	14	14	14	13	9	4	2	1
Ov	19	19	19	18	14	8	2	1	
Ob	11	11	11	11	11	8	5	3	1

Figure 22

Kaplan-Meier Curve for Time To a 6MWD <325m Stratified by BMI Status at The First Available Measure

Table 23

BMI Status at Earliest Measure as a Predictor of a 6MWD < 325m Using a Cox Proportional Hazards Model [1]

BMI status	**Hazard Ratio**	**95% CI lower**	**95% CI upper**	**P-value**
Overweight	1.628	0.498	5.324	0.420
Obesity	0.691	0.209	2.279	0.543

[1] Censored n=24, missing n=114, cesnored cases before the earliest event in a stratum n=3
Reference category is no overweight or obesity

BMI status at ages five to nine:

For ages five to nine years, BMI status did not predict time to a 6MWD of <325m (Supplementary Table 15).

Box 7

Summary of Findings for the Impact of BMI Status on Time to a 6MWD <325m

There was no statistically significant impact of BMI status at the first available measure or at ages five to nine on time to a 6MWD of <325m. .

2.5.6 Impact of BMI Status on Time to First Fracture

BMI status at the first available measure:

Across the sample there were 68 (43.0%) young people with DMD who sustained a fracture during follow-up period (Table 24), of these 57 (80.3%) initially sustained a crush fracture and 14 (19.7%) other bone fractures (e.g. femoral, foot). Of the remaining patients 81 (51.3%) did not have a fracture during the follow-up period (censored) and nine (5.7%) were excluded due to missing data. There were 19 boys who received zoledronic acid prophylactically.

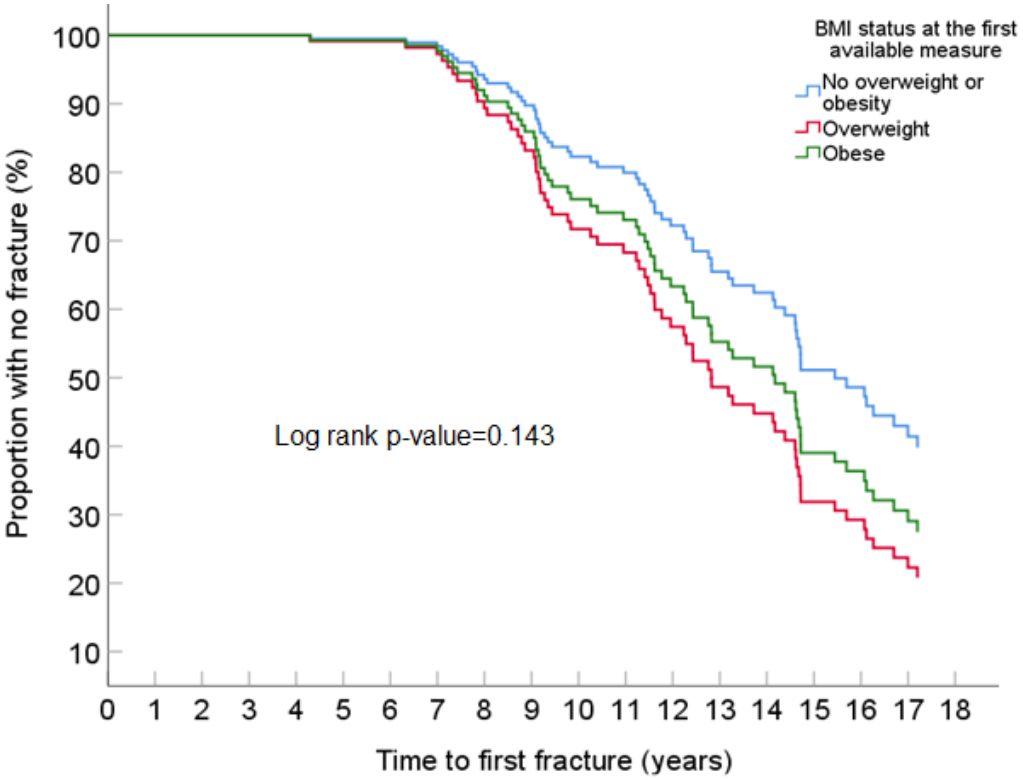
Table 24

Description of A Fracture Across BMI Status at First Available Measure of BMI (n=158) [1]

	Fracture, n (N%)	**Median time to first fracture (95% CI)** [2]
No overweight or obesity	28 (41.2)	16.1 (13.7-18.4)
Overweight	26 (38.2)	12.8 (11.5-14.1)
Obesity	14 (20.6)	12.4 (8.7-16.1)
Total	68 (100)	14.6 (13.3-16.0)

[1] Censored n=81, missing n=6, excluded BMI not measured prior to fracture n=3
[2] Log rank p-value=0.143

There were no differences across BMI status categories at the first available BMI measure for time to first fracture, in unadjusted analysis and adjusted for zoledronic acid treatment (Figure 23, Table 25).



Number at risk

No ov/ob	67	67	65	61	52	40	31	27	18	6
Ov	49	49	49	45	36	26	18	10	5	2
Ob	33	33	32	28	22	15	11	8	5	2

Figure 23

Kaplan-Meier Curve Time to First Fracture Stratified by BMI Status at the First Available Measure

Table 25

BMI Status at Earliest Measure as a Predictor of First Fracture Using a Cox Proportional Hazards Model [1]

BMI status	**Hazard Ratio**	**95% CI lower**	**95% CI upper**	**P-value**
Overweight	1.704	0.993	2.923	0.053
Obesity	1.402	0.737	2.669	0.303

[1] Censored n=80, missing n=6, censored cases before the earliest event in a stratum n=1, excluded BMI not measured prior to fracture n=3
Reference category is no overweight or obesity

Impact of BMI status at different ages:

In the unadjusted analysis, obesity at age six did not significantly impact time to first fracture (Table 26). However, when adjusting for zoledronic acid treatment those with obesity at 6 years were 2.3 times as likely to sustain a fracture earlier compared to those without overweight or obesity (HR 2.327 95% CI 1.055-5.134), see Figure 24. There were no significant differences across BMI status categories at five, seven or eight years for time to first fracture in both unadjusted analyses and adjusted for zoledronic acid treatment.

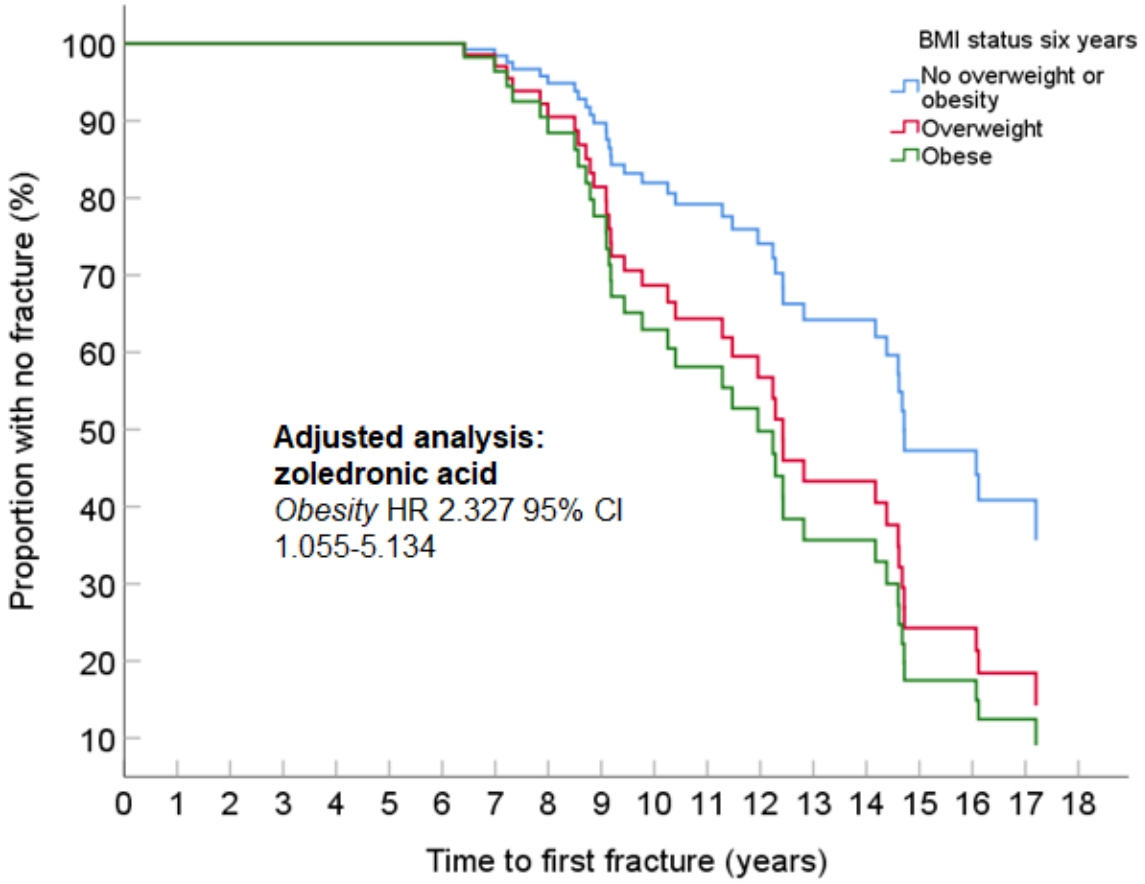
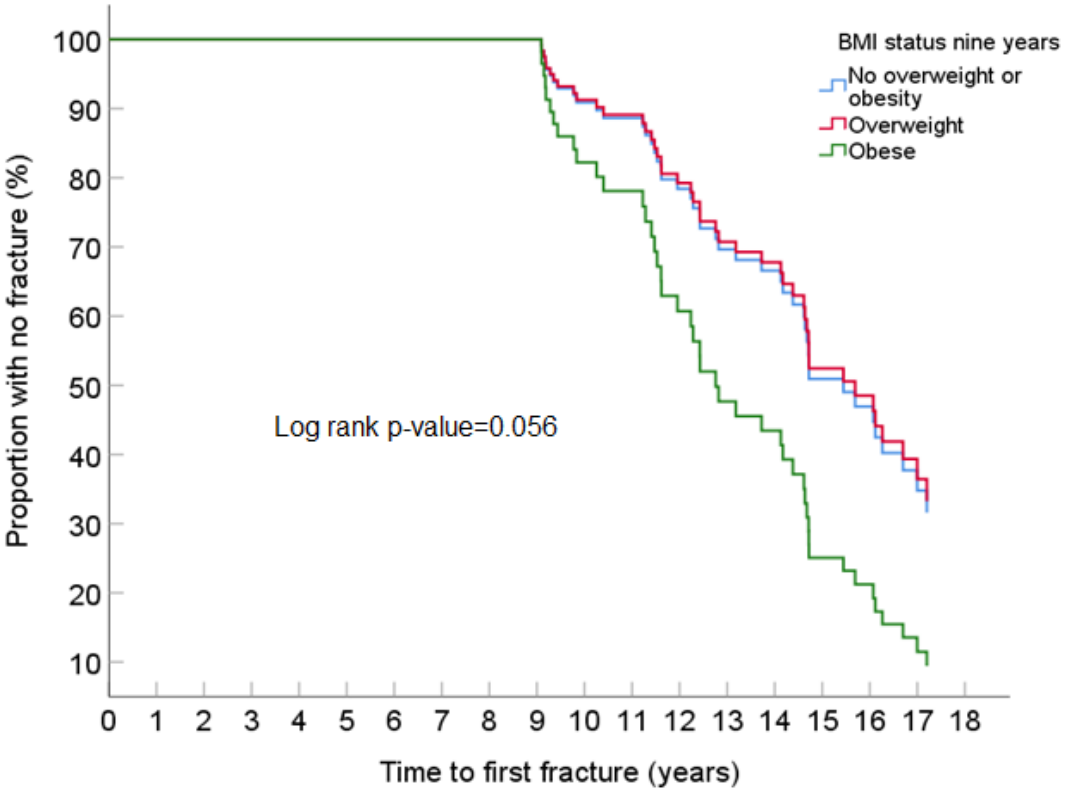


Figure 24

Kaplan-Meier Curve Time to First Fracture Stratified by BMI Status at Age Six Years Adjusted for Zoledronic Acid Treatment

Those with obesity at nine years sustained a fracture earlier compared to those without overweight or obesity; median time to first fracture no overweight or obesity 16.1 years (95% CI 13.9-18.3), overweight 14.7 years (95% CI 14.1-15.4) and obesity 12.3 years (95% CI 11.3-13.3), see Figure 25. This remained significant when adjusting for zoledronic acid treatment (obesity HR 2.191 95% CI 1.094-4.387) and when only including those who sustained a crush fracture (obesity HR 2.106 95% CI 1.009-4.394, adjusted for zoledronic acid treatment).



Number at risk

No ov/ob	29	29	29	29	29	26	20	15	11	3
Ov	19	19	19	19	19	18	14	10	4	1
Ob	34	34	34	34	31	17	11	8	2	

Figure 25

Kaplan-Meier Curve Time to First Fracture Stratified by BMI Status at Age Nine Years

Table 26

BMI Status at Ages Five to Nine Years of as a Predictor of First Fracture Using a Cox Proportional Hazards Model (Unadjusted) [1]

Age at BMI measure	BMI status [2]	Hazard Ratio	95% CI lower	95% CI upper	P-value
Five years	*Overweight*	0.523	0.241	1.135	0.101
	Obesity	2.197	0.970	4.975	0.059
Six years	*Overweight*	2.022	0.930	4.396	0.076
	Obesity	2.082	0.970	4.470	0.060
Seven years	*Overweight*	1.256	0.622	2.539	0.525
	Obesity	1.776	0.875	3.605	0.112
Eight years	*Overweight*	1.404	0.676	2.915	0.363
	Obesity	1.862	0.927	3.739	0.081
Nine years	*Overweight*	0.957	0.437	2.096	0.912
	Obesity	2.050	1.038	4.046	**0.039***

[1] *Five years*: event n=37, censored n=36, missing n=79, censored cases before the earliest event in a stratum n=4, excluded first fracture before five years n=2. *Six years*: event n=40 censored n=44, missing n=71, censored cases before the earliest event in a stratum n=1, excluded first fracture before six years n=2. *Seven years*: event n=47, censored n=46, missing n=60, excluded first fracture before seven years n=5. *Eight years*: event n=47, censored n=39, missing n=58, excluded first fracture before seven years n=13. *Nine years*: event n=45, censored n=37, missing n=57, excluded first fracture prior to nine years n=19

[2] Reference category is no overweight or obesity

Box 8

Summary of Findings for the Impact of BMI Status on Time to First Fracture

When adjusting for zoledronic acid treatment, boys with obesity at six years were over twice as likely to sustain a fracture earlier compared to their peers without overweight or obesity. Having obesity at nine years increased the likelihood of sustaining a fracture earlier. In these boys with obesity at nine years, the first fracture occurred approximately four years earlier than those without overweight or obesity. There were no significant differences for time to first fracture across BMI status categories at five, seven and eight years.

2.5.7 Impact of BMI Status on Time to Scoliosis Diagnosis

BMI at the first available measure:

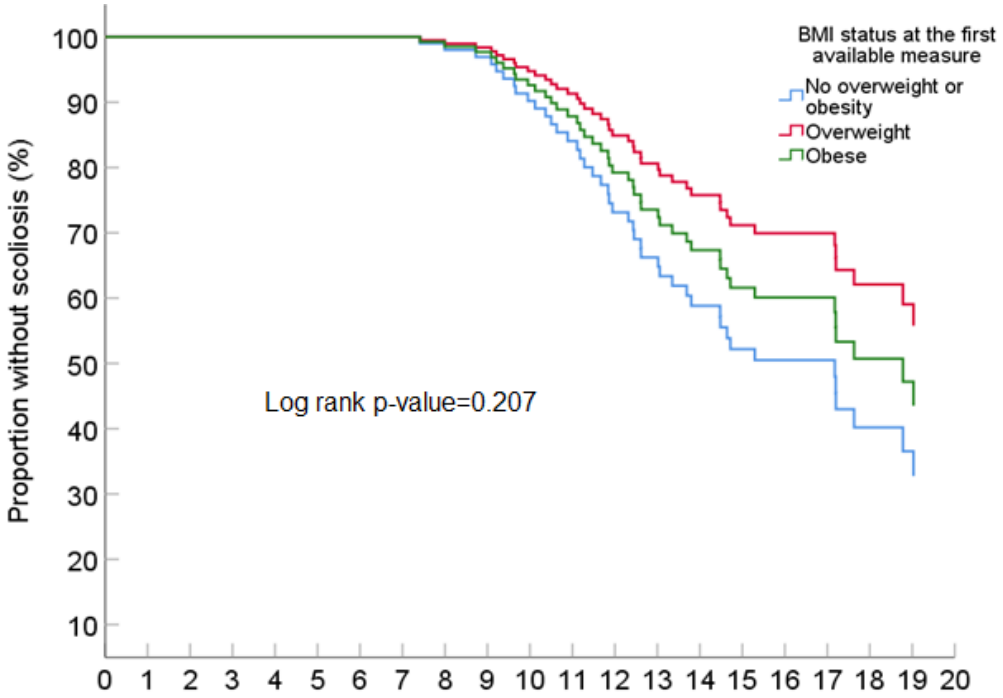
There were 48 (27.2%) patients who developed scoliosis (event), 106 (67.1%) who did not develop scoliosis (censored) and data was missing for nine (5.7%) patients (Table 27). In both models unadjusted and adjusted for ambulatory status there was no difference across BMI status categories for time to scoliosis diagnosis (unadjusted analysis see Figure 26 and Table 28).

Table 27

Description of Scoliosis Across BMI Status at First Available Measure of BMI (n=158) [1]

	Scoliosis diagnosis, n (N%)	**Median time to scoliosis diagnosis (95% CI)**
No overweight or obesity	25 (58.1)	17.2 (13.9-20.5)
Overweight	10 (23.3)	-
Obese	8 (18.6)	-
Total	43 (100)	17.6 (15.9-19.3)

[1] Censored n=106, missing n=4, excluded BMI not measured prior to scoliosis diagnosis n=5
Scoliosis diagnosis did not reach 50% for the overweight and obese categories, median time to data (time to scoliosis diagnosis for 50% of the population) is therefore not available



Number at risk											
No ov/ob	67	67	65	61	55	42	30	20	12	5	1
Ov	47	47	47	44	37	29	20	14	11	7	1
Ob	35	35	34	29	23	19	13	8	4	1	1

Figure 26

Kaplan-Meier Curve Time to Scoliosis Stratified by BMI Status at the First Available Measure

Table 28

BMI Status at The First Available Measure as a Predictor of Scoliosis Diagnosis Using a Cox Proportional Hazards Model [1]

BMI status	**Hazard Ratio**	**95% CI lower**	**95% CI upper**	**P-value**
Overweight	0.523	0.251	1.092	0.084
Obesity	0.745	0.336	1.654	0.470

[1] Event n=43, censored n=85, missing n=4, censored cases before the earliest event in a stratum n=21, excluded BMI not measured prior to fracture n=5
Reference category of no overweight or obesity

BMI status at ages five to nine years

BMI status at five to nine years not significantly impact time to scoliosis diagnoses (Supplementary Table 16).

Box 9

Summary of Findings for the Impact of BMI Status on Time to Scoliosis Diagnosis

There was no impact of BMI status at the first available measure or at ages five to nine on time to scoliosis diagnosis.

2.5.8 Impact of BMI Status on Time to Diagnosis of OSA

BMI status at the first available measure:

In this cohort, 69 (43.7%) boys were diagnosed with OSA (event), 82 (51.9%) did not have OSA (censored) and seven (4.4%) were excluded or had missing data (Table 29). BMI at the first available measure did not impact time to OSA diagnosis (Figure 27, Table 30).

Table 29

Description of OSA Diagnosis Across BMI Status at First Available Measure of BMI (n=158) [1]

	OSA diagnosis (event), n (N%)	**Median time to OSA diagnosis (95% CI)** [2]
No overweight or obesity	31 (44.9)	15.3 (14.5-16.1)
Overweight	23 (33.3)	14.9 (14.0-15.9)
Obesity	15 (21.7)	14.1 (12.1-16.2)
Overall	69 (100)	15.0 (14.2-15.8)

[1] Censored n=82, missing n=6, excluded BMI not measured prior to OSA diagnosis n=1
[2] Log rank p-value=0.172

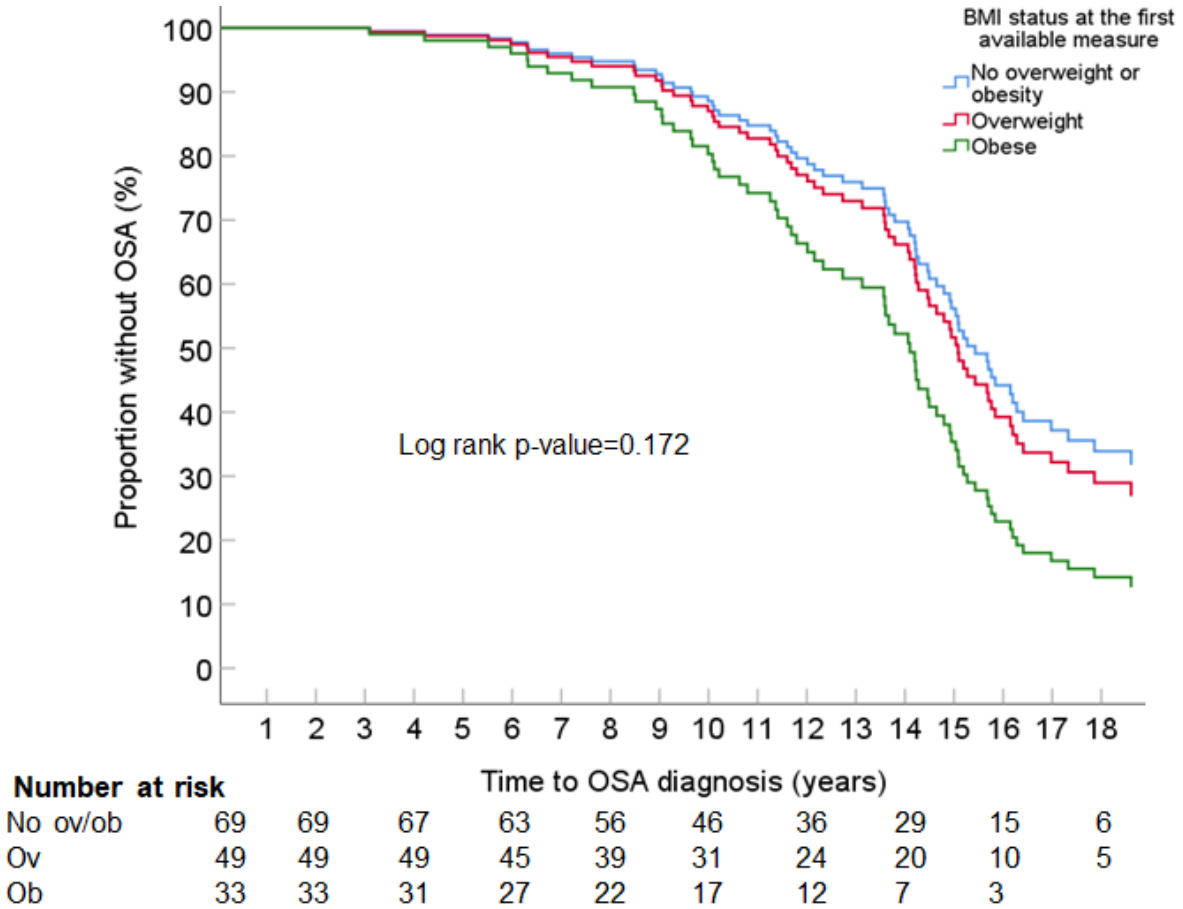


Figure 27

Kaplan-Meier Curve Time to OSA Stratified by BMI Status at the First Available Measure

Table 30

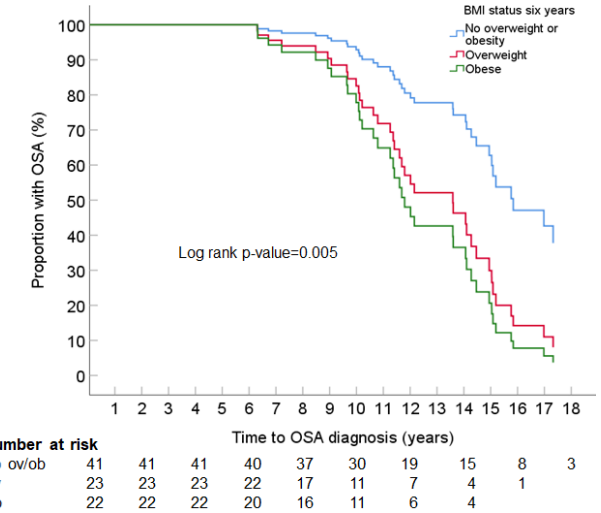
BMI Status at The First Available Measure as a Predictor of Diagnosis of OSA Using a Cox Proportional Hazards Model [1]

BMI status	**Hazard Ratio**	**95% CI lower**	**95% CI upper**	**P-value**
Overweight	1.145	0.667	1.965	0.622
Obesity	1.803	0.964	3.374	0.065

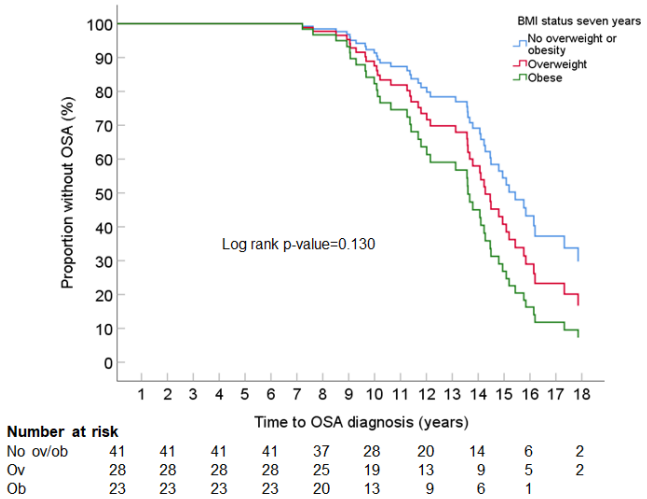
[1] Censored n=82, missing n=6, excluded BMI not measured prior to OSA diagnosis n=1
Reference category is no overweight or obesity

BMI status at ages five to nine years:

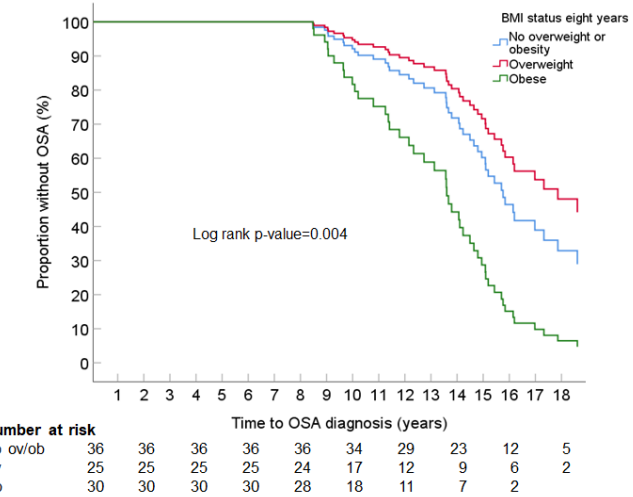
Those with obesity at six to nine years, were 2.2 to 3.4 times more likely to be diagnosed with OSA at any time point compared to those without overweight or obesity (Figure 28, Table 31). Median time to OSA diagnosis was significantly earlier for those with obesity at six years (13.6 years 95% CI 10.6-16.6) compared to no overweight or obesity (15.8 years 95% CI 13.7-18.0), overall log-rank p-value=0.005. Boys with obesity at both eight and nine years were predicted to be diagnosed with OSA approximately two years earlier than those without overweight or obesity. Median time to OSA diagnosis for no overweight or obesity at eight years was 15.8 years 95% CI 15.0-16.6 vs. obesity 13.6 years 95% CI 10.8-16.4, log rank p-value=0.004. Median time to OSA diagnosis for no overweight or obesity at nine years was 15.3 years 95% CI 14.3-16.2 vs. obesity 13.6 years 95% CI 10.8-16.4, log rank p-value<0.001. The Cox proportional hazards model indicated higher likelihood of earlier diagnosis of OSA for those with obesity at age seven, however the overall distribution across BMI status categories was not significantly different (log rank p-value=0.130).



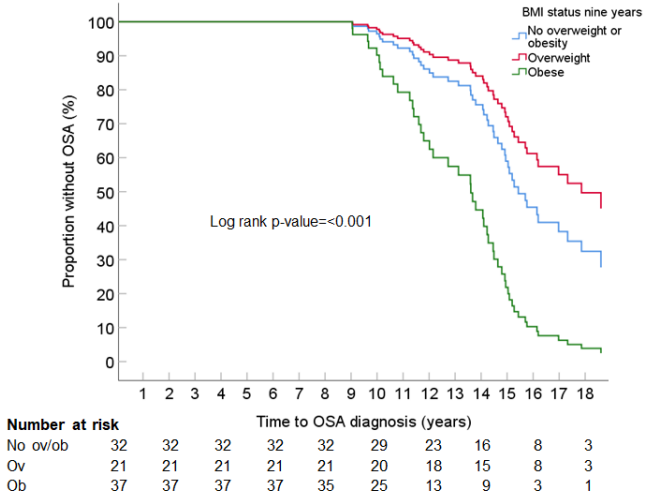
a.Six years (log rank p-value=0.005)



b.Seven years (log rank p-value=0.130)



c.Eight years (log rank p-value=0.004)



d.Nine years (log rank -value=<0.001)

Figure 28a-d

Kaplan-Meier Curves for Time to OSA Stratified by BMI Status at Six to Nine Years

Table 31

BMI Status at Ages Five to Nine Years as a Predictor of OSA Using a Cox Proportional Hazards Model [1]

Age at BMI measure	BMI status [2]	Hazard Ratio	95% CI lower	95% CI upper	P-value
Five years	*Overweight*	1.212	0.585	2.510	0.605
	Obese	1.257	0.444	3.561	0.667
Six years	*Overweight*	2.590	1.175	5.711	**0.018**
	Obese	3.389	1.469	7.815	**0.004**
Seven years	*Overweight*	1.476	0.737	2.955	0.272
	Obese	2.163	1.004	4.660	**0.049**
Eight years	*Overweight*	0.659	0.281	1.546	0.338
	Obese	2.461	1.245	4.863	**0.010**
Nine years	*Overweight*	0.621	0.274	1.411	0.255
	Obese	2.883	1.481	5.612	**0.002**

[1] *Five years*: event n=35, censored n=41, missing n=78, censored cases before the earliest event in a stratum n=1, excluded OSA diagnosis before five years n=3 *Six years*: event n=37, censored n=49, missing n=67, excluded OSA diagnosis before six years n=5. *Seven years*: event n=44, censored n=48, missing n=58, excluded OSA diagnosis before seven years n=8. *Eight years*: event n=45, censored n=46, missing n=57, excluded OSA diagnosis before eight years n=10. *Nine years*: event n=47, censored n=43, missing n=55, excluded OSA diagnosis prior to nine years n=13

[2] Reference category is no overweight or obesity

Box 10

Summary of Findings for The Impact of BMI Status on Time to OSA Diagnosis

Those with obesity at six through to nine years were between two and three times more likely to be diagnosed with OSA at any time point compared to those without overweight or obesity. From age seven through to nine years, the median time to OSA diagnosis was approximately 1.5-2 years earlier for those with obesity compared to those without overweight or obesity.

2.5.9 Impact of BMI Status on Time to CPAP Initiation

BMI status at the first available measure:

In this sample, CPAP was initiated for 26 (16.5%) patients (event), 128 patients (81.0%) did not require CPAP and four patients (2.5%) had missing BMI data and were excluded (Table 32).

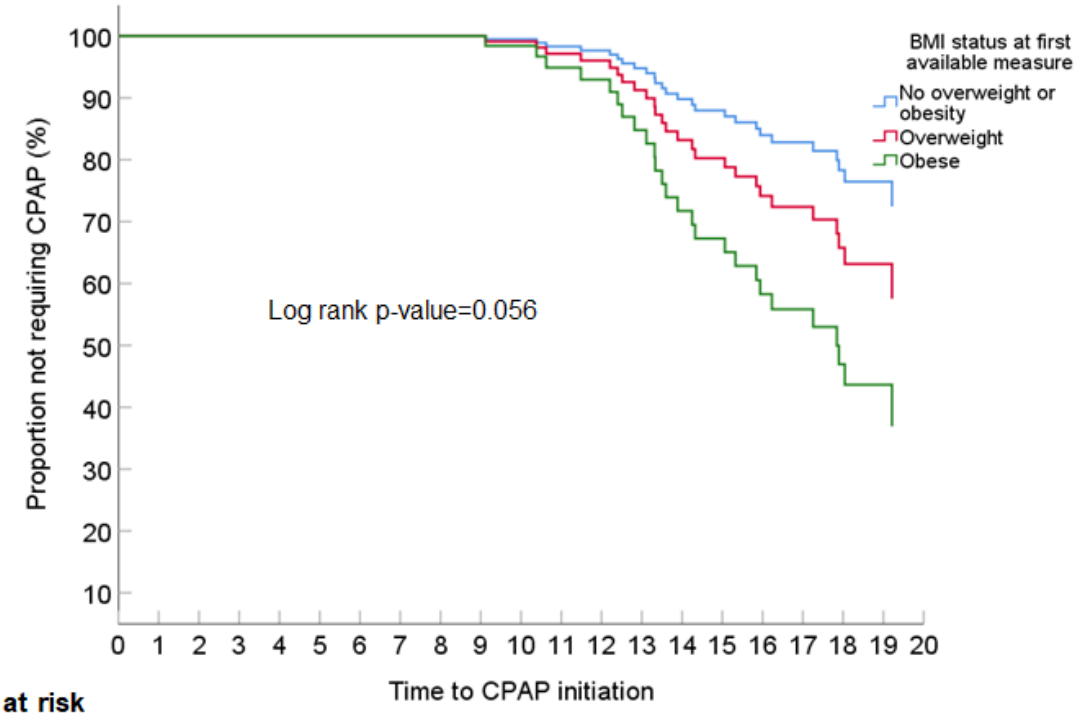
Table 32

Description of CPAP Initiation Diagnosis Across BMI Status at First Available Measure of BMI (n=158) [1]

	CPAP initiation (event), n (N%)	**Median (95%CI) time to CPAP initiation** [2]
No overweight or obesity	9 (34.6)	-
Overweight	9 (34.6)	-
Obese	8 (30.8)	17.9 (14.9-20.9)
Total	26 (100)	-

[1] Censored n=93, missing n=4, censored cases before the earliest event in a stratum n=35
[2] Probability of CPAP did not reach 50% for the no overweight and obesity and overweight categories, median time to data (time to CPAP initation for 50% of the population) is therefore not available

Distributions across BMI status categories for time to CPAP initiation were not significantly different (log rank p-value=0.056), see Figure 29. However, when using the Cox proportional hazards model, compared to those without overweight or obesity, boys with obesity at the first available BMI measure were over three times as likely to commence CPAP at any time point (Table 33).



Number at risk											
No ov/ob	70	70	68	64	58	50	44	33	26	14	2
Ov	49	49	49	46	39	32	24	20	15	7	1
Ob	35	35	34	29	24	20	16	9	6	3	1

Figure 29

Kaplan-Meier Curve Time to CPAP Initiation Stratified by BMI Status at the Earliest Measure

Table 33

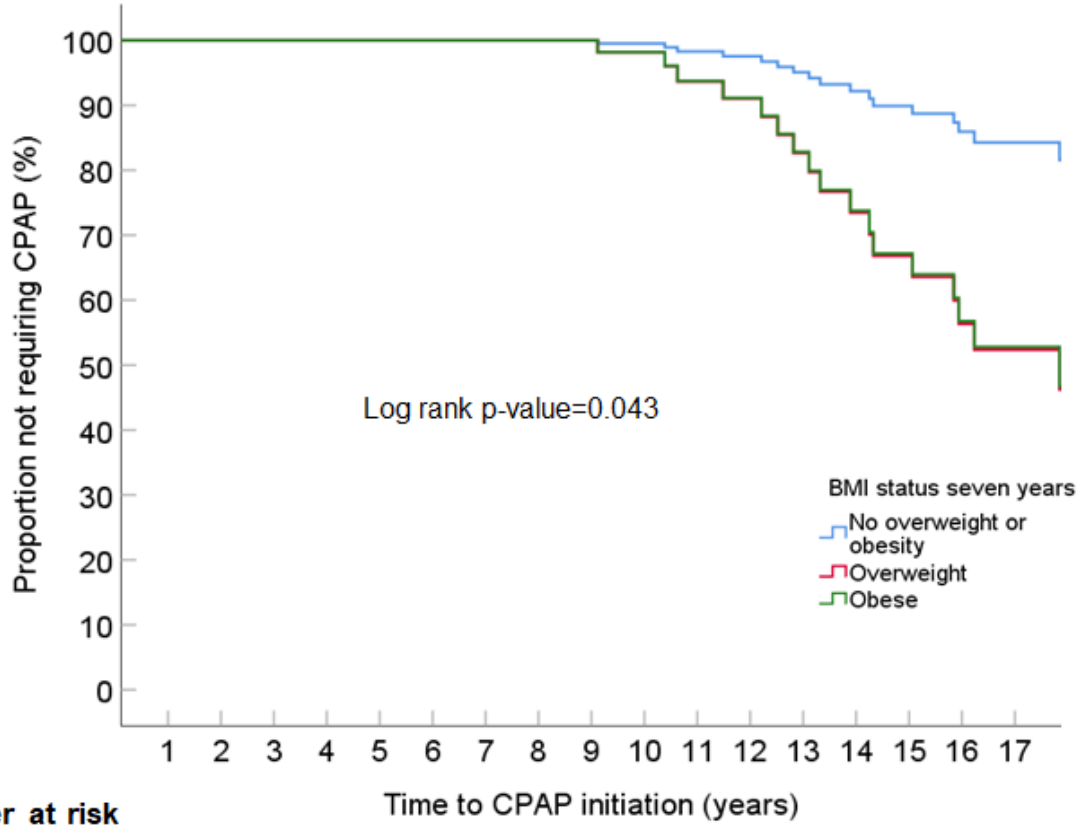
BMI Status at Earliest Measure as a Predictor of Time to Commencement of CPAP Using a Cox Proportional Hazards Model [1]

BMI status	Hazard Ratio	95% CI lower	95% CI upper	P-value
Overweight	1.715	0.680	4.322	0.253
Obesity	3.094	1.187	8.062	**0.021***

[1] Censored n=93, missing n=4, censored cases before the earliest event in a stratum n=35
Reference category is no overweight or obesity

BMI status at five to nine years:

Boys with obesity at seven years were more likely to commence CPAP earlier compared to those without overweight or obesity (Figure 30). There was no significant difference in time to CPAP initiation for six, eight and nine years (Table 34). For all BMI categories, the probability of CPAP initiation did not reach 50% and therefore median time-to-event data is not available.



Number at risk										
No ov/ob	42	42	42	42	39	32	27	19	12	5
Ov	29	29	29	29	26	19	13	9	6	2
Ob	26	26	26	25	21	15	10	7	4	1

Figure 30

Kaplan-Meier Curve Time to CPAP Initiation Stratified by BMI Status at Seven Years

Table 34

BMI Status at Ages Five to Nine Years as a Predictor of CPAP Initiation Using a Cox Proportional Hazards Model [1]

Age at BMI measure	BMI status [2]	Hazard Ratio	95% CI lower	95% CI upper	P-value
Six years	*Overweight*	0.528	0.065	4.313	0.551
	Obesity	2.716	0.904	8.155	0.075
Seven years	*Overweight*	3.785	1.137	12.598	0.030
	Obesity	3.735	1.053	13.252	**0.041**
Eight years	*Overweight*	0.476	0.104	2.177	0.338
	Obesity	2.207	0.824	5.909	0.115
Nine years	*Overweight*	0.764	0.248	2.352	0.639
	Obesity	2.117	0.843	5.316	0.110

[1] *Five years*: not able to be performed as coefficients did not converge. *Six years*: event n=14, censored n=54, missing n=70, censored cases before the earliest event in a stratum=20. *Seven years*: event n=18, censored n=64, missing n=61, censored cases before the earliest event in a stratum n=15. *Eight years*: event n=19, censored n=70, missing n=61, censored cases before the earliest event in a stratum n=8. *Nine years*: event n=24, censored n=71, missing n=63

[2] Reference category is no overweight or obesity

Box 11

Summary of Findings for the Impact of BMI Status on Time to CPAP Initiation

Those with obesity at the first available BMI measure and at seven years were over three times as likely to be initiated with CPAP at any time point compared to those without overweight or obesity. At other ages there were no statistically significant differences across BMI status categories.

2.5.10 Impact of BMI Status on Time to Diagnosis of Nocturnal Hypoventilation

BMI status at the first available measure:

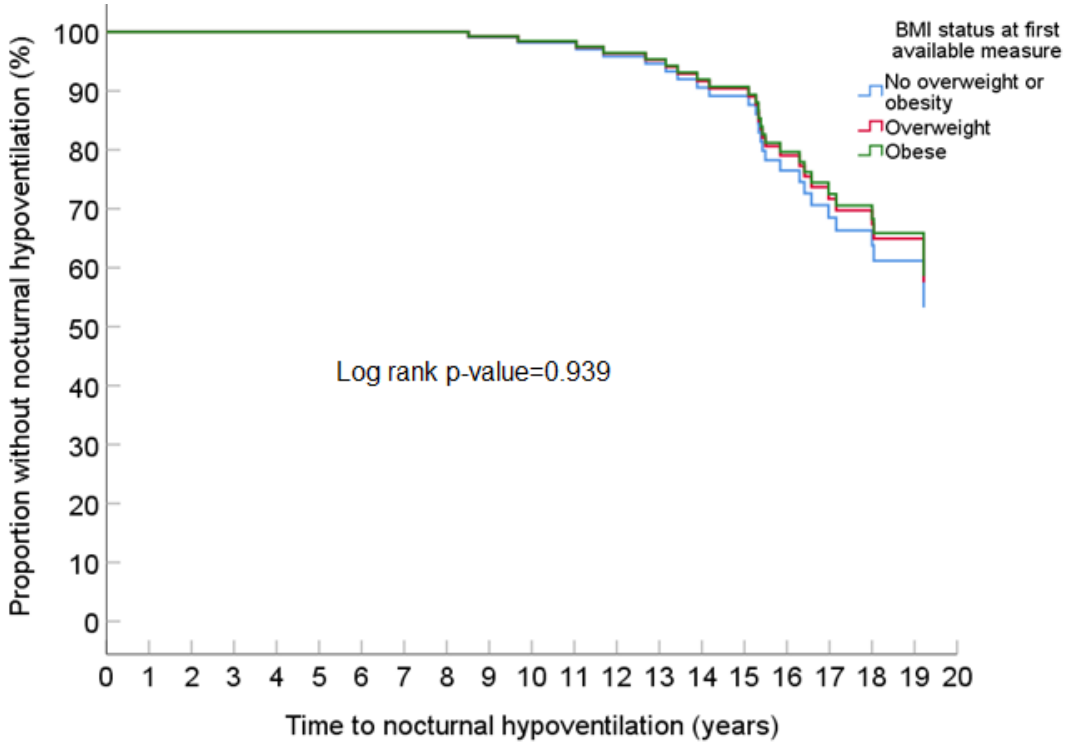
During the follow up period, 25 (15.8%) patients were diagnosed with nocturnal hypoventilation, 127 (80.4%) did not have a nocturnal hypoventilation and six (3.8%) were excluded due to missing data (Table 35). BMI status at the earliest measure did not impact time to nocturnal hypoventilation diagnosis (Table 36, Figure 31).

Table 35

Description of Nocturnal Hypoventilation Diagnosis Across BMI Status at First Available Measure of BMI (n=158) [1]

	Nocturnal hypoventilation diagnosis, n (N%)
No overweight or obesity	14 (56.0)
Overweight	7 (28.0)
Obese	4 (16.0)
Total	25 (100)

[1] Event n=25, censored n=127, missing n=6
Probability of nocturnal hypoventilation did not reach 50% for all groups, therefore median time to initiation is not available



Number at risk											
No ov/ob	69	69	67	63	57	49	42	34	20	9	1
Ov	48	48	48	45	38	29	23	18	13	6	1
Ob	35	35	34	29	24	20	14	10	6	3	1

Figure 31

Kaplan-Meier Curve Time to Nocturnal Hypoventilation Diagnosis Stratified by BMI Status at the First Available Measure

Table 36

BMI Status at Earliest Measure as a Predictor of Nocturnal Hypoventilation Diagnosis Using a Cox Proportional Hazards Model [1]

BMI status	Hazard Ratio	95% CI lower	95% CI upper	P-value
Overweight	0.878	0.353	2.186	0.780
Obesity	0.849	0.279	2.587	0.774

[1] Event n=25, censored n=127, missing n=6
Reference category is no overweight or obesity

BMI status at five to nine years:

Due to small a number of patients with nocturnal hypoventilation events for five to nine years (range n=7 to n=11), Cox proportional hazards model was not performed.

Box 12

Summary of Findings for the Impact of BMI Status on Time to Nocturnal Hypoventilation Diagnosis

BMI status at the first available measure did not impact time to nocturnal hypoventilation diagnosis. We were not able to perform analyses at other ages due to low sample sizes.

2.5.11 Impact of BMI Status on Time to Initiation of Bi-Level

BMI status at the first available measure:

During the follow-up period bi-level was initiated for 22 (13.9%) patients (event), 136 patients (86.1%) not did require bi-level (censored) and four (2.5%) patients had missing BMI data and were excluded, see Table 37. BMI status at the first available measure did not impact time to bi-level (Table 38, Figure 32).

Table 37

Description of Bi-Level Initiation Across BMI Status at the First Available Measure of BMI (n=158) [1]

	Bi-level initiation, n (N%)	**Time to bi-level initiation, median (95% CI)**
Healthy weight	13 (59.0)	15.7 (14.1, 16.7)
Overweight	7 (31.8)	15.4 (13.7, 15.7)
Obesity	2 (9.1)	14.1 (11.6, 16.5)
Total	22 (100)	15.5 (14.1, 16.4)

[1] Event n=22, censored n=73, missing n=4
Log rank p-value=0.575

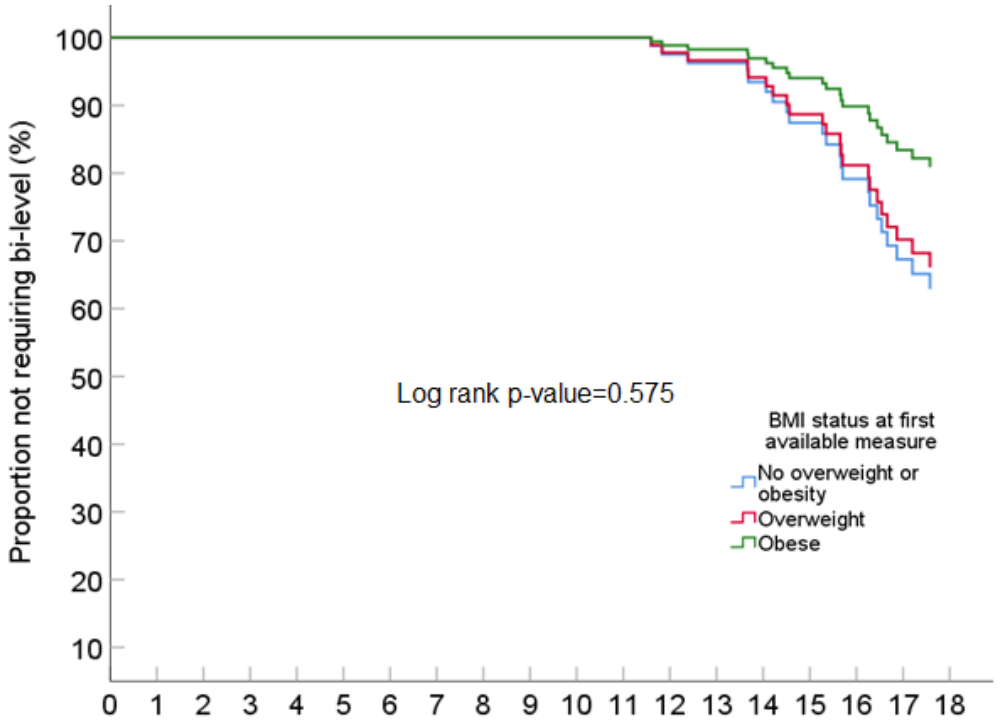
BMI status at five to nine years:

Due to small a number of patients with nocturnal hypoventilation events for five to nine years (range n=7 to n=11), Cox proportional hazards model was not performed.

Box 13

Summary of Findings for The Impact of BMI Status on Time to Bi-Level Initiation

BMI status at the first available measure did not impact time to bi-level initiation. We were not able to perform analyses at other ages due to low sample sizes.



Number at risk										
No ov/ob	70	70	68	64	58	50	43	36	24	8
Ov	49	49	49	46	39	32	26	20	14	6
Ob	35	35	34	29	24	20	14	10	6	2

Figure 32

Kaplan-Meier Curve Time to Bi-Level Initiation Stratified by BMI Status at the First Available Measure

Table 38

BMI Status at Earliest Measure as a Predictor of Time to Commencement of Bi-Level Using a Cox Proportional Hazards Model [1]

BMI status	Hazard Ratio	95% CI lower	95% CI upper	P-value
Overweight	0.893	0.356	2.240	0.810
Obesity	0.458	0.103	2.029	0.304

[1] Event n=22, censored n=73, missing n=4, censored cases before the earliest event in a stratum n=59
Reference category is no overweight or obesity

2.5.12 Impact of BMI on Time to FVC <1L

BMI status at the first available measure:

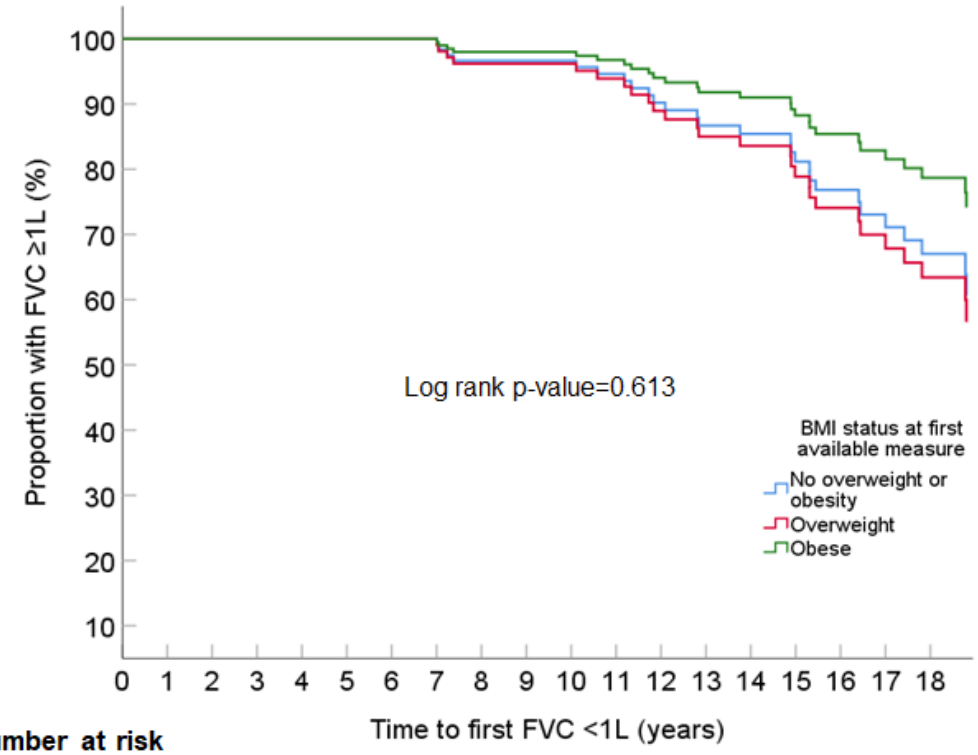
During the follow-up period, 27 (17.1%) patients had a recorded FVC of <1L (event), for 98 (62.0%) patients all recorded FVCs were ≥1L (censored) and 33 (20.9%) had missing data and were excluded from the analysis (Table 39). BMI status at the first available measure did not predict time to a recorded FVC <1L (Figure 33, Table 40).

Table 39

Description of FVC <1L Across BMI Status at the First Available Measure of BMI (n=158) [1]

	FVC <L, n (N%)	**Median time to bi-level initiation (95% CI)**
Healthy weight	14 (51.9)	12.5 ± 3.9
Overweight	10 (37.0)	14.0 ± 4.0
Obesity	3 (11.1)	14.2 ± 2.7
Total	27 (100)	13.3 ± 3.6

[1] Censored n=98, missing n=33
Log rank p-value=0.613



Number at risk										
No ov/ob	58	58	58	57	51	46	40	32	22	10
Ov	42	42	42	42	37	31	23	19	14	6
Ob	25	25	25	24	23	20	14	9	6	2

Figure 33

Kaplan-Meier Curve for Time to FVC <1L Stratified by BMI Status at the First Available Measure

Table 40

BMI Status at Earliest Measure as a Predictor of Reaching FVC <1L Using a Cox Proportional Hazards Model [1]

BMI status	Hazard Ratio	95% CI lower	95% CI upper	P-value
Overweight	1.138	0.505	2.565	0.755
Obesity	0.599	0.171	2.089	0.421

[1] Event n=27, censored n=97, missing n=33, censored cases before the earliest event in a stratum n=1
Reference category is no overweight or obesity

BMI status at five to nine years:

Time to FVC <1L did not significantly differ across BMI status at five through to nine years (Supplementary Table 17).

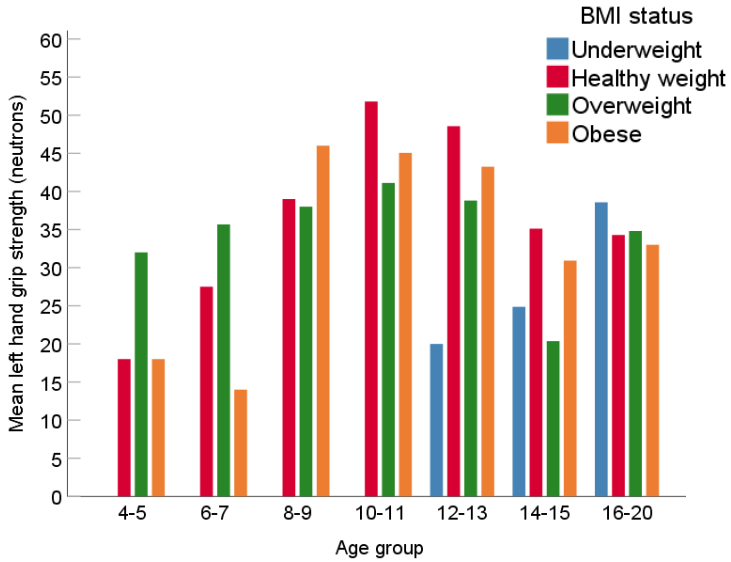
Box 14

Summary of Findings for the Impact of BMI Status on Time to FVC <1L

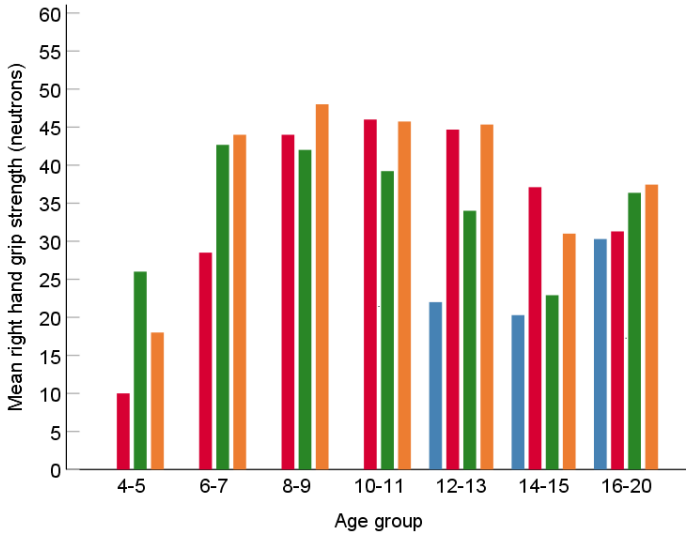
There was no impact of BMI status at the first available measure or at ages five to nine on time to FVC <1L.

2.5.13 Hand Grip Strength Across BMI Status

The mean left and right hand grip strength across BMI status categories and age groups are shown in Figure 34 and in Supplementary Table 18. There was a trend for those who were underweight at ages 12-13 years and 14-15 years having a lower mean hand grip strength compared to those who were a healthy weight. No other trends were observed for BMI status categories at other ages.



a. Left hand grip



b. Right hand grip

Figure 34

a (Top) Left Grip Strength and b (Bottom) Right Grip Strength Across BMI Status

2.6 Discussion

In our sample, the incidence of obesity in young people with DMD ranged from one in ten to one in two, which is between two to six times higher than the general population of Australian children and adolescents. (6) With increasing age FM% increases and LM% decreases, however steroids may provide some protection against this progression of body composition changes. Young people with DMD and obesity are diagnosed with OSA and sustain an initial fracture earlier than their peers without overweight or obesity. It remains unclear what impact obesity has on physical function; obesity at age eight was protective against a slower (7-10 second) 10m walk/run, however there was no impact of BMI status on any other measure of physical function.

2.6.1 Discussion of Key Findings From Aim 1

In this predominantly steroid-treated (90%) cohort, boys had short stature from early in childhood which was exacerbated with increasing age. BMI measures are extreme both within underweight and overweight ranges. These trends align with findings from other steroid-treated international cohorts (see section 1.6). (43,44,47) In our cohort, the median BMI z-score was well into the overweight range from three years of age and steadily increased during childhood. Obesity peaked at age 11 years (51%) when just over one quarter of boys with DMD in the cohort have severe obesity (class 1 or 2 or a BMI ≥120% of the 95th percentile). Comparison of obesity prevalence within our study with international cohorts is limited due to use of different BMI cut-off values, reporting of data according to broad age ranges rather than individual age groups and some studies including steroid-naïve cohorts. In one Argentinian steroid-treated cohort who utilised local growth chart cut-off values, the prevalence of obesity amongst those aged 5-19 years was 28% (compared to 16-50% in our sample for the same age range). (61)

Descriptive analysis of old vs. new era cohorts (1997 to 2009 (5) vs. 2010 to 2018) suggests underweight in Victorian males with DMD may have decreased over time. Concomitantly, obesity appears to now be more persistent into adolescence as the rate of obesity amongst those aged 13 to 16 years in the new era cohort was up to three times higher than in the old era cohort. This is likely related to improved management with steroids over time which maintain function and strength but also lead to higher body weight. (32,44) Our data

suggests young people attending the neuromuscular clinic at RCH have on average biannual monitoring of a linear growth and weight, which aligns with recommended care guidelines. (24) Regular monitoring of growth, appetite and nutritional intake is essential for early identification and prevention of obesity.

We identified a number of factors associated with both increased and decreased odds of obesity. From the included variables, seeing the neuromuscular clinic dietitian was associated with an increased odds of obesity. This is likely related to those who have already developed obesity being referred to the neuromuscular clinic dietitian for weight management advice. We also observed an association between taking deflazacort and increased odds of obesity. This is likely due to the prescription of deflazacort as an alternative to prednisolone in response to steroid-related weight gain. There is some data from retrospective and low quality RCTs that there is less gain with deflazacort for young people with DMD. (32,47) Scoliosis surgery was associated with reduced odds of obesity. Underweight is more likely to be present in those who undergo scoliosis surgery due to postoperative hypermetabolic state and weight loss. Complications such as infections are not uncommon after scoliosis surgery (138) which may further increase energy and protein requirements which, if not managed appropriately, can lead to malnutrition. Both extremes of BMI status (underweight and obesity) are important considerations pre- and post-operatively for scoliosis correction and other major surgeries. In a large (n=1291) cohort of young people with neuromuscular disorders (diagnoses were unspecified) who underwent posterior spinal fusions, those with obesity had a higher risk of surgical site infections, wound dehiscence, urinary tract infections and hospital readmissions. (139) Interestingly, we observed a decreased likelihood of obesity in those with neurodevelopmental disabilities. In those without DMD, neurodevelopmental disabilities are commonly associated with an increased risk of obesity. (140,141) A lower likelihood of obesity in our cohort of boys with DMD and neurodevelopmental disabilities may be due to the presence of feeding difficulties, sensory preferences or use of stimulant medications. (141,142)

Increasing age was also associated with a higher FM% and lower LM%. This reflects disease progression characterised by muscle wasting, fatty infiltration of lean tissue and excess adipose tissue. We observed little differences in BMI z-scores between those who were ambulant and non-ambulant, however being ambulant at the time of DXA scan was associated with a 5% lower FM. Weight gain during the non-ambulatory period will likely consist of a higher proportion of FM as opposed to lean tissue. We expected to see an

association with steroid treatment and increased lean mass, as this has previously been shown in prospective research. (54) However, we were likely limited by the small number of steroid-naïve boys in the cohort.

2.6.2 Discussion of Key Findings From Aim 2

The key findings from Aim 2 of this study are summarised throughout the results and in the infographic in Figure 35. We observed little effect of obesity on time to clinical milestones related to physical function. Obesity at only one of the analysed age groups (eight years) was protective against a slower time (7-10 seconds) in a 10m walk/run. We are unable to draw conclusions from this finding as this relationship was not observed for obesity at other ages groups, nor for other functional outcome measures. Furthermore, the time cut-off of 7-10 seconds was included as an exploratory outcome which has not been used previously. A time cut-off of >10 seconds for the 10m walk/run is used in prior literature and is a marker of loss of ambulation in the following 12 months. (24,132) Anecdotally, a time of 7-10 seconds is indicative of a period of rapid functional decline following this milestone. Body composition is a potential mediating factor in the relationship between obesity and a later time to a 7-10 second 10m walk/run. Ambulant boys with a higher BMI may also have a higher muscle mass (54) and therefore may maintain strength, function and walking/running speed for longer. The response to steroids may also play a role in protecting against a slower walk/run but also causing a higher BMI and short stature which may have functional benefits. (48,97) It is well documented in our cohort and in existing literature that steroid-treated boys with DMD have short stature from early in childhood and that finding is exacerbated with increasing age. (43,44,47) As obesity becomes more severe, weight may impact functional mobility, but however we were unable to stratify the obesity category further according obesity severity due to small sample sizes.

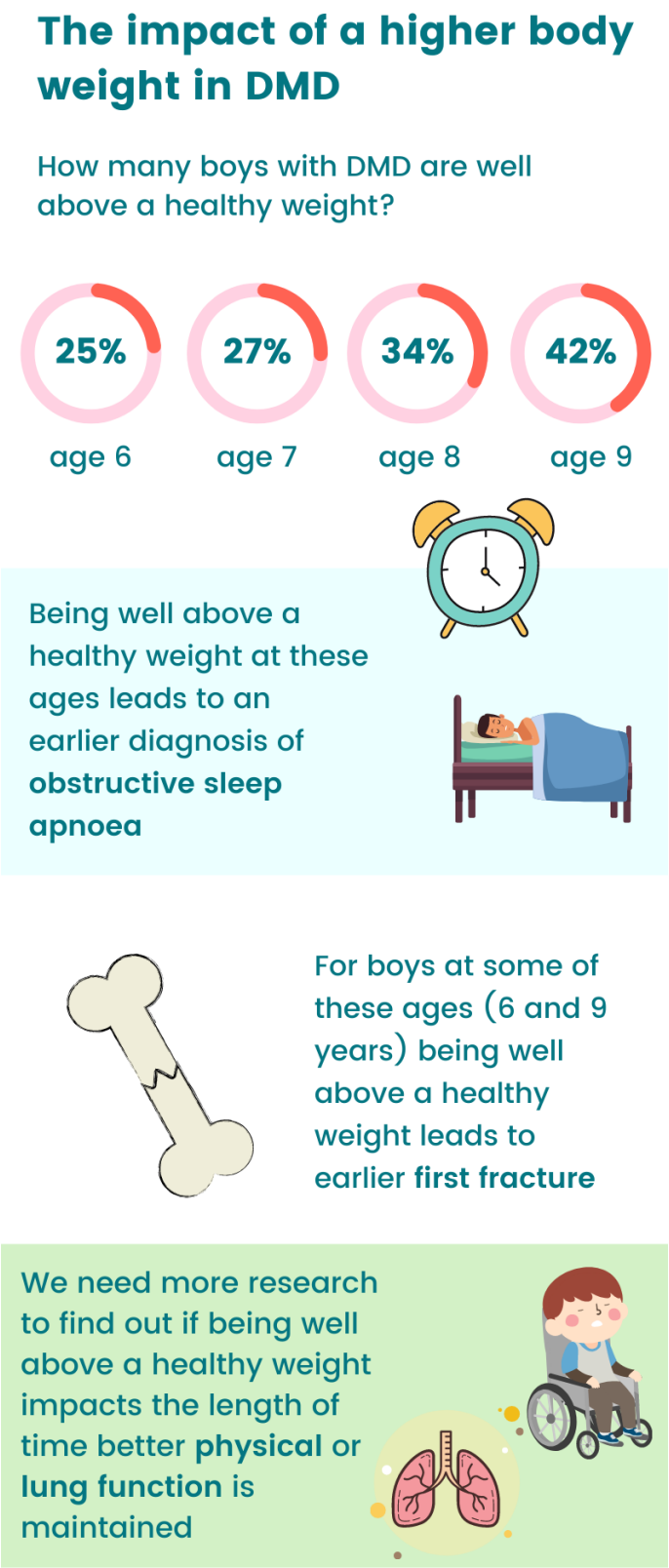


Figure 35

Infographic Summarising the Key Findings for Chapter 2

We analysed one measure of strength (grip strength), for which we were unable to perform time-to-event analysis as there are no known clinically meaningful milestones. There was a small trend for those who were underweight at 12-15 years having a lower mean hand grip strength, however this needs to be confirmed with further research. Strength as a potential mediator between obesity and physical function requires further exploration, for example, considering the differences between boys with obesity who have greater or lower strength and how this impacts physical function and biomechanics. Other recommendations for future research which were outside the scope of this study include the effect of BMI status on individual NSAA items, upper limb function and activities of daily living.

Obesity at two time points, six and nine years, increased the likelihood of sustaining a fracture earlier. Analysis at other ages may have been limited by small sample sizes. Increased risk of fractures in children with obesity has also been observed in typically developing populations. (143) In DMD, response to steroids may be a mediator in this scenario; steroid treatment can cause weight gain (32) and can also impact bone mineral density and fractures in DMD. (144) Young people with DMD treated with deflazacort have a shorter time to first fracture, higher fracture incidence and lowest height growth compared to those on other steroid regimens. (47) In our sample, those treated with deflazacort were also more likely to have obesity. This is likely due to the prescription of deflazacort in this country as an alternative to prednisolone for patients who have experienced significant steroid-related weight gain. It may be hypothesised that in this Australian cohort, the impact of both deflazacort and obesity is interrelated and that both are associated with increased fracture risk. In those with obesity and/or those taking deflazacort, there is a need for close surveillance of fracture risk factors such as vitamin D deficiency, low dietary calcium intake and falls. Dietitians and physiotherapists play an integral role in advising families on how to mitigate these risk factors to help prevent fractures, which cause significant burden and can lead to loss of ambulation and decline in function and strength. (145)

Diagnosis of OSA was up to two years earlier in those with obesity compared to those without overweight or obesity. Young people with DMD who have obesity may also require CPAP earlier, however our analyses exploring this was limited by small sample sizes. OSA and other sleep disturbances can have a significant impact on the quality of life and fatigue in young people with DMD (see section 1.5.4). The relationship between obesity and OSA may be cyclical and poses challenges in the clinical management of both conditions: obesity causes OSA due to anatomical obstruction, while sleep disturbance causes fatigue and

reduced perceived quality of life which may create barriers to weight management strategies (e.g. fatigue as a barrier to participating in physical activity). As well as the burden of OSA on individual patients and families, there are also significant economic implications due to the increased need for healthcare services. (146,147) We did not find an association between BMI status and time to FVC <L, a milestone that negatively predicts survival in DMD. (148) Previous literature has shown a lower BMI is associated with a lower FVC, (5,53) however as we had few in our sample that were underweight we were unable to observe this effect.

2.6.3 Strengths and Limitations

Strengths of this study include the substantial number of anthropometric observations collected across both ambulatory and non-ambulatory phases of disease progression and the longitudinal nature of these data. The number of observations analysed is comparative to previous large international studies of growth in DMD. (44,45) To the authors' knowledge, this is also the first study internationally to comprehensively explore the effect of BMI status on time to clinical milestones in a contemporary population with DMD. This study builds upon previous research which has typically explored the effect of BMI on single clinical outcomes (Table 7) by analysing multiple outcomes related to physical and respiratory function and bone health. Our cohort was also predominantly steroid-treated which is the mainstay management strategy for DMD. A limitation of this study was its retrospective design, we were only able to record the time of milestones when they appeared in medical records rather than prospectively screening for events. For example, time of loss of ambulation was identified from clinician notes and therefore depends on the frequency of contact between families and clinicians and the timeliness of parent reporting. Conducting longitudinal, prospective and multi-site studies that explore the impact of BMI status on clinical milestones would overcome this. While we had a large sample of anthropometric observations (Aim 1), patient sample sizes for clinical milestones analyses (Aim 2) were often small due to missing data. In some clinical milestones such as timed function tests, there may have been insufficient power to detect differences across BMI status. We analysed data for 156 individuals with DMD from the largest paediatric neuromuscular clinic in Australia (at RCH) with an average of approximately nine years of follow-up data. Therefore, to obtain sufficient power for time-to-event analysis in future studies, data from multiple sites will be required. Larger sample sizes would enable further exploration of the impact of minority BMI status categories such as underweight and severe obesity class 2 on

clinical outcomes. This study was also limited by adult data not being available. Some milestones are more likely to occur in adulthood, such as FVC <1L which occurs early in the second decade of life. (134) Tracking patient data into adulthood through collaboration with adult neuromuscular clinics is recommended to understand the impact of BMI status on clinical outcomes occurring during the late ambulatory phase (other examples include cardiomyopathy and dysphagia).

2.7 Conclusion

Young people with DMD can experience extremes in their BMI status in both the underweight and overweight ranges over their lifetime. With increasing age and disease progression, FM% increases and LM% decreases. Treatment with steroids provides some protection against declining LM. Obesity disproportionally affects young people with DMD compared to general populations and this can lead to earlier fractures and OSA diagnosis. It remains unclear what impact obesity had on physical function. Close monitoring of growth, fracture risk factors and OSA symptoms is recommended for all young people with DMD, but especially for those who above a healthy weight range. There is a need for larger prospective studies that track data into adulthood to understand the effect of all BMI status categories, including underweight and severe obesity, on clinically meaningful milestones. A summary of what this study contributes to knowledge can be found in Box 15.

Box 15

Contribution to Knowledge Gaps (Chapter 2)

For young people with DMD this study contributes…

- Contemporary data describing growth, body composition and BMI status, including obesity severity in Victoria, Australia
- Knowledge that currently up to one in two have obesity which persists into adolescence (13-16 years)
- Identification that those who saw a dietitian or who were taking deflazacort were more likely to have obesity
- Identification that ambulatory status has little effect on BMI, however being able to independently ambulate is associated with a lower FM
- Identification that obesity may lead to earlier fractures and earlier OSA diagnosis
- There remains no clear effect of BMI status on physical function

Chapter 3.

Dietary Factors Contributing to Weight Gain in DMD

Peer-reviewed journal article:

Title: Are dietary factors associated with body habitus in ambulant boys with Duchenne muscular dystrophy?

Authors: Natassja Billich, Maureen Evans, Helen Truby, Monique Ryan, Zoe Davidson

In preparation for *Journal of Human Nutrition and Dietetics*

Conference abstract:

Dietitians Australia Conference 2019, Gold Coast.

Oral presentation.

3.1 Preamble

Little is known about the dietary intake of young people with DMD, see Box 16. This chapter will explore potential dietary factors that may contribute to excess weight gain in a cohort of ambulatory boys with DMD in Australia.

Box 16

Identified knowledge gaps (Chapter 3)

- Only one study from Mexico has conducted an analysis of energy and macronutrient intake of young people with DMD
- Dietary intake of Australian boys with DMD has not been explored
- There has been no analysis of micronutrient or food group intake in boys with DMD

3.2 Aims and Objectives

In ambulatory boys with DMD this study aims to:

1. Conduct a comprehensive dietary analysis of energy, macro- and micro-nutrients, core and discretionary foods and drinks.
2. Explore the relationship between dietary factors and body habitus and motor function.

The objectives of this study are to:

i. Describe energy, macro- and micro-nutrient, core food group and discretionary food and drink intake and compare differences across boys who are within a healthy weight range with those above a healthy weight range.
ii. Determine the relationships between BMI z-score, body composition and energy intake using correlation analysis.

3.3 Methods

3.3.1 Study Design and Setting

This study is a cross-sectional secondary data analysis of food diaries collected for the *Nutriceuticals in DMD* study. (27) *Nutriceuticals in DMD* was a multicentre, double blind, randomised, controlled cross-over trial which aimed to test the efficacy of an enhanced nutritional supplement on motor function outcomes in boys with DMD. A full methodology and results from this study has been described previously. (27) At each six visits across 18 months a three-day food diary (including two weekdays and one weekend day) was completed by parents to assess the impact of the supplement on dietary intake. Parent-reported energy intake using food diaries has shown to accurately reflect measured total energy expenditure in the DMD population. (90) The present study is a comprehensive analysis of the baseline food diaries from participants enrolled in the *Nutriceuticals in DMD* study and collected prior to commencing the intervention. Local Research Ethics and Governance office approved all study procedures for the original *Nutriceuticals in DMD* study at each study site. (27)

3.3.2 Participants

For *Nutriceuticals in DMD*, eligible participants were ambulatory boys aged 5 to 13 years with a definite diagnosis of DMD. Boys with dietary allergies were excluded. To be eligible for inclusion in this dietary analysis, participants had to have completed a food diary for at least one day at baseline.

3.3.3 Outcome Measures

In addition to three-day food diaries, baseline assessment included collection of information on demographics, steroid type and duration of treatment, nutritional supplements taken prior to the intervention, anthropometry, body composition and six-minute walk test.

Measures of anthropometry and body composition were BMI z-score, FM% and LM%. BMI z-scores were used to determine weight status categories based on the CDC reference values (Box 2). FM% and LM% were measured using total body DXA scan.

The six-minute walk test data was used as a measure of motor function ability. For this analysis, percent predicted 6MWD (%Pred6MWD), which considers age and height (and associated stride length) was calculated using the Geiger equation (149) which has been validated in children with DMD. (150)

3.3.4 Study Procedure

Quantitative and qualitative analysis of three-day food diaries was performed by one APD (NB). Quantitative analysis included assessment of dietary energy, macro- and micro-nutrient intake using data from FoodWorks nutrient analysis software (FoodWorks (Version 9) [Computer software], 2015). Micro-nutrient intake was calculated from food and drink intake, intake from supplements was not analysed. Energy intake was compared against the estimated energy requirements (EER) of boys aged 3-10 years and 10-18 years determined by the Schofield weight only equation (28) with a 1.4 physical activity level (PAL) factor applied (Box 17). This method has proven to accurately reflect measured total energy expenditure when compared to indirect calorimetry, the gold standard reference method in boys with DMD. (87) Energy intake was reported as a daily total, as kJ/kg of total body weight (BW) and kJ/kg LM.

Box 17

EER Equations

Boys 3-10 years:

$EER\ (kJ) = ((0.095 \times weight\ (kg) + 2.110) \times 1000) \times 1.4\ PAL$

Boys 10-18 years:

$EER\ (kJ) = ((0.074 \times weight\ (kg) + 2.754) \times 1000) \times 1.4\ PAL$

To determine under-reporting of energy intake, the Goldberg cut-off limits for energy intake to basal metabolic rate ratio of 0.9 were applied. (151) Macro-nutrient intake was compared against the recommended Acceptable Macronutrient Distribution Ranges for Australia and New Zealand. (110) Energy density was calculated as kJ of energy per gram of food and drinks (kJ/g). A higher energy density is associated with higher total energy intake in typically developing children. (152) The protein to energy ratio (P:E) was also determined, calculated by grams of protein/418.4kJ (equivalent to 100 kilocalories). The P:E ratio, or the percentage of energy from protein in the diet, can be used as a measure of dietary quality by defining safe levels of protein intake when a diet is consumed to meet energy needs. (153) The value of an adequate P:E ratio forms the basis of the "protein leverage hypothesis" which suggests that an intrinsic drive to maintain a target protein intake of approximately 15% of dietary energy, could result in an excessive energy intake if the diet consists of low protein density but high fat and/or carbohydrate (low P:E). (154)

Micro-nutrient intake was compared against various Nutrient Reference Values (NRVs) for Australia and New Zealand. (110) NRVs used were: Estimated Average Requirements and; Adequate Intake. (110) A summary of the NRVs and other dietary factors used are summarised in Box 18.

Box 18

Definitions of Nutrient Reference Values and Other Dietary Factors Analysed

Energy density (152) = kJ of energy per gram of food and drinks (kJ/g)

Protein to energy ratio (P:E) (153) = grams protein/418.4kJ (equivalent to 100 kilocalories).

Acceptable Macronutrient Distribution Range (110) = The estimated range required for each macronutrient (expressed as a % contribution to energy) that would allow for an adequate intake of all other nutrients, whilst maximising general health.

Estimated Average Requirements* (110) = daily nutrient level estimated to meet the requirements of 50% of healthy individuals in a particular life stage and gender group.

Adequate Intake (110) = average daily nutrient intake level based on observed or experimentally-determined approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people that are assumed to be adequate.

* Estimated Average Requirements are used to determine inadequacy when dietary intake is below the reference value, whereas intake above a Recommended Daily Intake has a low probability of inadequacy (110)

Qualitative analysis of food diaries included the classification of foods and drinks consumed into the Five Food Groups (fruit, vegetables, grains, meat/fish/poultry/alternatives and dairy) or discretionary foods (foods or drinks high in added sugar, saturated fat or salt). The Australian Guide to Healthy Eating was used to classify food and drinks as one of the Five Food Groups or discretionary foods and to determine the number of serves consumed. (155) The proportion of total energy and protein derived from discretionary foods was also determined. Discretionary foods were further classified into sub-categories (e.g. sugar-sweetened drinks or processed meats) to determine which types of foods were contributing the most to this category. Serves consumed were compared to the Australian Guide to Healthy Eating recommended serves for the relevant sex and age. Water intake was poorly reported in food diaries and was therefore not analysed.

3.3.5 Data Analysis

Data was analysed using SPSS statistical software (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp). Normality of the data was assessed visually using frequency distribution. For normally distributed and non-parametric data the mean and SD and median IQR are reported, respectively. Participants were initially stratified by BMI status – healthy weight, overweight and obesity – and a one-way analysis of variance with Tukey post-hoc test was used to determine differences across groups for clinical characteristics. Due to the small sample size in the overweight group (n=4), the overweight and obesity group was then combined and re-named 'above a healthy weight'. To test for differences across boys who were a healthy weight and above a healthy weight, an independent t-test was used for normally distributed data and a Mann-Whitney U test was used for non-parametric data. To determine dietary components associated with BMI z-score, FM%, LM% and total energy intake correlation analysis was used. Dietary factors included in the correlation analysis were: energy, energy/kg BW, energy/kg LM, P:E ratio, % energy intake from discretionary foods, energy density, age and %Pred6MWD. For correlation analyses the Pearson correlation (r) is reported. For r values <0.3 the relationship was considered to be no relationship/very weak, 0.3 to 0.5 weak, 0.5 to 0.7 moderate and >0.7 strong. To determine which foods/drinks contributed the most to discretionary food intake, the proportion of total energy from each discretionary food category (e.g. fried potatoes) was calculated. For all analysis a p-value of <0.05 was considered to be statistically significant.

3.4 Results

3.4.1 Clinical Characteristics

The clinical characteristics of the 37 participants with DMD across weight status categories (healthy weight, overweight and obese) are described in Table 41. The median age across all participants was 8.5 years [IQR 7.2, 10.5] and was not different across weight status categories. Sixty percent of participants had obesity. Children with obesity had a significantly greater BMI z-score and %FM and significantly lower %LM compared to overweight and healthy weight children. The majority of the cohort was steroid treated. In steroid treated boys, those with obesity had a significantly longer steroid treatment duration than their overweight and healthy weight peers. Only one boy was not able to complete the 6-minute walk test and was excluded from analysis of 6MWD. There were no significant differences across weight status categories for 6MWD outcomes. Due to the small number of participants classified as overweight, the overweight and obese groups were combined into a single category "above a healthy weight" for subsequent analysis. All food diary data was analysed although, some parents recorded less than three days food intake (n=1) and some recorded more than three days (n=7), mean 3.2 (SD 0.7) days.

Table 41

Clinical Characteristics of Ambulant Boys with Duchenne muscular dystrophy (n=37) [1]

	Healthy weight	Overweight	Obesity	Total
n (%)	11 (30)	4 (11)	22 (60)	37 (100)
Age (years)	7.7 (6.5, 10.4)	7.5 (6.2, 8.8)	9.6 (8.0, 10.8)	8.5 (7.2, 10.5)
Height z-score	-1.07 ± 1.24	-0.82 ± 1.04	-1.73 ±1.12	-1.43 ±1.18
Weight z-score	-0.58 ±1.11	0.47 ±0.35	1.15 ± 0.84 [a] ***	0.56 ± 1.17
BMI z-score	0.24 (-0.35, 0.96)	1.23 (1.13,1.31)	2.20 (1.77, 2.37) [a] *** [b] ***	1.72 (0.97, 2.22)
FM%	22.6 ± 7.0	23.7 ± 5.7	38.6 ± 9.5 [a] *** [b] **	32.2 ± 11.4
LM%	74.8 ± 6.1	73.6 ± 5.9	59.8 ± 9.3 [a] *** [b] *	65.7 ± 10.9
Deflazacort	1 (9.1)	1 (25.0)	8 (36.4)	10 (27.0)
Prednisolone	7 (63.6)	3 (75.0)	14 (63.6)	24 (64.9)
Steroid duration (years)	1 (0, 5)	2 (1, 3)	4 (2, 6) [b]*	3 (1, 5)
6MWD (metres)	363 ± 55	400 ± 58	362 ± 106	366 ± 88
6MWD % predicted	65 (56, 72)	68 (61, 79)	60 (44, 76)	63 (47, 75)

[1] Weight status is presented as row percentages in parenthesis, steroid types and 6MWD (6-minute walk distance) are presented as column percentages
[a] Significantly different to healthy weight [b] Significantly different to overweight *p<0.05 **p<0.01 ***p<0.001
Median and interquartile range is reported in parenthesis, mean ± SD

3.4.2 Energy Intake

For boys who were a healthy weight, the median energy intake was 316 kJ/kg BW [IQR 276, 355] which was greater than the median EER, see Table 42. For boys who were above a healthy weight, energy intake was 185kJ/kg BW [143, 214] which was lower than the median EER. Boys who were above a healthy weight had a significantly lower energy intake per BW and LM than those who were a healthy weight. Energy density (kJ/g) was 5.8 [IQR 4.2, 6.3] for healthy weight and 4.7 [IQR 4.0, 5.7] for those above a healthy weight, however these differences were not significant. According to Goldberg cut-offs, three parents underestimated their son's food intake (energy intake to basal metabolic rate ratios were 0.76, 0.81 and 0.88). When these three participants were excluded from the analysis, there was an increase in energy intake (+25kJ/kg/day) for the above a healthy weight group. However, differences between groups for energy/kg BW and LM remained significant ($p=<0.01$) when they were excluded, thus these three participants were included in all subsequent analyses.

Table 42

Estimated Energy Requirements (EER) and Intakes of Ambulant Boys with Duchenne muscular dystrophy (N=37) [1]

	Healthy weight (n=11)	**Above a healthy weight (n=26)**	**Total (n=37)**
EER (kJ)/day	6622 [5667, 6760]	7934 [6798, 8480]	-
EER (kJ/kg BW)	248 [238, 278]	208 [194, 235]	-
Energy (kJ)	7359 [6688, 8359]	6367 [5594, 7414]	6881 [5806, 7533]
% of EER	124 [115, 132]	88 [75, 96] *	91 [77, 118]
Energy (kJ/kg BW)	316 [276, 355]	185 [143, 214] **	198 [176, 284]
Energy (kJ/kg LM)	448 [384, 467]	305 [272, 328] **	321 [278, 420]
Energy density (kJ/g of food or drink)	5.8 [4.2, 6.3]	4.7 [4.0, 5.7]	5.1 [4.2, 6.0]
P:E ratio (protein g/418.4kJ)	4.5 [3.9, 5.1]	4.7 [4.0, 5.2]	4.6 [4.0, 5.1]

[1] Values are presented as median with interquartile range.
*p<0.05 **p<0.01 ***p<0.001 significant differences between healthy weight and above a healthy weight
Abbreviations: EER, estimated energy requirements; P:E, protein to energy

3.4.3 Macro- and Micro-nutrient Intake

For macro- and micro-nutrient intake, healthy weight participants (mean age 7.7 years) were compared to the Australian Nutrient Reference Values for four to eight year old boys and above a healthy weight participants (mean age 9.1 years) were compared to the Nutrient Reference Values for those aged nine to 13 years (Table 43). For all participants the percentage of energy from protein, fat and carbohydrates were within recommended limits when compared to Acceptable Macronutrient Distribution Ranges. Saturated fat intake was 13% of total energy, slightly above the recommended intake of <10% of energy intake (110). All boys met the Estimated Average Requirement for protein intake, and the P:E ratio was 4.5 (g protein/100kcal) [IQR 4.0, 5.1] or approximately 18% of dietary energy intake. For all measures of macronutrients, there were no significant differences between the healthy weight and above a healthy weight group. Intake of fibre was low across all participants with 84% consuming below the Adequate Intake.

Calcium intake was inadequate for 35% of participants, however of these 13 participants eight were taking a calcium supplement prior to commencing the *Nutriceuticals in DMD* study. Most participants consumed adequate amounts of other micronutrients. Daily micronutrient intake was not significantly different across weight status categories.

Table 43

Macro- and Micro-nutrient Intakes Compared to Nutrient Reference Values

		Healthy weight (mean age 7.7 years, n=11)		Above a healthy weight (mean age 9.1 years, n=26)		Total (n=37)	
				% energy intake			
Macronutrients (g)							
	AMDR	**Daily intake (g)**	**% energy intake**	**Daily intake**	**% energy intake**	**Daily intake**	**% energy intake**
Protein	15-25%	77.4 (20.1)	18 (2.9)	73.7 (13.6)	19 (3.6)	74.8 (15.6)	19 (3.4)
Fat	20-35%	64.2 (13.5)	34 (5.0)	58.1 (17.5)	33 (4.7)	59.9 (16.4)	33 (4.7)
Saturated fat	≤10%	24.5 (7.68)	13 (3.4)	23.2 (7.5)	13 (2.5)	23.6 (7.5)	13 (2.8)
Carbohydrate	45-65%	204.3 (44.9)	47 (3.6)	185.9 (44.2)	46 (4.6)	191.4 (44.6)	47 (4.2)
Micronutrients							
	NRV [1]	**Daily intake**	**Below NRV (%)**	**Daily intake**	**Below NRV (%)**	**Daily intake**	**Below NRV (%)**
Dietary fibre (g)	AI: 18	16 [13, 17]	82	15 [12, 18]	84.6	16 [12, 18]	84
Calcium (mg)	4-8: 520 9-13: 800	766 [599, 899]	18	726 [589, 920]	42.3	727 [599, 899]	35
Iron (mg)	4-8: 4 9-13: 6	10 [6, 13]	0	8 [6, 9]	15.4	8 [6, 9]	11
Zinc (mg)	4-8: 3 9-13: 5	10 [7, 12]	0	8 [7, 10]	0	8 [7, 10]	0

Table 43

Macro- and Micro-nutrient Intakes Compared to Nutrient Reference Values

		Healthy weight (mean age 7.7 years, n=11)		Above a healthy weight (mean age 9.1 years, n=26)		Total (n=37)	
				% energy intake			
	NRV	**Daily intake**	**Below NRV (%)**	**Daily intake**	**Below NRV (%)**	**Daily intake**	**Below NRV (%)**
Thiamine (mg)	4-8: 0.5 9-13: 0.7	1.5 [0.9, 2.2]	0	1.5 [1.0, 1.9]	0	1.5 [1.0, 2.1]	0
Riboflavin (mg)	4-8: 0.5 9-13: 0.8	2.0 [1.1, 2.7]	0	1.7 [1.3, 2.2]	0	1.8 [1.3, 2.3]	0
Niacin (mg)	4-8: 6 9-13: 9	32.7 [30.7, 35.7]	0	33 [30, 35]	0	33 [31, 36]	0
Vitamin C (mg)	4-8: 25 9-13: 28	93 [50, 184]	9	99 [55, 179]	19	93 [55, 179]	16
Vitamin B12 (µg)	1.0	4.3 [3.1, 5.3]	9	3.6 [2.5, 4.8]	0	3.8 [2.8, 4.9]	3
Vitamin A (µg)	4-8: 275 9-13: 445	455 [330, 742]	9	517 [370, 616]	19	503 [338, 637]	16
Dietary folate equivalents (µg)	4-8: 160 9-13: 250	540 [453, 806]	0	661 [516, 798]	0	633 [514, 798]	0

[1] NRVs are EAR unless otherwise stated, some nutrients have different values for 4-8 years (healthy weight) and 9-13 years (above a healthy weight)
**significant difference between healthy weight and overweight/obese $p<0.01$ *significant difference between healthy weight and overweight/obese $p<0.05$
Abbreviations: AI, Adequate Intake; AMDR, Acceptable Macronutrient Distribution Ranges; EAR, Estimated Average Requirement; NRV, Nutrient Reference Values

3.4.4 The Five Food Groups and Discretionary Food Intake

The Five Food Groups and discretionary food intake was compared to the Australian Guide to Healthy Eating (Figure 36 and Supplementary Table 19). No participants consumed the recommended five serves of vegetables, with a median <1 serve/day. Across all participants, 46% consumed less than the recommended two fruit serves however this increased to 81% for fresh fruit only (the Australian Guide to Healthy Eating also classifies pure fruit juice as fruit). Most boys consumed less than the recommended serves of grain foods, meat/fish/poultry/alternatives and dairy foods (65%, 70% and 81%, respectively).

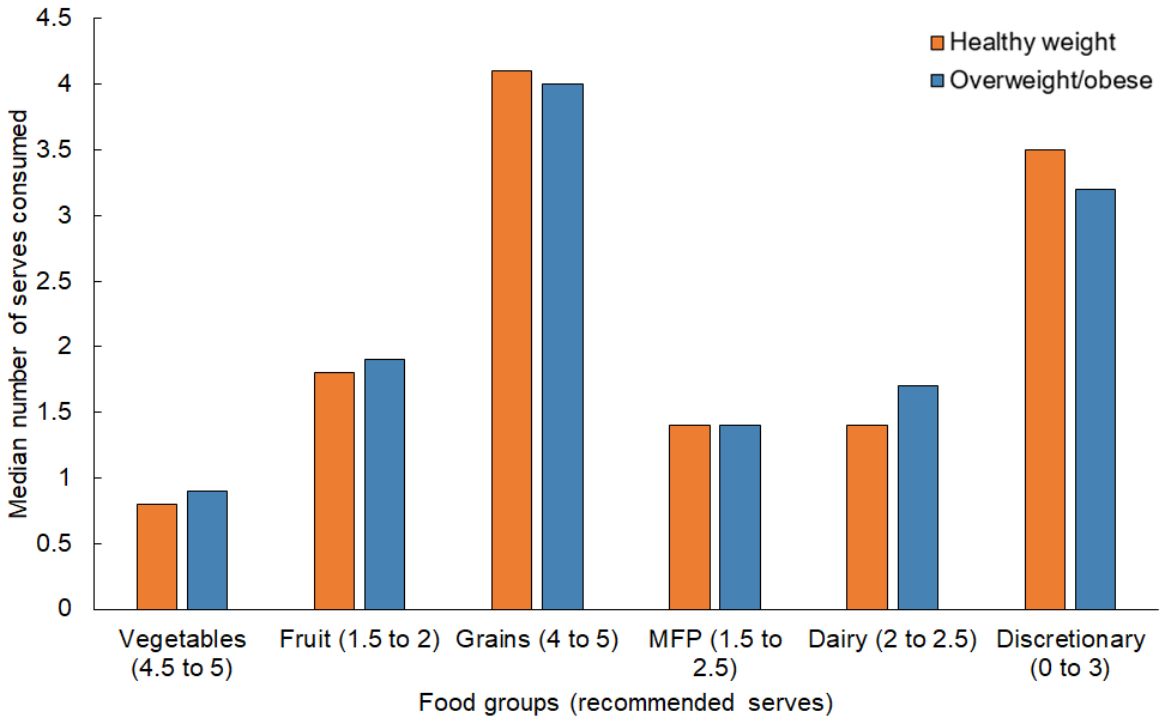


Figure 36

Dietary Intake of Core and Discretionary Food Groups [1]

[1] MFP, meat, fish, poultry and alternatives

The median number of serves of discretionary foods consumed by all participants was 3.3 [IQR 2.0, 4.7] and ranged from 0 to 10.9 serves. Discretionary foods contributed 27% [IQR 21, 42] of energy intake for all participants. The median proportion of total protein derived from discretionary foods was 23% (IQR 11, 38). Processed meats (e.g. chicken nuggets), fried potatoes (e.g. fries) and savoury snacks (e.g. potato crisps) contributed to 24% [IQR 6, 32], 7% [IQR 0, 19] and 4% [IQR 0, 17] of energy from discretionary foods, respectively.

There was no significant difference between the healthy weight and above a healthy weight groups for intake of the Five Food Groups, discretionary food serves or the proportion of energy or protein derived from discretionary foods.

3.4.5 Factors Associated with BMI z-score and Body Composition

Correlation analysis determined the relationship between dietary factors and BMI z-score, FM% or LM%, see Table 44. Energy/kg BW and energy/kg LM was negatively associated with BMI z-score and FM% and positively associated with LM%. There was no relationship between total daily energy intake, energy density, P:E ratio, % EI from discretionary food and BMI z-score, FM% or LM%.

3.4.6 Factors Associated with Energy Intake

Factors associated with energy intake were also explored using correlation analysis (Table 44). There was a weak positive relationship observed between %Pred6MWD and energy intake, that is, those participants who were able to walk further for their age and height consumed more energy. As P:E ratio decreased, energy intake increased. As the percentage of energy intake from discretionary foods and energy density increased so did the total energy intake. Age was not significantly correlated with total energy intake. However, there was a moderate negative association with age and energy intake per kg BW and LM with younger boys having a higher energy intake.

Table 44

Correlation Analysis Between Dietary Factors, Age, Body Habitus and Functional Outcomes. [1]

Factors	BMI z-score		FM%		LM%		Energy intake		Energy kJ/kg BW		Energy kJ/kg LM	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*	*r*	*p*
Energy intake kJ	-0.100	0.56	-0.236	0.16	0.229	0.17	-	-	-	-	-	-
Energy kJ/kg BW	**-0. 650**	**<0.01**	**-0.817**	**<0.01**	**0.805**	**<0.01**	-	-	-	-	-	-
Energy kJ/kg LM	**-0.564**	**<0.01**	**-0.563**	**<0.01**	**0.547**	**<0.01**	-	-	-	-	-	-
Energy density kJ/g	-0.147	0.38	-0.171	0.31	0.166	0.33	**0.424**	**<0.01**	**0.393**	**0.02**	**0.485**	**<0.01**
P:E ratio g protein/418.4 kJ	0.262	0.12	0.284	0.09	-0.295	0.08	**-0.422**	**<0.01**	**-0.383**	**0.02**	**-0.388**	**<0.01**
% EI from discretionary food	-0.260	0.12	-0.284	0.09	0.280	0.09	**0.461**	**<0.01**	**-0.393**	**0.02**	**0.417**	**0.01**
Age (years)	0.111	0.51	**0.592**	**<0.01**	**-0.581**	**<0.01**	0.002	0.99	**-0.609**	**<0.01**	**-0.499**	**<0.01**
%Pred6MWD	-	-	-	-	-	-	**0.364**	**0.03**	**0.427**	**<0.01**	0.249	0.143

[1] Abbreviations *r*, Pearson correlation coefficient; *p*, p-value; %Pred6MWD. % predicted 6-minute walk test; %FM fat mass percentage; LM%, lean mass percentage; P:E, protein to energy; BW, body weight;

3.5 Discussion

This study provides a novel dietary analysis of boys with DMD as it includes micro-nutrients, food groups and discretionary foods in addition to energy and macronutrients. We have identified that steroid-treated, ambulant boys with DMD who are a healthy weight and have lower adiposity may be consuming more than their energy requirements. These boys are also younger and able to walk further. This analysis suggests boys who are in a healthy weight range may be consuming more energy than their peers who are above a healthy weight. Dietary factors associated with a higher energy intake were: a higher percentage of energy intake from discretionary foods, higher energy density and a lower P:E ratio, however these findings should be interpreted with caution as associations were weak. We observed poor adherence to population based healthy eating recommendations, as most participants did not meet recommended serves of grains, meat and alternatives or dairy, and none met recommended serves of vegetables. More than a quarter of energy was derived from discretionary foods and drinks with processed meat products (e.g. chicken nuggets) being the main single food category contributing to these items. The intake of discretionary foods is comparable to the broader population of children in Australia who consume approximately one third of total energy from discretionary foods and drinks. (156)

Our study suggests boys with DMD who are a healthy weight, younger and who have better motor function may be eating more than their energy requirements. Only one other study has explored the dietary intake of individuals with DMD. This analysis included energy and macronutrient intakes of a large Mexican sample (n=101) of both ambulant and non-ambulant steroid-naïve males with DMD. (60) In the Mexican cohort, pre-school and school-aged participants consumed a higher energy intake compared to dietary reference values. (60) Participants who were ambulatory consumed a higher energy intake than non-ambulatory participants, which is consistent with our findings of a higher energy intake in those with better motor function. The Mexican study found that total daily energy intake was not associated with body FM or LM. (60) These findings concur with the Mexican study as these Australian children had a total daily energy intake which did not have a clear relationship with fat or lean mass. However, when using energy per kilogram of BW or LM in the correlation analysis, the leaner participants had the highest energy intakes. Considering energy intake per kilogram of body weight may be particularly useful for healthy weight boys with DMD when aiming for target energy intake in order to prevent

excessive weight gain. In clinical practice, the daily energy requirements estimated by the Schofield weight equation (28) with a physical activity factor of 1.3-1.4 for ambulatory boys and 1.0-1.1 for non-ambulatory boys applied can be divided by total body weight as a reference value for energy intake. (27) For boys with obesity and when weight loss is clinically indicated (e.g. post-pubertal), clinicians could consider using an adjusted body weight to estimate requirements.

The finding that boys with the highest BMI z-scores and FM consumed the least amount of energy appears counter intuitive. However, there are several hypotheses that may explain these results. During the early ambulatory phase, boys with DMD might consume a higher energy intake because of an increased appetite due to commencement of steroids and/or higher activity levels. These higher intakes can contribute to weight gain in early childhood. As physical function and muscle mass declines as the diseases progresses, resting and/or total energy requirements may decrease and if energy intakes aren't adjusted appropriately, further weight gain may occur. The low energy intake observed in boys who were above a healthy weight may be due to a restricted energy intake (to stabilise weight) or a reduced appetite as energy requirements and activity levels decrease. The cause of obesity in this population is likely a complex combination of sub-optimal diet, decreased physical activity as functional decline occurs, potentially decreased energy requirements as loss of muscle mass occurs, poor sleep, increased appetite and reduced satiety induced by steroid treatment and other metabolic disturbances. (24,127)

Our study suggests that the early ambulatory phases of DMD when energy intakes are highest and may be above estimated requirements, is a key time to implement strategies to prevent excessive weight gain. Strategies may include increasing the P:E ratio which may assist adequate protein status to support optimal body composition, and minimise excessive energy consumption by supporting satiety. (157) As this study demonstrates approximately a quarter of total protein was derived from discretionary foods and 30% were below the recommended served of lean meat/fish/poultry and alternatives, it is recommended that dietary strategies focus on lean, unprocessed, high biological value sources of protein. To support protein utilisation and appetite management, protein should be evenly distributed across the day e.g. small portions of protein-containing foods at each meal and snack. Furthermore, reducing the energy density of the diet may decrease energy intake and assist in weight management. The energy density (kJ/g) of the dietary intakes of our sample was

5.8 for boys who were a healthy weight and 4.7 for those who were above a healthy weight and a higher energy density was associated with a higher total, per kg and per kg of LM energy intake. Energy density for the healthy weight DMD group was slightly higher than a recently reported large European cohort of typically developing male children (n=4390) which was 1.33 Kcal/g (equivalent to 5.5 kJ/g). (158)

For all boys with DMD, diet quality could be improved to assist in optimising health outcomes. In our study, approximately one third of energy intake was from discretionary foods and drinks (those high in energy, saturated fat, sugar and/or salt) which may displace foods from the Five Core Food Groups. Low adherence to healthy eating recommendations is not only observed in DMD but also the wider population of Australian children. (156) While improving dietary quality is important for all children, it is particularly valuable for boys with DMD. As physical ability declines with disease progression, modifications to diet, such as increasing vegetable intake to reduce energy density is one of the key strategies to attenuate weight gain. (159) Improving diet quality is also important to prevent or assist in the management of diet- or obesity-related co-morbidities which are prevalent in DMD. For example, young males with DMD are at risk of insulin resistance and hypertension. (61,96,99) By improving diet quality such as by increasing the amount of wholegrains and fibre and reducing the glycaemic load, insulin sensitivity may be improved. (160) Increasing fibre-rich foods with adequate fluid intake can also help in the management of constipation, which is a common issue in DMD. (161)

This study has several limitations. The small sample size of ambulatory boys aged five to 13 years means that the findings may not be applied to non-ambulatory or older males with DMD. We also do not describe the changes in dietary intake as boys' transition from the ambulatory to non-ambulatory phase, which will be important to explore further. This study is also observational and therefore does not describe causality between dietary intake and BMI z-score and body composition outcomes. There are known limitations in accurate reporting of food and drink intake and therefore estimating dietary intake, however, the parent-reported three-day food diary methods used in this study have been previously demonstrated to be accurate for energy intake when compared to energy expenditure using the reference method of doubly labelled water. (90) Water intake was poorly reported in food diaries and was therefore not analysed, this will be important to explore in future research as the importance of fluids to prevent constipation and renal dysfunction is

specifically highlighted in clinical care guidelines. (24) This study is strengthened by providing the first comprehensive analysis of dietary intake beyond energy and macronutrients. Majority of the participants in our study were also steroid-treated which is acknowledged best practice internationally.

3.6 Conclusion

This is the first dietary analysis of boys with DMD in Australia (see Box 19). We observed that boys with the highest BMI z-scores and FM have the lowest energy intakes. So, the cause of excessive weight gain in the DMD population remains poorly understood and may not solely be attributed to excess energy intake. The early ambulatory stages of disease when energy intakes are highest may be a key time period to implement obesity prevention strategies and improve food eating behaviours and food choices. Addressing poor dietary quality is an important factor to address to attenuate weight gain and manage diet-related co-morbidities in the non-ambulatory phase.

Box 19

Contribution to Knowledge Gaps (Chapter 3)

In Australian ambulatory boys with DMD…

- Those who are younger and have better motor function may have excessive energy intakes.
- Majority of boys have adequate intake of micronutrients.
- Consumption of discretionary food intake may be excessive and consumption of core food groups such as fruit and vegetables low, although comparable to healthy Australian children
- A lower protein to energy ratio and higher discretionary food intake may drive higher total energy intakes.

Chapter 4.

Consulting the Evidence Base Regarding Weight Management Strategies for Young People with Chronic Healthcare Needs

Peer reviewed journal article:

Title: Weight Management Interventions That Include Dietary Components for Young People with Chronic Healthcare Needs: A Systematic Review

Authors: Natassja Billich, Isabella Maugeri, Lara Calligaro, Helen Truby, Zoe Davidson

Manuscript in press for *Nutrition & Dietetics*

Conference abstract:

Australia and New Zealand Obesity Society Annual Scientific Meeting 2018

Melbourne

Poster presentation

4.1 Preamble

High rates of obesity are not only observed in young people with DMD. The World Health Organization estimates the global prevalence of overweight and obesity in children and adolescents to be approximately 18-19% and 6-8%, respectively. (162) However, young people with chronic healthcare needs have a higher risk of overweight and obesity compared to general populations.(141,163) Young people with chronic healthcare needs refers to those having a disease or condition that is chronic and difficult to treat or incurable and who require health services beyond what is usually required.(164,165) For the purpose of this systematic review, populations of interest were those with chronic healthcare needs whose condition or its management or treatment increases the risk of overweight or obesity. Examples include young people with autism spectrum disorder, intellectual disabilities and survivors of cancers. The prevalence of obesity is approximately twice as high in young people with autism spectrum disorder (18%) and intellectual disabilities (13-15%) and up to six times as high for DMD (13-47%) and survivors of acute lymphoblastic anaemia (6-48%).(5,140,166,167) Weight management in young people with chronic healthcare needs poses unique and complex challenges for clinicians and families. For example, these young people may have higher learning needs, limited mobility, require medication that affects appetite, have particular food preferences or feeding difficulties in the context of managing complex healthcare needs. (141,168,169)

The World Health Organization recommends that a family-based multicomponent approach involving diet, physical activity and psychosocial support should be the foundation for all overweight and obesity interventions for children and adolescents.(170) Dietary components within weight management interventions may attain greater importance for young people with chronic healthcare needs, where physical activity interventions may not be feasible and/or where drugs or surgery are not appropriate first line therapies. Questions arise as to what and how dietary interventions for weight management should be delivered for these populations so that the complexity of managing chronic health conditions is taken into consideration. Whilst numerous dietary strategies both with and without physical activity or behaviour interventions have been evaluated in typically developing paediatric populations, the evidence base on dietary strategies for young people with a broad range of chronic healthcare needs has not been systematically reviewed.(115,116,120-122) Two scoping reviews exist that focus on weight management for young people with disabilities: one

focussing on obesity prevention and the other obesity management.(171,172) Within the scope of these reviews were young people with physical disabilities (obesity prevention) and those with a range of disabilities including intellectual and physical disabilities (obesity management). The latter scope of the literature from 2007-2017 identified five studies which indicated tailored weight management programs for children with disabilities that are family-focussed may contribute to successful weight management. (172)

Considering the paucity of evidence for weight management in DMD, this systematic review will draw upon the broader literature for young people with chronic healthcare needs. This review will build upon existing knowledge for young people with chronic healthcare needs by identifying and describing the scope of weight management interventions available, and to identify evidence for optimal dietetic management (see Box 20). This systematic review will also build upon a previous scoping review to provide an updated search for weight management interventions for those with disabilities. (172)

Box 20

Identified Knowledge Gaps (Chapter 4)

In young people with chronic healthcare needs…

- The scope of weight management interventions that are available for this broad population.
- Optimal dietetic management strategies.
- The effect of weight management strategies on BMI, weight and other health outcomes.

4.2 Aims

The aims of this systematic review are:

1. To determine what weight management interventions that include a dietary component are available for young people with chronic healthcare needs who have overweight or obesity.
2. The effect of weight management interventions that include a dietary component on BMI or weight for young people with chronic healthcare needs.

4.3 Methods

The reporting of this systematic review complies with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statements. (173,174) The study protocol was registered with PROSPERO on 23rd October 2017 (Registration number: CRD42017079036).

4.3.1 Search Strategy

The initial search was conducted on 19 October 2017 and updated on 1 June 2020. Six databases were searched: Ovid MEDLINE, Ovid Embase, Ovid AMED, Ebsco CINAHL, Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews and Scopus. Briefly, search terms were determined using the PICOS (Population, Intervention, Comparator, Outcome, Study type) framework: children AND "chronic disease" (P); "weight management" AND intervention (I); and weight OR "body mass index" (O). See Appendix I for the full search strategy in Ovid MEDLINE. Comparator and study type were not used to develop the search. Where possible, limits were applied for English language articles only. The search strategy was validated by identifying five articles that met the inclusion criteria and verifying that the search terms retrieved these articles when entered into Ovid MEDLINE and Ovid Embase. Reference lists of relevant literature reviews and of the final included studies were hand searched for any relevant articles (backwards citation searching). Included studies were also searched in Scopus to identify any relevant citing literature (forward citation searching).

4.3.2 Study Eligibility Criteria

For inclusion in the review, study populations were required to be a young person (0-18 years) with chronic healthcare needs and overweight or obesity. Two definitions were used to guide the population inclusion criteria. The first was for children and youth with special healthcare needs: "those who have or are at risk for a chronic physical, developmental, behavioural, or emotional condition and who also require health and related services of a type or amount beyond that required by children generally". (165) The second was a definition of chronic disease in childhood, that is, a disease or condition that is diagnosable, chronic (likely to be present for > 3 months) and difficult to treat or incurable. (164) Also within the scope of this review were young people who had undergone treatment for a chronic condition such as survivors of cancers or those with congenital heart disease who had undergone surgery. These populations were included due to the long-term effects of their chronic condition or its treatment, including an ongoing increased risk for overweight or obesity. (175-179) It was required that overweight and obesity were classified using appropriate paediatric reference sets e.g. CDC growth charts. (40) The wide age criteria of 18 years or less was used to identify the scope of literature available for younger children through to adolescents.

For the purposes of this systematic review, the definition of young people with chronic healthcare needs was further refined into subcategories that describe the relationship between the condition and overweight and obesity: 1) chronic conditions that cause an increased susceptibility to overweight or obesity due to the nature of the condition and/or its management (e.g. physical disabilities); 2) conditions that are directly caused by overweight or obesity (e.g. type 2 diabetes mellitus); 3) conditions that have a bi-directional relationship with overweight or obesity (e.g. polycystic ovarian syndrome) and; 4) genetic causes of overweight/obesity and appetite dysregulation (e.g. Prader-Willi syndrome), see Table 45. To align with the intention of the review and its aim, this review focuses on studies where the majority of the study population align with subcategory 1). Overweight and obesity is likely amenable to dietary intervention in this subcategory; and combining subcategories would introduce considerable heterogeneity.

Table 45

Prevalence of Obesity and Associated Factors Among Young People with Chronic Healthcare Needs and The Population Scope of This Systematic Literature Review

Population group	Obesity prevalence	Factors associated with overweight and obesity
Examples of populations with increased susceptibility to obesity (within the scope of this systematic review)		
Autism spectrum disorder	18% (140)	Psychotropic medications, (140,180-182) feeding difficulties and limited food acceptance, (141,183) sleep problems, (140) food as behavioural reinforcement. (141)
Intellectual disabilities	13-15% (166)	Psychotropic medications, low physical activity. (184)
Down syndrome	0–63% (185)	Leptin resistance, low physical activity, (185) reduced energy requirements and hypotonia. (141)
Learning & behavioural disabilities	10-20% (186,187)	Abnormal eating patterns, low physical activity, food as behavioural reinforcement, binge eating, frequent snacking. (188,189)
Muscular dystrophy	13-47% (5)	Reduced muscle mass, mobility, physical activity and energy expenditure, steroid treatment. (24,33,61,168)
Cerebral palsy	12% (169)	Reduced muscle mass, mobility, physical activity, hypothalamic damage. (169)
Hearing/visual impairments	20% (187)	Low physical activity, poor food choices, less aware of appearances (visual impairments). (190,191)
Spina bifida	8-18% (192)	Reduced mobility and physical activity, reduced LM and reduced energy expenditure. (193,194)
Survivors of cancers	6-48% (167)	Cranial radiotherapy, (167,195) steroid treatment, (33,167) obesogenic behaviours during treatment. (167)

Examples of populations outside the scope of this systematic review			
Children and youth with overweight or obesity who are otherwise healthy	**Conditions caused by overweight and obesity:** Type 2 diabetes mellitus, non-alcoholic fatty liver disease, OSA, hypertension, hypercholesterolaemia and dyslipidaemia	**Conditions with a bi-directional relationship with overweight and obesity:** Asthma, polycystic ovarian syndrome	**Genetic causes of overweight and obesity and appetite dysregulation:** Prader-Willi syndrome, individuals with variants affecting *LEP*, *MC4R* and *BDNF* genes

We initially searched for some conditions which were later excluded: asthma was initially included due to some evidence suggesting it increases susceptibility to weight gain and; Prader-Willi syndrome due the condition having features of neurodevelopmental disabilities such as intellectual disability and hypotonia. (196,197) However, on review, these conditions were thought to be more appropriately classified as having a bi-directional relationship with overweight and obesity (asthma) and genetic causes of overweight and obesity and appetite dysregulation (Prader-Willi syndrome). (198-200)

Eligible interventions included a dietary component as a treatment strategy for overweight or obesity. Interventions could be diet-only or multicomponent including behavioural therapy, physical activity, drugs or surgery. Diet-only interventions were defined as those involving dietary components only (e.g. prescription of energy intake), whereas interventions that utilised behaviour change techniques (e.g. Cognitive Behavioural Therapy) or physical activity counselling, encouragement or prescription were considered to be diet + behavioural and diet + physical activity respectively. There were no criteria set for the type of comparator. Eligible outcomes were measured BMI (body mass index, as kg/m^2 or z-score values) or weight.

All experimental study designs were eligible for inclusion, as well as systematic literature reviews and meta-analyses. We excluded qualitative studies, case reports and those reported in grey literature. There were no restrictions on length of intervention, setting, who delivered the intervention or the date of publication. Only articles published in English were eligible for inclusion.

4.3.3 Study Selection Procedures

All citations identified through the search strategy were imported into EndNote (*Endnote Version 8.1*. Philadelphia: Clarivate Analytics; 2017). After removal of duplicates in Endnote remaining citations were imported into Covidence (*Covidence systematic review software*. Melbourne: Veritas Health Innovation) for management of the review process including study selection, data extraction and quality appraisal. Information extracted from studies included: study identification, conflicts of interest, study methodology, population characteristics, intervention details and outcomes. The Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence (201) and the Cochrane Risk of Bias tool (202) was

applied to included studies. NB and IM independently screened articles (titles and abstracts and full texts) and NB and LC independently performed data extraction and risk of bias assessment. Discrepancies were resolved by a discussion and if a consensus could not be reached a third researcher was consulted (ZD). NB performed forwards and backwards citation searching to identify any additional relevant articles.

4.3.4 Outcome Measures

Primary and secondary outcomes were pre-defined in the review protocol and subsequently data were analysed and reported according to these outcomes. Primary outcomes were BMI (kg/m^2 or z-score) or weight. Secondary outcomes were overweight or obesity prevalence, body composition, dietary intake, physical activity, metabolic markers, disease-related markers, psychological outcomes and adverse events.

4.3.5 Data Synthesis and Analysis

Due to the scoping nature of this review, the heterogeneity of included populations and the small number of RCTs available in the literature (n=5), it was not appropriate to conduct a meta-analysis. All primary and secondary outcomes were synthesised narratively according to primary diagnosis.

4.4 Results

The combined initial and updated literature search identified 15293 references from which 12 studies were identified from 13 publications (see Appendix D for PRISMA flow diagram). (203-215) One study reported both short- and long-term outcomes in two separate articles, results from both were included. (205,212) There were no systematic reviews or meta-analyses that met the eligibility criteria.

Table 46 summarises the characteristics of included studies. Of the 12 included studies, five were RCTs and seven were single arm before and after comparisons. Eight studies were conducted in the United States of America (USA), (204,205,207,209-211,213,214) two in Canada (203,206) and one from Hong Kong, (208) and Italy. (215) The mean ages of the participants recruited ranged from nine to 16 years old. Study sample sizes ranged from 9 to 135.

Table 46

Study characteristics of studies included in the systematic review, structured by participant diagnosis [1]

Study ID	Design: LoE	Country; Setting; recruitment sources	Intervention name (baseline n)	Participant primary diagnosis	Ov/ob; age; % female; medications
Brown 2015 (204)	BA: 4	USA; Outpatient clinic; Specialist weight management clinic	*Brenner FIT* (111)	Attention deficit hyperactivity disorder 16%, learning disabilities 12%, intellectual disabilities 5%, autism spectrum disorder 3%, cerebral palsy, auditory processing disorder, Down & Williams syndrome 1%	Ob; 12y; 56% F; not reported
Gillette 2014, Pona 2017 (205)-(212)	BA: 4	USA; Outpatient clinic; Specialists and primary care	*Special Needs Weight Management Clinic* (76)	Autism spectrum disorder 50%, Down syndrome 24%, developmental delay 16%, intellectual disabilities 5%, Prader-Willi syndrome 3%, cerebral palsy 3%	Ob; 10y; 36% F; not reported
Lee 2017 (208)	RCT: 2	Hong Kong; School and community; Special development schools	*a. School Based Weight Management Program* (63) *b. Control* (52)	Mild intellectual disabilities	Ov + ob; a. 13y 24% F b. 15y 35% F; not reported

Table 46

Study characteristics of studies included in the systematic review, structured by participant diagnosis [1]

Study ID	Design: LoE	Country; Setting; recruitment sources	Intervention name (baseline n)	Participant primary diagnosis	Ov/ob; age; % female; medications
Matheson 2019 (210)	BA: 4	USA; Unclear; Flyers, email mailing lists, physician referrals	*TEAM UP* (20)	Autism spectrum disorder	Ov + Ob; 10y; 10% F; 20% stimulants, clonidine fludrocortisone or antipsychotics
Nicol 2019 (211)	RCT: 2	USA; Outpatient clinic; Primary care	*a. Behavioural Weight Loss Intervention* (19) *b. Recommended Care* (7)	Neurodevelopmental disabilities (autism spectrum disorder, learning disabilities, intellectual disabilities) 62%, attention deficit hyperactivity disorder 19%, mood 12%, anxiety 4%, psychotic 4% disorders	Ov + Ob; a. 13y 26% F b. 13y 14% F; 100% antipsychotics
Ptomey 2015 (213)	RCT: 2	USA; Community; Community programs, flyers, e-mail	*a. Enhanced Stop Light Diet* (10) *b. Conventional Reduced Energy Diet* (10)	Autism spectrum disorder 45%, Down syndrome 40%, other neurodevelopmental disabilities 15%	Ov + Ob; a. 16y 50% F b. 14y 40% F; not reported
Hamilton 2011 (206)	BA: 4	Canada; Outpatient clinic; Specialist clinic	*Lifestyle + metformin + diazoxide* (9)	Craniopharyngioma (benign) tumour with hypopituitarism	Ob; 15y; 44% F; 78% growth hormone; 89% sex steroid

Table 46

Study characteristics of studies included in the systematic review, structured by participant diagnosis [1]

Study ID	Design: LoE	Country; Setting; recruitment sources	Intervention name (baseline n)	Participant primary diagnosis	Ov/ob; age; % female; medications
Huang 2014 (207)	RCT: 2	USA; Community; Specialist clinic	*a. Fit4Life* (19) *b. Control* (19)	Acute lymphoblastic leukaemia	Ov + Ob; median 13y; a. 37% F b. 42% F; not reported
Lustig 1999 (209)	BA: 4	USA; Outpatient clinic; Specialist clinic	*Lifestyle + octreotide* (9)	Brain tumour 78%, acute lymphoblastic leukaemia 22%, all with cranial insult and a hypothalamic endocrinopathy secondary to tumour, surgery or radiation	Ob; 10-18y; 56% F; 100% thyroxine, 56% hydrocortisone, 33% outpatient clinic, 22% desmopressin & carbamazepine, 11% leuprorelin & testosterone
Stern 2018 (214)	RCT: 2	USA; Outpatient clinic; Specialist clinic	*a. NOURISH-T* (27) *b. Enhanced Usual Care* (26)	Lymphoma or acute lymphoblastic leukaemia 56%, sarcoma 7%, brain cancer 19%, other/unknown diagnosis 19%	Ov + Ob (Ob=96%); a. 9y 48% b. 11y; 58%; nil meds affecting weight
Altamirano-Diaz 2017 (203)	BA: 4	Canada; Community; Specialist clinic	*Smart Heart -operated* (19) & *non-operated* (15)	Congenital heart disease with or without corrective surgery	Ov + Ob; 14y; 44% F; nil confounding meds

Table 46

Study characteristics of studies included in the systematic review, structured by participant diagnosis [1]

Study ID	Design: LoE	Country; Setting; recruitment sources	Intervention name (baseline n)	Participant primary diagnosis	Ov/ob; age; % female; medications
Verrotti 2013 (215)	BA: 4	Italy; Outpatient clinic; Specialist clinic	*Weight Loss Program* (135)	Chronic migraine	Ob; 16y; 58% F; 62% migraine meds

[1] Age is reported as mean unless otherwise specified
Abbreviations: BA, before and after comparison; F, female; LoE, Level of Evidence; Ob, obese; Ov, overweight; RCT, randomized controlled trial

Across the 12 studies, six involved young people with neurodevelopmental disabilities such as autism spectrum disorder or intellectual disabilities who were mostly recruited from the community or primary care. (204,205,208,210-213) One study included participants treated with anti-psychotics with a neurodevelopmental disability or a mood, anxiety or psychotic disorder. (211) Another study had a small number of participants (3%) with Prader-Willi syndrome, however as the majority of participants had a neurodevelopmental disability diagnosis this study remained included. (205) Majority of neurodevelopmental disabilities across studies were autism spectrum disorder, intellectual disabilities or other diagnoses affecting cognition (e.g. attention deficit hyperactivity disorder). There were no studies that exclusively recruited young people with physical disabilities however a small percentage of participants with diagnoses such as cerebral palsy, Down syndrome and Williams syndrome were included in three studies. (204,205,212,213) There were four studies in survivors of cancer or tumours, (206,207,209,214) one in young people with congenital heart disease with both operated and non-operated groups (203) and one in chronic migraine, all of whom were recruited from specialists clinics. (215)

Due to the inclusion of all study designs, a high risk of bias was detected in at least one domain for all studies. (203-215) The main sources of bias were selection bias, as majority of the studies (n=7) were before and after comparisons that did not randomly allocate participants; (203-206,209,210,212,215) and performance bias, due to lack of blinding of participants for lifestyle interventions. (203-213,215) The assessment of the methodologic quality of each study is summarised in Appendix D.

Interventions and the summary of their effect on BMI (absolute values or z-score) are described in detail in Table 47. Most studies (n=10) evaluated multi-component lifestyle interventions including dietary, behavioural and physical activity. (203,204,206-208,210,211,213-215) One study had dietary and behavioural components only. (205,212) Two studies included drugs in their intervention. One used octreotide which attenuates insulin secretion, compliance was with medication was high (8 out of 9 participants were compliant). (209) The other used a combination of diazoxide and metformin to simultaneously decrease insulin secretion (diazoxide) and improving response to insulin (metformin), compliance was measured using medication counts however compliance rate was not reported. (206) A dietitian was involved in the delivery of the intervention in seven studies (203-206,208,212-214) and a nutritionist in one study. (215) There were no studies

that evaluated bariatric surgery in their intervention. Across studies, seven reported to specifically tailor the intervention to participants' diagnoses. For young people with neurodevelopmental disabilities strategies to tailor interventions included: focussing on feeding difficulties and food acceptability, (205) using social stories, rewards and planning for high risk situations (210) and reducing the cognitive load of interventions e.g. by using visual cues rather than written lists. (211) For survivors of cancers and tumours interventions used targeted drugs (206,209) or in two studies focus groups with patients and care teams informed the development of interventions. (207,214) Of the ten studies not including drugs in the intervention, compliance to the intervention was reported in four studies measured by study visit attendance. (205,212) Retention at last follow-up ranged from 48-95% (from n=11 studies), majority of studies reported high retention (>80%).

Table 47

Description of Weight Management Interventions That Include a Dietary Component and Comparator Arms.

Study ID; Study arm (length of intervention) [1]	Delivery mode and timing; Delivery personnel	Family-focussed; Tailored	Diet	Other components (behaviour- theory or methods/physical activity- type/Drug) [2]	Adherence/ compliance; Retention at last follow-up	BMI/Wt [3]
Neurodevelopmental disabilities (n=5)						
Brown 2015(204); *Brenner FIT* (4m)	Biweekly F2F; MDT paed, counsellor, dietitian, physio, exercise specialist	Y; N	Nutrition counselling on grocery shopping, meal tracking, drink choices	*Behaviour* - Goals, behaviour modification, motivational interviewing/ *Physical activity* - Individual	Not reported; 61%	≈/ not reported
Gillette 2014, Pona 2017(205,212); *Special Needs Weight Management Clinic* (12m)	Face-to-face at mo 1, 2, 3, 6, 12; MDT psych, nurse, paed, dietitian, occupational therapist	Y; Y	Individual diet, focus on feeding difficulties and food acceptability	*Behaviour* - Stimulus control, goals	2.9 ± 1.5 sessions attended; 48%	↓/ not reported
Lee 2017(208); *a. School Based Weight Management Program*	Face-to-face family group× 16 + online × 8; physical activity specialist, dietitian, psych, nurses	Y; N	Education on healthy diet & parenting skills. Games & activities	*Behaviour* - Social Cognitive Theory, parental & social support/ *Physical activity* - Education	Not reported; not reported	?/?
b. Routine Care (24w)	Biweekly routine physical activity classes, unclear frequency of health talks; Unclear	N; N	Posters promoting healthy lifestyle & health talks on dietary habits	*Physical activity* - Structured		?/?

Table 47

Description of Weight Management Interventions That Include a Dietary Component and Comparator Arms.

Study ID; Study arm (length of intervention) [1]	Delivery mode and timing; Delivery personnel	Family-focussed; Tailored	Diet	Other components (behaviour- theory or methods/physical activity- type/Drug) [2]	Adherence/ compliance; Retention at last follow-up	BMI/Wt [3]
Matheson 2019(210); *TEAM UP* (16w)	Face-to-face weekly parent sessions, 1 session child included; Graduate student trained in parent-based training	Y; Y	20% energy reduction aim 1000–1200 kcals for 5/7 days & 5 fruit/veg servings/day, written info	*Behaviour* - Family-based therapy, parenting advice, goals, motivational interviewing, self-monitoring, planning, relapse prevention/ *Physical activity* – Encouraged + structured (1 class)	63% attended >80% treatment sessions; 85%	↓/ not reported
Ptomey 2015(213); *a. Enhanced Stop Light Diet*	Face-to-face × 1 + weekly video chat, Lose It! App to track diet + FitBit™; dietitian	N; N	Low energy portion-controlled entrees (×2) + shakes (×2) provided + 5 fruit/veg serves/day + 'green' or 'amber' TLS foods if hungry.	*Behaviour* - Social support, self-monitoring, environmental control, self-efficacy/ *Physical activity* - Individual	Not reported; 95%	≈/↓
b. Conventional Reduced Energy Diet (8w)	Face-to-face × 1 + weekly video chat, Lose It! App to track diet + FitBit; dietitian	N; N	500-700 kcal/day deficit, high volume, low fat diet, ≥ 5 fruit/veg serves/day.	As above		≈/↓

Table 47

Description of Weight Management Interventions That Include a Dietary Component and Comparator Arms.

Study ID; Study arm (length of intervention) [1]	Delivery mode and timing; Delivery personnel	Family-focussed; Tailored	Diet	Other components (behaviour- theory or methods/physical activity- type/Drug) [2]	Adherence/ compliance; Retention at last follow-up	BMI/Wt [3]
Neurodevelopmental disabilities and mental illness (n=1)						
Nicol 2019(211); *a. Behavioural Weight Loss Intervention*	Face-to-face weekly; social worker or counsellor	Y; Y	Dietary advice using traffic light system	*Behaviour* - Socio-ecological framework, self-monitoring, goals, problem solving/ *Physical activity* - Individual	64% sessions attended, compliance assessed by homework completion and quality; 79%	↓/≈
b. Recommended Care (16w)	Face-to-face monthly; social worker or counsellor	Y; N	Dietary advice using traffic light system	*Behaviour* - Problem solving only/ *Physical activity* - Individual	79% sessions attended; 86%	≈/≈
Survivors of cancers or tumours (n=4)						
Hamilton 2011(206); *Lifestyle + metformin + diazoxide* (6m lead-in/treatment)	Monthly face-to-face + weekly phone call in 1st mo; MDT: nurse, dietitian, exercise physiologist, psych, social worker	N; Y	Dietary counselling (lead-in and treatment)	*Behaviour* - Psych counselling for behaviour change/ *Physical activity* – Individual/*Drug* - metformin + diazoxide (treatment phase)	Compliance measured by tablet count; 78%	↓/↓ during treatment phase only

Table 47

Description of Weight Management Interventions That Include a Dietary Component and Comparator Arms.

Study ID; Study arm (length of intervention) [1]	Delivery mode and timing; Delivery personnel	Family-focussed; Tailored	Diet	Other components (behaviour- theory or methods/physical activity- type/Drug) [2]	Adherence/ compliance; Retention at last follow-up	BMI/Wt [3]
Huang 2014(207); *a. Fit4Life*	Phone call weekly mo 1, biweekly mo 2-4 + weekly resources + SMS 2/day; health coach	Y; Y	Dietary counselling for calorie reduction	*Behaviour* - Social Cognitive Theory, goals, self-monitoring/ *Physical activity* - Individual	80% of the intervention was received; 95%	≈/≈
b. Control (4m)	phone call biweekly mo 1, monthly mo 2-4 + monthly resources; health coach	Y; N	Written nutrition materials for weight management	*Physical activity* - Education	50% of the intervention was received; 90%	≈/≈
Lustig 1999(209); *Lifestyle + octreotide* (6m lead-in/treatment)	Monthly face-to-face; Unclear	N; Y	Dietary counselling-calorie restrictions (lead-in & treatment)	*Physical activity* – Encouraged/*Drug* - octreotide	1/7 non-compliant with medication; 89%	↓/↓ during treatment phase only

Table 47

Description of Weight Management Interventions That Include a Dietary Component and Comparator Arms.

Study ID; Study arm (length of intervention) [1]	Delivery mode and timing; Delivery personnel	Family-focussed; Tailored	Diet	Other components (behaviour- theory or methods/physical activity- type/Drug) [2]	Adherence/ compliance; Retention at last follow-up	BMI/Wt [3]
Stern 2018*(214)* ; *a. NOURSH-T*	6 individual/small caregiver group, face-to-face session 1/6 + phone call sessions 2-5 + 1 group + 1 booster session; group leaders, 1 session oncology dietitian & physio	Y; Y	Education; ov/ob & healthy eating post cancer treatment, portion control, mindful eating, fruit/veg	*Behaviour* - Social & Cognitive Behavioural Theory, parenting advice, goals, self-monitoring, contingency management, stimulus Control/ *Physical activity* - Education	Not reported; 67%	≈/ not reported
b. Enhanced Usual Care (6w/4 m)	1 face-to-face group & 1 booster session + resources; unspecified	Y; N	Generic weight management advice (We Can! Manual)	*Physical activity* - Education	Not reported; 73%	≈/ not reported
Congenital heart disease (n=1)						
Altamirano-Diaz 2017*(203)*; *Smart Heart* (12m)	Weekly phone call (50 in total) ≤30 min each; dietitian + fitness specialist	Y; N	Tailored dietary counselling on set topics	*Behaviour* - Planning, goals, overcoming barriers, routine/ *Physical activity* – Individual	Not reported; 94%	↓ operated group only/ not reported

Table 47

Description of Weight Management Interventions That Include a Dietary Component and Comparator Arms.

Study ID; Study arm (length of intervention) [1]	Delivery mode and timing; Delivery personnel	Family-focussed; Tailored	Diet	Other components (behaviour- theory or methods/physical activity- type/Drug) [2]	Adherence/ compliance; Retention at last follow-up	BMI/Wt [3]
Chronic migraine (n=1)						
Verrotti 2013(215); *Weight loss program* (12m)	Face-to-face weekly for diet/ physical activity + 4 monthly for behaviour; Nutritionist, psych & physio	Y; N	15–20% energy deficit. Increased fibre, decreased fat & sugar sweetened beverages	*Behaviour* - Cognitive behavioural therapy/*Physical activity*– Individual	Not reported; 90%	↓/↓

[1] Where only one time is specified intervention length=follow-up length, for all RCTs studies intervention length/follow-up was the same for both arms. Intervention length is in months unless otherwise specified.
[2] Physical activity categories: Structured= group exercise or organised fitness, individual= counselling or individual advice, education= information delivered or lectures, encouraged= encouraged only
[3] BMI refers to effect of the intervention on absolute BMI or z-score; ≈ no significant effect; ↓ significant decrease; ? unclear effect due to insufficient information
Abbreviations: d, day; kcal, kilocalorie; MDT, multidisciplinary team; m, months; N, no; ob, obesity; ov, overweight; physio, physiotherapist; psych, psychologist; w, week; Y, yes

Primary outcome data for BMI (as kg/m2, percentile or z-score) and weight is detailed in Table 48. Eight studies observed significant reductions in BMI or weight following the interventions. Two of these studies utilised individual dietary counselling and goal-setting: one including young people with neurodevelopmental disabilities (*Special Needs Weight Management Clinic*) and the other congenital heart disease (*Smart Heart – operated group*). (203,205) One study including young people with autism spectrum disorder (*TEAM UP*) focussed on parental behaviours, prescribed an energy deficit of 20% and set specific fruit and vegetable targets. (210) For young people with migraine (*Weight loss program*), a 15-20% energy deficit prescription with a focus on increased fibre and decreased fat and sugar-sweetened beverages, cognitive behavioural therapy and individual physical activity advice was associated with reductions in BMI. (215) The remaining two interventions both for survivors of cancer or tumours (*Lifestyle + metformin + diazoxide* and *Lifestyle + octreotide*) observed significant decreases in BMI during the drug treatment phases only. (206,209) One RCT including young people with neurodevelopmental disability observed a significant reduction in weight (but not BMI) in both study arms; one intervention included portion-controlled meals and shakes (*Enhanced Stop Light Diet*) and the other a prescribed 500-700 kcal energy deficit (*Conventional Reduced Energy Diet*), both were delivered by a dietitian. (213)

Table 48

Effects of Weight Management Interventions That Include a Dietary Component on Primary and Secondary Outcomes.

Study ID	Study group	Outcome	Baseline (n)	Post-int. or change Δ (n) [1]	Secondary outcomes key findings [2]
Neurodevelopmental disabilities (n=5)					
Brown 2015(204)	*Brenner FIT*	BMIz	2.5 ± 0.5 (111)	Δ -0.09 ± 0.17 (56)	**Metabolic:** Within group comparison over time not tested
Gillette 2014, Pona 2017(205),(212)	*Special Needs WM Clinic*	BMIz	2.42 ± 0.47 (63)	1-6 mo: 2.37 ± 0.51 (63)*, 12 mo: Δ -0.02/mo	**Diet:** ↑ types of fruits, vegetables, grains, meats, no change to dairy foods.
Lee 2017(208)	*a. School-based WM program*	BMI	NR	25.7 ± 0.18 (63)	Baseline or change data for secondary outcomes not recorded.
		Wt	NR	62.7± 0.36	
	b. Routine Care	BMI	NR	25.9 ± 0.16 (52)	
		Wt	NR	63.2 ± 0.35	
Matheson 2019(210)	*TEAM UP*	BMIz	2.17 ± 0.46 (20)	1.92 ± 0.59 (17)**	**Diet:** ↑ vegetables **Physical activity:** ↑ episodes of PA
Ptomey *et al.* 2015(213)	*a. Enhanced Stop Light Diet*	BMI	30.7 ± 7.3 (10)	Δ -1.6 ± 0.9 (10)	**Body composition:** (a) -2.8cm, (b) -3.2cm waist circumference**,** significance not recorded **Diet:** (a, b) ↓ kcal (-845 and -675, respectively), (a)>(b). (a, b) ↓ carbohydrate, protein and fat intake, ↑ diet quality **Physical activity:** (a,b) ↓ sedentary activity
		Wt	82.3 ± 29.8	Δ-3.9 ± 2.7**	
	b. Conventional Reduced Energy Diet	BMI	26.9 ± 5.3 (10)	Δ -1.0 ± 0.4 (10)	
		Wt	65.1 ± 25.3	Δ-2.2 ± 1.4**	

Table 48

Effects of Weight Management Interventions That Include a Dietary Component on Primary and Secondary Outcomes.

Study ID	Study group	Outcome	Baseline (n)	Post-int. or change Δ (n) [1]	Secondary outcomes key findings [2]
Neurodevelopmental disabilities and mental illness (n=1)					
Nicol 2019(211)	*a. Behavioural Weight Loss Intervention*	BMIz	2.01 ± 0.52 (19)	Δ -0.13 ± 0.17 (15)§	**% overweight/obese:** (a) ↓ % overweight. **Body composition:** (a,b) no change waist circumference, FM % (a) no change lean mass kg (b) ↑ LM 1.6kg **Metabolic:** (a,b) no change hepatic fat, carotid intima-media thickness, fasting glucose, cholesterol, HDL. (b) ↑ triglycerides (a) no change. (b) ↓ LDL (a) no change. **Condition-related:** No change in the Abberant Behaviour or Child Behaviour Checklist scores. **Adverse events:** Nil.
		Wt	78.0 ± 33.3	Δ -0.12 ± 3.04	
	b. Recommended Care	BMIz	2.08 ± 0.23 (7)	Δ -0.03 ± 0.13 (6)	
		Wt	68.6 ± 13.8	Δ 2.42 ± 2.36	
Survivors of cancers or tumours (n=4)					
Hamilton 2011(206)	*Lifestyle + MET + diazoxide*	BMIz	2.3 ± 0.3 (7)	Lead-in: Δ 0.11 ± 0.08, treatment: Δ -0.04 ± 0.15 (7)*	**Metabolic and condition-related outcomes:** No change triglycerides, cholesterol, HDL or LDL, insulin sensitivity, oral glucose tolerance test insulin or glucose, adiponectin, lepin, HbA1c, aspartate aminotransferase, alanine aminotransferase. **Adverse events:** Treatment phase oedema (n=1), elevated hepatic enzymes & vomiting (both n=1)
		Wt	99.7 ± 26.3	Lead-in: Δ 9.5 ± 2.7, treatment: Δ +1.2 ± 5.9**	

Table 48

Effects of Weight Management Interventions That Include a Dietary Component on Primary and Secondary Outcomes.

Study ID	Study group	Outcome	Baseline (n)	Post-int. or change Δ (n) [1]	Secondary outcomes key findings [2]
Huang 2014(207)	*a. Fit4Life*	BMIz	1.84 ± 0.32 (18)	Δ -0.08 ± 0.15 (18)	**Diet & physical activity:** (a,b) no change moderate-vigorous activity or energy intake. **Psychological:** (a) improved Children's Depression Inventory negative mood domain only.
		Wt	65.6 ± 19.5	65.5± 18.8	
	b. Control	BMIz	2.00 ± 0.41 (17)	Δ -0.01 ± 0.13 (17)	
		Wt	70 ± 17.6	71.4 ± 18.1	
Lustig 1999(209)	*Lifestyle + octreotide*	BMI	36.3 ± 2.2 (9)	Lead-in: Δ 2.1 SE 0.3, treatment: Δ -2.0 SE 0.7 (8)**	**Diet:** ↓ calories. **Metabolic:** ↓ insulin. **Condition-related:** ↓ insulin like growth factor 1**.** **Adverse Events:** gastrointestinal symptoms (n=7), gallstones (n=4), oedema (n=1).
		Wt	102.0 ± 10.0	Lead-in: Δ 6.0 SE 0.7, treatment: Δ -4.8 SE 1.8**	
Stern 2018(214)	*a. NOURSH-T*	BMI %	NR (27)	↓ (18) [3]	**Body composition:** waist:hip ratio (a) ↓, (b) no change. **Diet:** (a) ↓ sugar sweetened beverages, (b) no change however lower sugar sweetened beverages at baseline **Physical activity:** (a) ↑ (b) ↓ daily steps & self-reported activity.
	b. Enhanced Usual Care	BMI %	NR (26)	No change (19)	

Table 48

Effects of Weight Management Interventions That Include a Dietary Component on Primary and Secondary Outcomes.

Study ID	Study group	Outcome	Baseline (n)	Post-int. or change Δ (n) [1]	Secondary outcomes key findings [2]
Congenital heart disease (n=1)					
Altamirano-Diaz 2017(203)	*a. Smart Heart operated*	BMIz	2.06 ± 0.37 (18)	Δ -0.14 (95% CI -0.28, -0.002) (18) *	**Body composition:** (a) ↓ waist circumference (b) no change. (a,b) ↑ LM kg, no change waist:height ratio, FM %, LM% **Metabolic and condition-related:** No change heart rate, systolic BP, diastolic BP, HDL and LDL cholesterol, triglycerides, fasting glucose, HbA1c, insulin, HOMA-IR, max volume oxygen.
	b. Smart Heart non-operated	BMIz	1.63 ± 0.49 (14)	Δ 0.07 (95% CI -0.10, 0.24) (14)	
Chronic migraine (n=1)					
Verrotti 2013(215)	*Weight loss program*	BMI	32.9 ± 4.6 (135)	29.9 ± 6.0 (n=135) **	**Body composition:** ↓ waist circumference**. Condition-related:** ↓ headache frequency, intensity, medication, impairment (Paediatric Migraine Disability Assessment).
		Wt	85.2 ± 8.2	76.9 ± 9.1 **	

[1] *P<0.05 compared to baseline, **p<0.01 compared to baseline, § significant within group difference but p-value not reported, †p<0.05 between group comparison, ± indicates mean and standard deviation, square brackets indicates median and inter-quartile range, values separated by a hyphen in parenthesis indicates range
[2] Changes are within group comparison from baseline
[3] Results interpreted from graph, raw BMI values NR. Significant decrease when analysis was controlled for caregiver BMI & BMI percentile at baseline, however unadjusted analysis not significant.
Abbreviations: Δ, change; BMI, body mass index; BMIz, body mass index z-score; mo, months; BP, blood pressure; HbA1c, glycated haemoglobin A1c; HDL, high density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment insulin resistance; LDL, low density lipoprotein cholesterol; wt, weight (in kg)

Secondary outcomes measured were: body composition (n=5), diet (n=5), physical activity (n=4), metabolic (n=5), condition-related (n=5), and psychological outcomes (n=1) and adverse events (n=3), see Table 48. All studies that measured dietary outcomes observed positive changes including increased fruit or vegetable consumption (n=2), decrease in energy (n=2) and decrease in sugar-sweetened beverages (n=1). Majority of studies that measured metabolic markers did not observe significant changes following interventions. Disease-related outcomes measured were behaviour change in young people with neurodevelopmental disabilities or mental illness (n=1), metabolic markers and hormones in survivors of cancers and tumours (n=2), cardiovascular outcomes in young people with congenital heart disease (n=1) and measures of headache frequency, intensity, impairment and medication use in young people with chronic migraine (n=1).

4.5 Discussion

This extensive literature search demonstrates there is currently limited evidence available on the management of overweight and obesity in young people with chronic healthcare needs. In eight out of the 12 included studies, weight management interventions with a dietary component significantly reduced BMI or weight. There were also numerous beneficial effects on secondary outcomes including: improved dietary intake, body composition and physical activity levels. When considering the studies that were effective in reducing BMI or weight, potential themes across the types of interventions emerge. Most studies that were effective (except those with drug interventions) were family focused, delivered weekly by a multidisciplinary team including a dietitian or nutritionist and used individualised dietary counselling or negative energy balance to achieve weight change. Of the six lifestyle-only (without drugs) studies that demonstrated a significant decrease in BMI or weight, three adapted or tailored the intervention specifically to the healthcare needs of the participants based on their diagnoses. (205,210,211) These may be useful starting considerations to guide clinicians working with young people with chronic healthcare needs and may be useful for some dietitians to advocate for their role as a part of the multidisciplinary team.

There are many gaps in the evidence base for weight management in young people with chronic healthcare needs. Studies that are available cover specific conditions sporadically and many diagnoses are underrepresented or absent from the literature. For example, there were no studies that met the inclusion criteria that specifically recruited young people with physical disabilities. The paucity of high quality evidence on managing obesity in young people with chronic healthcare needs suggests, internationally, there is a lack of priority for weight management for these children. In a local context, there have been no studies conducted in Australia looking at obesity management in these populations. Yet, this is an overt problem recognised by bodies such as the CDC and Prevention and the Australian Institute of Health and Welfare. (163,216) Latest Australian data suggests 30% of children aged 5-14 years with a disability have overweight or obesity compared with 24% for those with no disability. (216) More research is urgently needed to identify effective weight management strategies in these vulnerable populations to ensure children and young people meet their growth and developmental milestones in the context of chronic health conditions and to reduce the risk of life-long morbidity related to overnutrition.

Across included studies, only five were RCTs and none could be included in an intervention vs. control meta-analysis. With the limited number of controlled trials, small sample sizes and heterogenous interventions, it is difficult to conclusively assess the impact of described interventions on primary outcomes or understand which intervention components are most effective. There may be several barriers to completing controlled trials in young people with chronic healthcare needs populations such as available funding, perceived low priority of weight management interventions in comparison to identifying treatments and the ethical issues associated with untreated groups in the context of weight management. Innovative trial designs, such as step-wedged or wait list controls, could be used in order to understand the effects of weight management interventions on BMI or weight status and other important outcomes such as metabolic health, physical function and quality of life. Younger children are also underrepresented with the mean age of participants across studies being nine years and older. This may be because we included only populations that already had overweight or obesity.

From this systematic review, several priority areas have been identified for future research planning with an understanding of how to manage overweight and obesity in young people with chronic healthcare needs. Managing overweight and obesity in the context of physical disabilities where the opportunity for increased physical activity is limited such as muscular dystrophies, cerebral palsy, skeletal dysplasia and brain and spinal cord injuries needs to be investigated. These populations present unique nutritional challenges in regards to weight management such as lower resting and/or total energy expenditure due to altered muscle mass and mobility, feeding difficulties and challenges regarding food provision and access. (141,168,169)

Psychological outcomes were measured in one study (changes in depressive symptoms) and none of the included studies reported on quality of life. Yet, depression, anxiety and eating disorders are common among young people with chronic healthcare needs (217) and there is a well established relationship between mental health concerns and overweight and obesity. (218) Outcome measures such as quality of life, symptoms of anxiety and depression and self-esteem as well as the involvement of mental health clinicians in the delivery of interventions will be paramount in future studies.

Whether interventions for young people with chronic healthcare needs should be specifically

tailored to individual conditions or groups of conditions (e.g. physical disabilities) needs further investigation. Future research should consider the implementation of weight management programs in these populations that considers competing healthcare priorities such as physical capabilities and function, regular therapy needs, medications, respiratory support and increased psychosocial concerns. Allied health professionals with expertise in different paediatric conditions are well placed to deliver tailored weight management interventions for young people with chronic healthcare needs. Adaptation and evaluation of existing community weight management programs for example, Mind Exercise Nutrition Do it (MEND) (219) (also translated to an Australian context as Go4Fun (220)), to these populations could be a potential strategy.

Strengths of this review include conducting a systematic and comprehensive search of the literature, including a broad scope of primary and secondary outcomes and a detailed description of interventions components and delivery. There are several limitations of this systematic review. Not all populations of young people with chronic healthcare needs were eligible for inclusion such as those with a condition that has a bi-directional relationship with obesity (e.g. polycystic ovarian syndrome) or those with genetic causes of obesity (e.g. MC4R deficiency). Lifestyle weight management interventions for young women with polycystic ovarian syndrome have previously been systematically reviewed, and show promising effects on clinical, metabolic and hormonal outcomes. (221) To systematically review the literature on the management of genetic obesity, a specialised and comprehensive search strategy of genetic variants will be required. (222) Another potential limitation of this study was the broad inclusion criteria including both those with an active chronic disease and those who had been treated and were in remission which introduced population heterogeneity. Included studies lacked robust methodological quality, introduced a high risk of bias and were limited by small sample sizes. There are also known flaws in using BMI z-score for obesity and alternative methods such as percentage of 95th percentile BMI should be considered in future research. (223) Our study was limited by only including studies published in English.

4.6 Conclusion

There is a concerning lack of evidence regarding the management of obesity on young people with chronic healthcare needs who have increased susceptibility to excessive weight gain. More robust, controlled trials need to be prioritised to understand how to optimally manage obesity in these populations and to what extent this may benefit physical and mental health. However, components of interventions that appear to lead to reduction in BMI or weight in young people with chronic healthcare needs are those that are multicomponent, family-focused interventions, delivered by a multidisciplinary team including a dietitian and use individualised dietary counselling or negative energy balance (see Box 21).

Box 21

Contribution to Knowledge Gaps (Chapter 4)

From a small amount of low quality evidence in young people with chronic healthcare needs…

- Weight management interventions including a dietary component may have beneficial effects on BMI, weight, dietary intake, body composition and physical activity levels.
- Interventions that are family focused, delivered weekly by a multidisciplinary team and use individualised dietary counselling or negative energy balance may assist in weight management.
- There are no studies that have specifically recruited young people with physical disabilities for weight management interventions.

Chapter 5.

Consulting Families and Healthcare Professionals to Develop a Weight Management Program for DMD

Peer reviewed journal article:

Ethics reference: HREC/51070/RCHM-2019

Peer-reviewed journal article:

Title: Consulting Families to Develop a Weight Management Program for Young People with Duchenne muscular dystrophy: A Multi-Site Survey

Authors: Natassja Billich, Paula Bray, Helen Truby, Maureen Evans, Monique Ryan, Kate Carroll, Katy de Valle, Daniella Villano, Andrew Kornberg, Bianca Sowerby, Michelle Farrar, Manoj Menezes, Sandra Holland, Rachel Lindeback, Anita Cairns, Zoe Davidson

In preparation

Conference presentation:

World Muscle Society 2020, virtual

Accepted poster with three-minute oral presentation

5.1 Preamble

Little is known about barriers and enablers to healthy eating and weight management for young people with DMD, see Box 22. There is a dearth of evidence regarding what weight management strategies are acceptable, feasible and important to families living with DMD. One approach to understanding what young people with DMD and their families want in weight management strategies is to consult with them using co-design processes. This has never been done before in DMD and is a key feature of this chapter.

Box 22

Identified Knowledge Gaps (Chapter 5)

Knowledge gaps regarding obesity management in DMD…

- There is limited evidence for obesity management in DMD, only two case studies have evaluated a weight management intervention for this population.
- Caregivers perceptions of the barriers and enablers to healthy eating and weight management have not been explored.
- For families with a young person with DMD, their preferences for the type of weight management strategies and their delivery is not known.

Co-design (also commonly referred to as participatory research) is an umbrella term that has been used to describe ways of involving consumers (e.g. patients and families) in research or healthcare interventions. (224) There is no best-practice method of conducting co-design research, (224) however there is potential to learn more from consumers the more that they are involved in research processes. (225) Co-design is recommended by the NHMRC who in 2016 released the *Statement on consumer and community involvement in health and medical research*. (226) The vision of the NHMRC statement is "consumers, community members, researchers and research organisations working in partnerships, to improve the health and well-being of all Australians through health and medical research.". (226) The NHMRC suggest effective strategies involve consumers and community members at various levels of research including; planning, seeking funding, conducting research and communicating the outcomes. (226)

This chapter describes the process and findings of co-designing a family-centred, lifestyle weight management program for young people with DMD. The steps in this co-process were: 1) a caregivers' survey; 2) development of a draft program of a draft program 3) further consultation with survey respondents; and 4) consultation with healthcare professionals. The proceeding chapter (Chapter 6) will then describe a feasibility and acceptability pilot study of the co-designed program. In the current and following chapter, the steps in developing and piloting this weight management program at a single site – RCH in Melbourne – are described. However, the caregivers survey described here has also be delivered at three additional sites: Sydney Children's Hospital Randwick and Children's Hospital at Westmead (part of the Sydney Children's Hospital Network in New South Wales) and Queensland Children's Hospital. This multi-site survey will form the submitted journal article associated with this chapter. Figure 37 provides an overview of the process for developing and piloting the weight management program at RCH and how findings from sites in New South Wales and Queensland will inform a future multi-site RCT. This multi-site RCT is described in further detail in Chapter 7 (future directions).

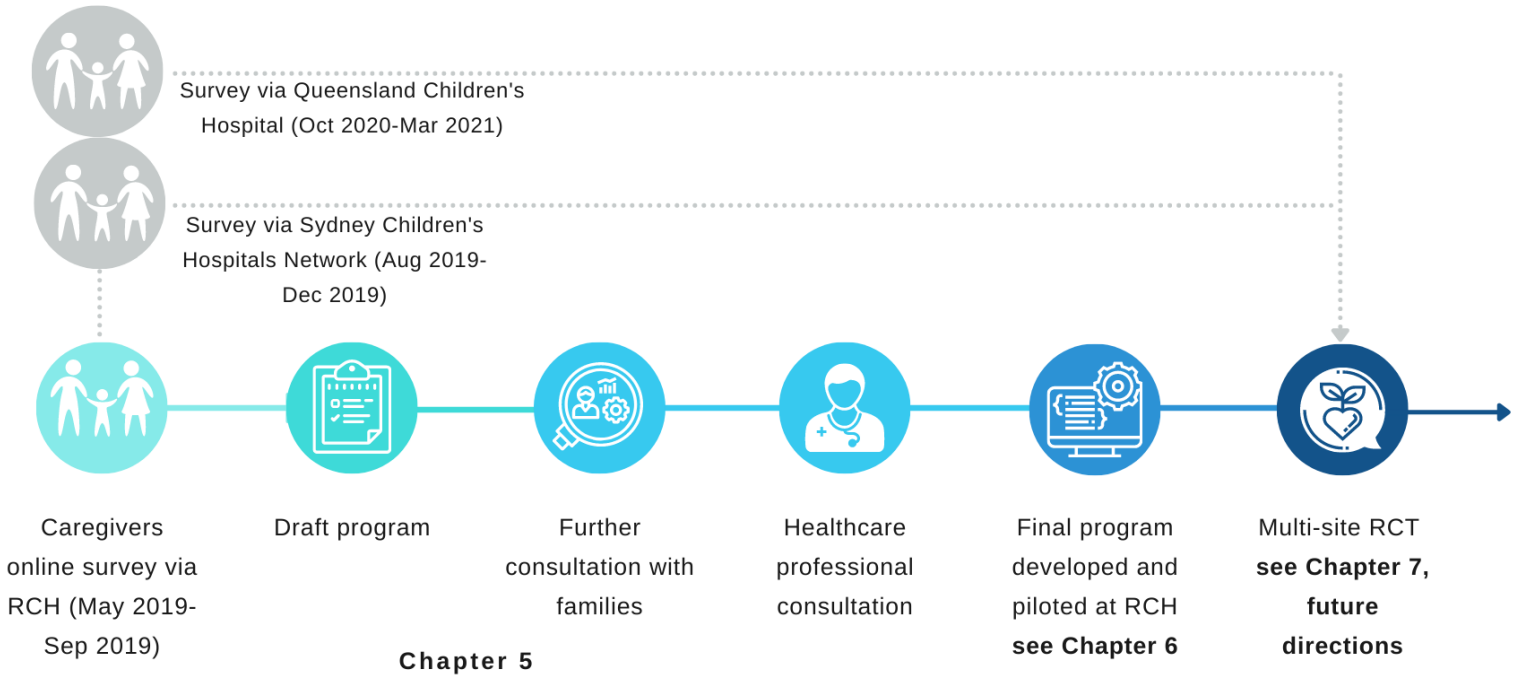


Figure 37

Overview of Processes for the Development of a Co-Designed Weight Management Program for DMD

5.2 Aims

The overarching aims of this study are to:

1. Identify barriers and enablers to managing weight for young people with DMD attending RCH and their families.
2. Partner with caregivers and healthcare professionals to co-design a lifestyle weight management program for young people with DMD.

The objectives of this study are to:

i. Identify the barriers to healthy eating experienced by families with a son with DMD.
ii. Explore caregivers' attitudes and beliefs about healthy eating and weight.
iii. Determine what influences caregivers' food provision and their son's food choices.
iv. Consult caregivers of a young person with DMD on their preferences for the design and delivery of a lifestyle weight management program.
v. Seek feedback and consult with survey respondents by sharing a proposed program outline.
vi. Consult with neuromuscular and nutrition healthcare professionals to inform the design of the weight management program.

5.3 Methods

5.3.1 Study Design, Setting and Participants

The first step of this study was a cross-sectional survey of caregivers of a young person with DMD from RCH in Melbourne. A convenience sample of caregivers were recruited if they had at least one child with a diagnosis of DMD who attended the neuromuscular clinic at RCH, were primarily responsible for the provision of food in their household, could read and understand English and, were willing to provide informed consent. There were no age limits for the young person with DMD, however as participants were recruited through a paediatric neuromuscular clinic they were likely 18 years or younger. Participants were excluded if they did not complete the survey in full, as it was assumed they were opting to withdraw from the study.

The survey consisted of two parts which addressed each of the primary aims of the study. The first part explored barriers and enablers to managing weight for young people with DMD (Aim 1); the second asked parents to co-design a weight management program for DMD (Aim 2).

Following the survey, caregivers who indicated they were willing to provide more feedback on the program's design were contacted via email. These caregivers were further consulted on a proposed program design and asked to record their feedback using a written questionnaire.

In the last step of this study, healthcare professionals were consulted on the program's design. A convenience sample of healthcare professionals from the research team's professional networks were invited to provide feedback on the proposed program. Healthcare professionals were recruited from a single site (RCH) and were chosen based on their expertise in neuromuscular disorders and/or paediatric nutrition and weight management. The RCH Research Governance Office approved all study procedures (HREC/51070/RCHM-2019).

5.3.2 Survey Development

The survey was developed by a multidisciplinary team of neuromuscular and nutrition researchers and clinicians including: dietitians, occupational therapists, physiotherapists and

neurologists. Demographic and clinical characteristics were first collected. Caregivers were asked to record information about their son's health including steroid treatment, self-reported height and weight (to enable calculation of BMI z-score) and functional mobility scale. The functional mobility scale scores functional mobility over three distinct distances which represents mobility in the home, at school and in the community. (227)

To explore the barriers and enablers to healthy eating and weight management (Aim 1) survey questions were informed by the Theoretical Domains Framework (TDF), see Table 49. (228) The TDF combines 33 theories of behaviour and behaviour change into 14 domains and aims to identify the cognitive, affective, social and environmental influences on behaviour. (228,229) Questions were also guided by previous literature which has described and used the TDF for survey development. (230)

To address Aim 2, caregivers were then asked to imagine their family was going to take part in a healthy lifestyle program and were asked to provide their preferences on various aspects of its design. See Table 49 for the aspects of the program design caregivers were consulted on. Caregivers were provided an opportunity to leave comments at the end of the first and second part of the survey. Caregivers could record their email address if they were willing to assist further developing the program and/or would like to receive more information about the program in the future.

Both parts of the survey were piloted amongst the multidisciplinary research team and with a convenience sample of caregivers recruited from personal and professional networks. Caregivers in the pilot phase of the survey did not have a son with DMD. This population for the piloting of the survey was chosen to avoid unnecessary burden on families who have a son with DMD. Furthermore, as DMD is a rare disease we wanted to optimise available participants for recruitment for the final survey. The purpose of piloting the survey was to test face validity by ensuring appropriate survey flow, readability, comprehension of questions and identify the time taken to complete the survey. During the piloting, particularly amongst those with neuromuscular expertise, content validity was tested by ensuring questions and responses

aligned with potential nutrition and weight management factors that are relevant to DMD. The final survey is included in Appendix E.

Table 49

Key Concepts and TDF Domains Addressed in the Survey [1]

Domain	Data collected
Screening questions	• Caregiver of someone with DMD • Primarily responsible for food provision in their household
Demographic and family characteristics	• Ethnicity • Postcode • Number of dependants with & without DMD in household
Health information	• Age • Height & weight to enable calculation of BMI z-scores • Functional mobility scale (227) • Steroid treatment and other medications or nutrition supplements • Diagnosis or investigation of neuropsychiatric disorders • Presence of feeding difficulties (231) • Access to a dietitian in the neuromuscular clinic or community
Physiological factors related to nutrition and weight	• Caregivers perceptions of their son's weight • Ease of maintaining a healthy weight • Weight gain in relation to steroids • Picky eating • Avoiding/choosing certain foods due to the texture, smell or taste
TDF: Knowledge	• General knowledge about healthy eating (155) • Knowledge about healthy eating for DMD
TDF: Skills, Beliefs about capabilities	• Skills to find, prepare and cook healthy foods • Desire to learn new skills • Barriers to learning new skills
TDF: Beliefs about consequences	• Beliefs about the consequences of excessive weight gain
TDF: Goals, Reinforcement	• Beliefs about the benefits of healthy eating • Consideration of health in food provision • Influences on provision of food (232) • Priority setting for healthy eating • Perceived consequences of food choices (233)

Table 49

Key Concepts and TDF Domains Addressed in the Survey [1]

Domain	Data collected
TDF: Intentions	• Intention to change their son's weight (e.g. stay the same or lose weight) • Son's intention for his weight
TDF: Environmental context and resources	• Household meal environment (234) • Perceived barriers to healthy eating
TDF: Social influences	• Social influences on son's food choices
TDF: Emotion, Behaviour regulation	• Appetite and emotional influences on son's food choices
Co-design of a healthy lifestyle program for DMD	• Caregiver preferences of: • The focus of the program (e.g. the whole lifestyle or diet only) • Topics and resources • Delivery mode (individual vs. group, face-to-face vs. virtual) • Timing (length of program, frequency of visits, time of day) • Options for other additional support (e.g. text messages) • Outcome measures • Name and email to receive further information

[1] TDF domains not covered in the survey: social/professional role and identity, optimism and memory attention and decision processing

5.3.3 Procedures for the Caregivers' Survey

The survey was developed and distributed using Qualtrics survey platform (Qualtrics, Provo, UT, USA. Available from: https://www.qualtrics.com). A paper version of the survey was also available at the participants' request. Any paper surveys were entered manually into Qualtrics by a member of the research team (NB). Young people with DMD were identified from a central clinic list and caregivers with email addresses available were invited to participate in the survey. Caregivers were also invited to participate during routine neuromuscular clinic visits and the survey was advertised in a research newsletter at RCH. After viewing the information statement and indicating consent by clicking a check box, participants proceeded to two screening questions (see Table 49) and the survey.

5.3.4 Development of a Draft Program

Following the initial survey at RCH, data were analysed to inform the development of a draft program outline. A one-page summary of the proposed program was created based on survey responses and distributed to both caregivers and healthcare professionals for further consultation.

5.3.5 Further Consultation with Caregivers

Caregivers who indicated in the survey they were willing to provide additional feedback were contacted by email. These caregivers were provided a document outlining the proposed program and were asked whether they agreed on the proposed: length of duration, frequency of sessions, feasibility of attending the hospital for visits, topics, resources and outcome measures. Parents were also given an opportunity to provide additional comments on the design of the program.

5.3.6 Consultation with Healthcare Professionals

Healthcare professionals were approached either by email, phone or in-person and provided the same one-page document outlining the proposed program as was provided to caregivers. Healthcare professionals were invited to provide feedback on the length of duration, structure,

delivery, frequency and timing of visits, topics offered, resources provided, outcomes measured or, any other aspect of the program. Informal feedback discussions were conducted in-person or over the phone with a member of the research team (NB) who documented key points and integrated these into the program.

Following the survey, development of a draft program outline and further consultation with families and healthcare professionals, data were collated to inform the final program. The feasibility and acceptability of the final program was tested during a pilot intervention study at a single site (RCH), which is described in full in Chapter 6.

5.3.7 Data Analysis

All data were analysed using SPSS statistical software (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). Data was presented graphically using either SPSS or Microsoft Excel (Microsoft Corp. Released 2019. Microsoft Excel. Redmond WA: Microsoft Corp.). For the online survey, all data is analysed descriptively. Nominal data are reported as frequencies and continuous data are reported as median or mean depending on the normality of the distribution. For survey questions where caregivers were asked to rank their preferred option, proportions of participants who selected the response as their first, second or third preference are presented graphically. Individual number of responses for first, second and third preferences are reported in text or in Appendix E. Raw data for additional comments recorded by caregivers are presented, these were not analysed qualitatively due to a small sample size for comments (n=5).

5.4 Results: Barriers and Enablers to Healthy Eating and Weight Management (Aim 1)

5.4.1 Family and patient characteristics

There were 35 survey respondents who commenced the survey, of these eight did not complete the survey and were excluded from the analysis. Data was analysed for the remaining 27 caregivers who completed the survey in full. Due to the sampling method, we were unable to identify the response rate as the survey was advertised publicly within the neuromuscular clinic. According to the postcodes recorded by families, 26 were from Victoria and one from Tasmania. Table 50 describes the characteristics of survey respondents and their families. Across all young people with DMD, majority were treated with steroids. Of neurodevelopmental disabilities or mental health conditions autism spectrum disorder was most commonly diagnosed or investigated. Approximately one third of families accessed a dietitian within the neuromuscular clinic.

Table 50

Demographic and Family Characteristics

Family characteristics (n=27)	
Ethnicity, n (N%)	
Australian	19 (70)
New Zealander [1]	1 (4)
Asian	3 (11)
European	3 (11)
South American	1 (4)
Dependants in household, n (N%)	
One	7 (26)
Two	11 (41)
Three or more	9 (33)
Families with one son with DMD, n (N%)	23 (85)
Families with more than one son with DMD, n (N%)	4 (15)
DMD characteristics (n=32)	
Age (years), mean ± SD	12.1 ± 4.3
Reported BMI z-score, median (IQR) *(n=20)*	1.37 (0.92, 1.95)
Reported functional mobility scale, n (N%)	
500m	14 (44)
50m	3 (9)
5m	4 (13)
Uses wheelchair	11 (34)
Steroid-treated, n (N%)	28 (93)
Nutritional supplements taken, n (%)	
Vitamin D	25 (78)
Calcium	12 (38)
Creatine	3 (9)
Multivitamin	5 (16)
Fish oil/Omega 3	6 (19)
Magnesium	2 (6)
Coenzyme Q10	3 (9)
Medications, n (%)	
Zoledronic acid	1 (3)
ACE Inhibitors	20 (63)
Pain medication	2 (6)
Stimulant	1 (3)
Selective serotonin reuptake inhibitor	3 (9)
Testosterone	10 (31)
Enrolled in a drug trial	5 (16)
Comorbidities, n (N%)	
ASD diagnosed/investigated	6 (19) / 3 (9)
ADHD diagnosed/investigated	1 (3) / 2 (7)
OCD diagnosed/investigated	2 (7) / 2 (7)

[1] Ethnicities also included those who additionally identified as Australian (multiple selection was allowed)

5.4.2 Physiological Factors Related to Nutrition and Weight

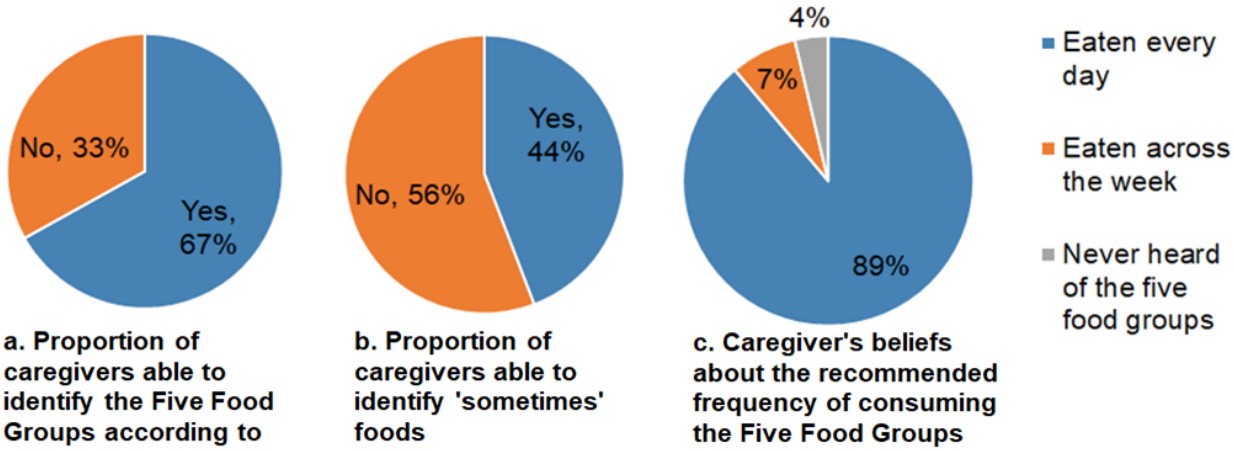
Across all young people with DMD, 20 (63%) were a healthy weight, 11 (35%) above a healthy weight and 1 (3%) below a healthy weight according to caregiver-reported height and weight data and calculation of BMI z-score. Caregivers were asked on a scale of 0 (not easy at all) to 5 (very easy) how easy it is for their son to achieve and maintain a healthy weight of which the median rating was 2.5 (IQR 1.0, 3.1). Of the 11 who were reported to be above a healthy weight, all caregivers believed their weight gain was related to steroids.

Across young people with DMD, 12 (41%) were reported to be fussy/picky eaters. Majority of caregivers reported that their son(s) avoid/choose certain foods due to the texture, smell or taste at least some (n=17, 53%) or most or all (n=5, 16%) of the time (n=10, 31% reported this rarely or never occurred).

The results will now be reported according to the relevant TDF domains.

5.4.3 Knowledge

Caregiver knowledge regarding the Five Food Groups and 'sometimes' foods are described in Figures 38a-c.



Figures 38a-c

Caregiver Knowledge Regarding the Five Food Groups and 'Sometimes' Foods.

5.4.4 Skills and Beliefs About Capabilities

Caregivers were asked on a scale from 0 to 5 to rate their confidence (a higher score indicating greater confidence) in their skills for both choosing and cooking/preparing healthy foods. Caregivers reported high confidence in their skills (median scores were 4.4 IQR 4.0, 5.0 and 4.3 IQR 4.0, 5.0 for choosing and preparing/cooking, respectively). Yet, majority (82%) of caregivers selected they would like to improve their skills in choosing, preparing and cooking healthy food. The most frequently selected skills caregivers wanted to improve were preparing healthy snacks and healthy lunchboxes and, buying and cooking healthy foods on a budget. Time was the most common barrier to improving these skills.

5.4.5 Beliefs About Consequences

All caregivers thought healthy eating was beneficial to both their family and their son(s) with DMD. Using a rating from 0 to 5, caregivers thought healthy eating was highly beneficial (ratings of 4 or 5) to their family (100% rated 4 or 5) and their son with DMD (96%).

Caregivers believed that not following a healthy eating pattern could have adverse consequences for both families and individuals with DMD (Figure 39, Supplementary Table 20). Weight gain was the most frequently selected consequence for both families and individuals with DMD. Over three quarters of caregivers thought not following a healthy eating pattern could affect muscle health for someone with DMD. All caregivers selected at least one adverse consequence.

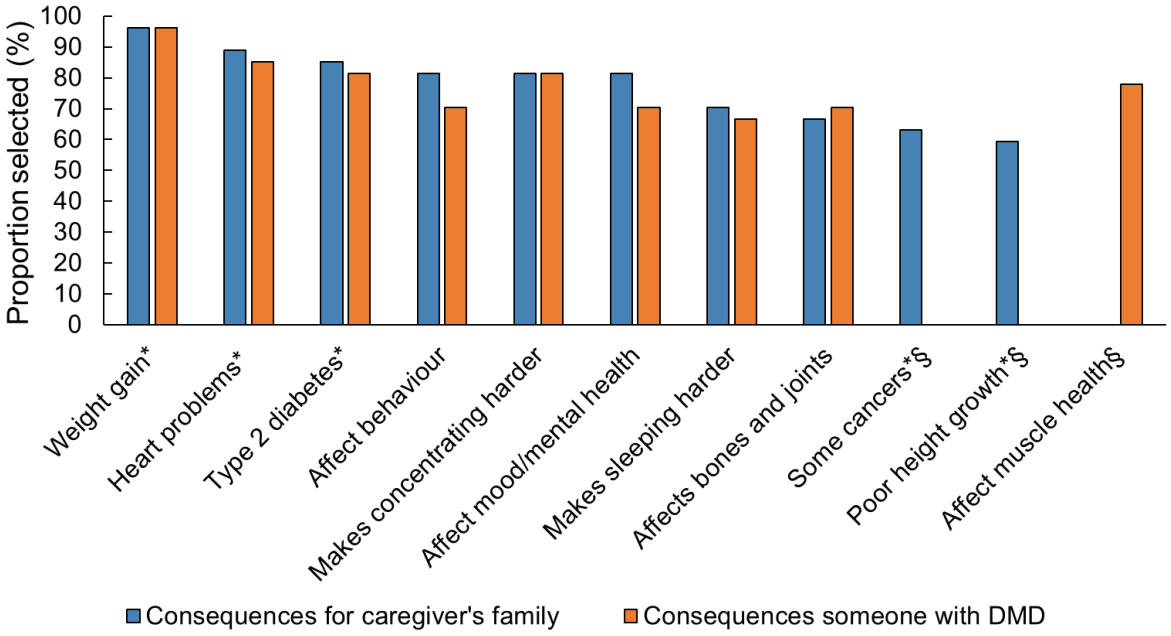


Figure 39

Beliefs about consequences for families and young people with DMD [1]

[1] * Responses were preceded with "at increased risk of…" § Not asked in regards to young people with DMD (some cancers or poor height growth) or families (affect muscle health)

Of young people with DMD, 11 were reported to be above a healthy weight. For these families, the consequences of their son being above a healthy weight are described in Figure 40-Figure 41.

Figure 40

Caregivers Perceptions of the Impact of Being a Above a Healthy Weight on Their Son

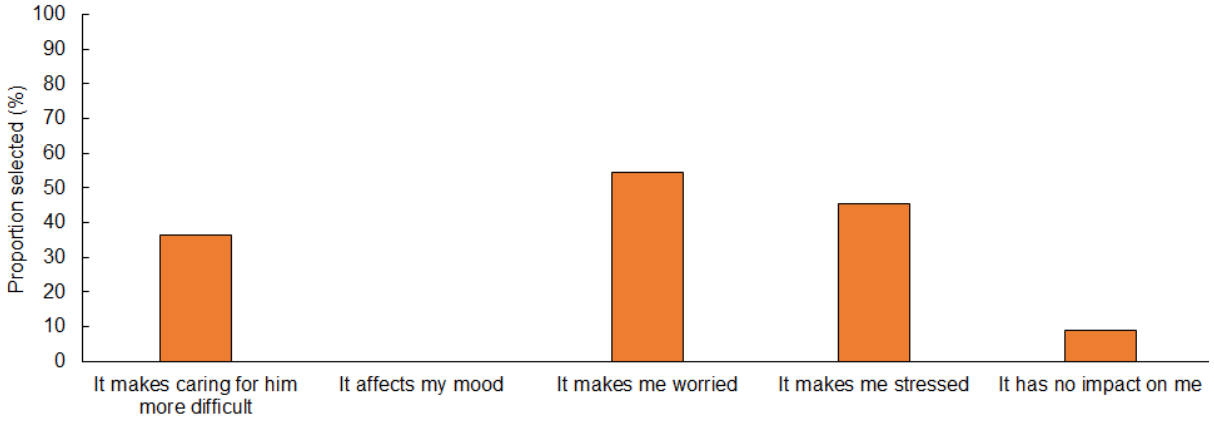


Figure 41

The Impact of Their Son Being Above a Healthy Weight on Caregiver

5.4.6 Reinforcement and Goals

In the context of their family's life, caregivers were asked to rate on a scale from 0 (not a priority at all) to 5 (highest priority) how much of a priority healthy eating was. Caregivers rated healthy eating as a high priority with a median score of 4.0 (IQR 3.5, 5.0). The majority of caregivers reported they considered the healthiness either most or all of the time when providing food to their son(s) with DMD and their family; and aimed to provide foods from the five food groups, reduce the amount of processed foods and reduce the amount of sugar (Figure 42 and Supplementary Table 21).

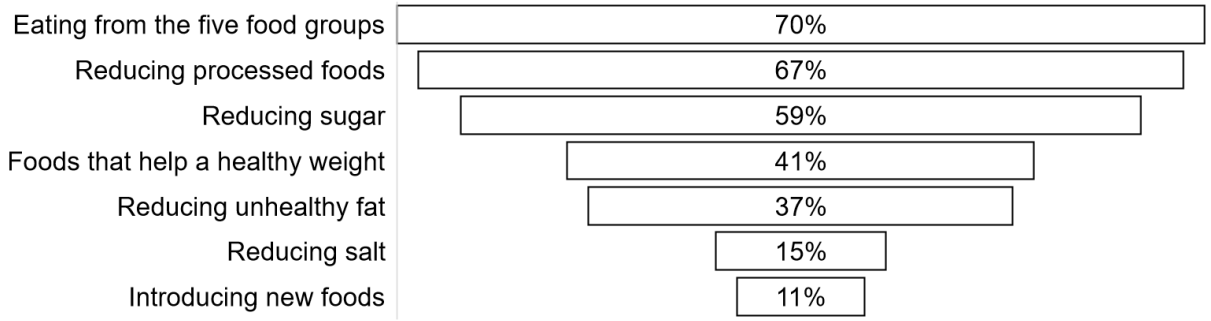
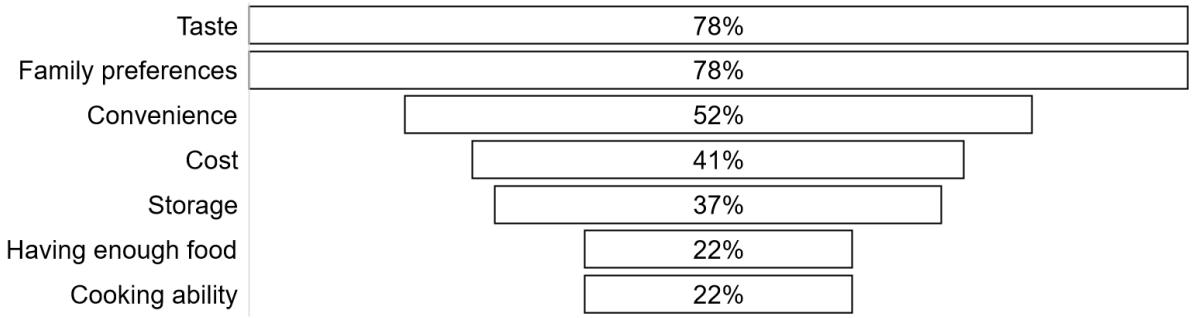


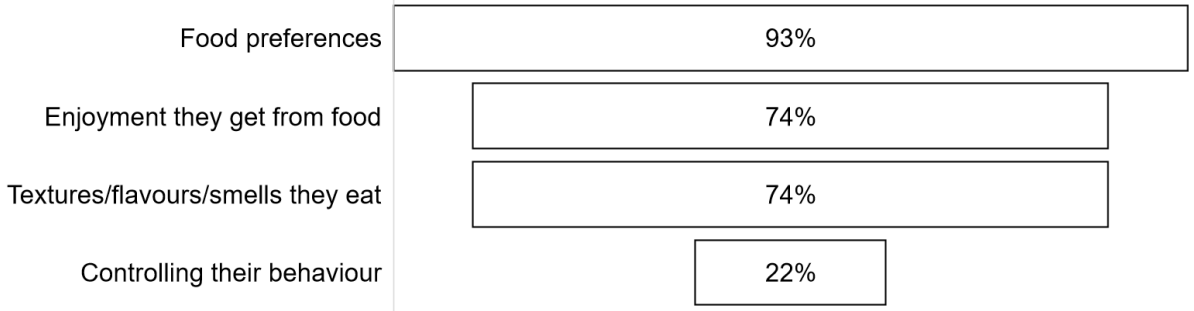
Figure 42

Considerations made by caregivers regarding the healthiness of foods provided

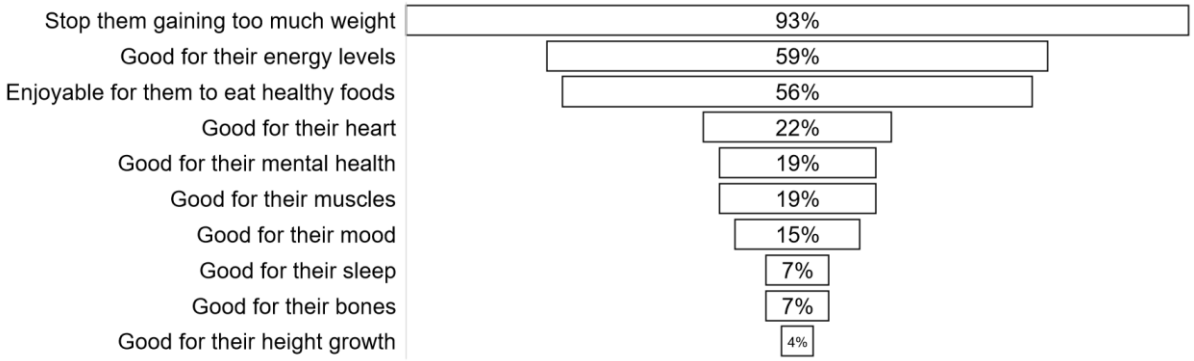
Besides the healthiness of the foods, taste and their family's food preferences were the most frequently selected consideration for caregivers when making food choices for their family (see Figure 43a-c, and Supplementary Table 22). When making food choices for their son(s) with DMD, food preferences, the enjoyment their son gets from food and the variety of textures, flavours and smells of the foods they eat were most frequently selected considerations (see Supplementary Table 23). The number one reason caregivers consider healthiness when providing food to their son was to stop then gaining too much weight (Supplementary Table 24).



a. Providing food to family



b. Providing food to son with DMD



c. Why caregivers consider the healthiness of food when providing food to their son

Figure 43a-c

Caregiver Considerations When Providing Food to Their Family and Their Son(s)

5.4.7 Intentions

For 59.4% of young people with DMD, it was their caregiver's intention to help their son stay the same weight. Fewer (18.8%) reported their son intended to stay the same weight and 34.4% reported their son intended to lose weight (Table 51).

Table 51

Intentions of Caregivers and Their Son(s) for Changing Weight

	Caregiver's intentions regarding son's weight, n (N%)	**Son's intentions for his weight, n (N%)**
Lose weight	8 (25)	11 (34)
Gain weight	1 (3)	1 (3)
Stay the same weight	19 (59)	6 (19)
No intention to do anything about his weight	4 (13)	6 (19)
I don't know what his intentions are	-	8 (25)

5.4.8 Environmental Context and Resources

Using an open-ended response, caregivers were asked to record and rank the first, second and third biggest barriers to providing healthy foods to their family (see Table 52). The most frequently recorded barrier was related to time followed by fussiness or preferences related taste, textures or smells of either their son(s) with DMD or other family members.

Table 52

Barriers to Providing Healthy Foods, n (N%)

	#1 barrier	**#2 barrier**	**#3 barrier**	**Any**
Time	5 (19)	2 (7)	3 (11)	10 (37)
Fussiness or preferences related to taste/textures/smells (son with DMD or other family members)	6 (22)	1 (4)	2 (7)	9 (33)
Lack of knowledge about what to prepare	3 (11)	0	0	3 (11)
Cost	1 (4)	1 (4)	0	2 (7)
Difficulty accessing a variety of foods due to available ingredients or recipe repertoire	0	2 (7)	0	2 (7)
Knowledge	0	1 (4)	0	1 (4)
Being prepared	0	1 (4)	1 (4)	2 (7)
No barrier recorded	12 (44)	19 (70)	21 (78)	-

In regards to the mealtime environment in their household, approximately three quarters of caregivers recorded that most or all of the time the family eats meals together at a table or bench (Figure 44, Supplementary Table 25). Screens were frequently used during mealtimes either eating in front of a screen or having the television (TV) on the in the background.

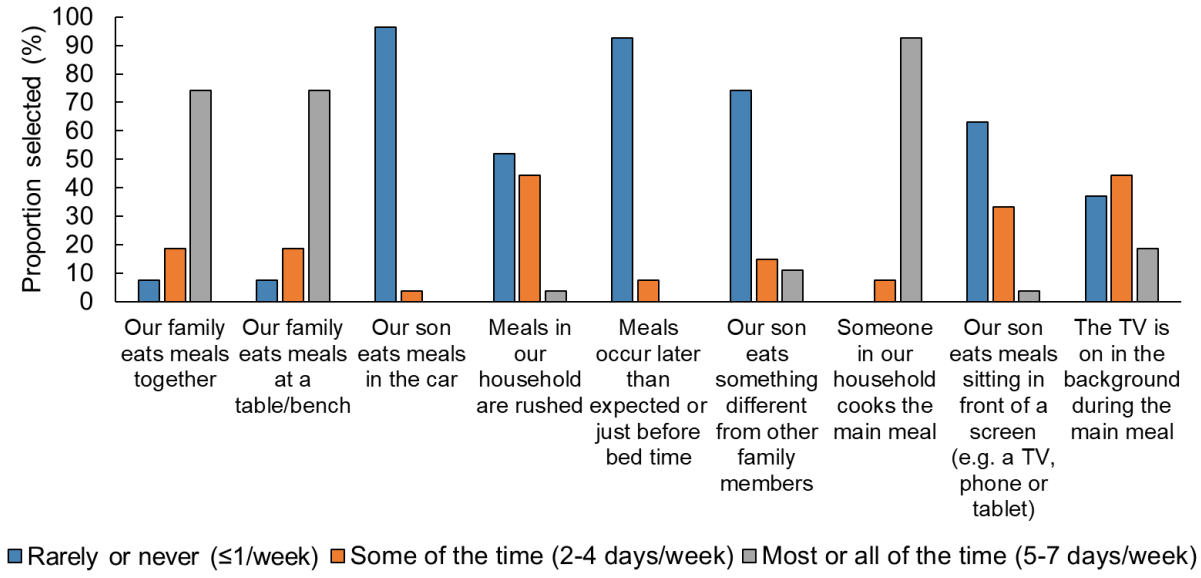


Figure 44

Mealtime Environment for Families with a Son with DMD

Of the seven caregivers that selected their son eats something different from other family members, reasons for eating something different included; that he avoids/chooses certain foods due to the texture, smell or taste of the food, he is a fussy eater, everyone in the family eats something different and because they try to prepare more healthier meals for their son (entered as other option).

5.4.9 Social Influences

Across young people with DMD, 20 (63%) were provided ‘sometimes’ foods some of the time (2-4 days per week) and 12 (38%) rarely or never (1 day or less per week). None of the caregivers reported to provide ‘sometimes’ foods most or all of the time. As reported by caregivers, 18 (56%) young people with DMD eat more ‘sometimes’ foods depending on what social situation they are in. Social situations were parties, family celebrations and when eating out.

5.4.10 Emotion and Behavioural Regulation

On a scale of 0 (not a problem at all/not difficult at all) to 5 (this is a big problem/extremely difficult), caregivers were asked to rate how problematic or difficult certain situations were related to eating, emotions and appetite. Caregivers rated an increased appetite because of medication as the most problematic (Figure 45, Supplementary Table 26). However, all situations were given low rating, indicating not problematic or difficult, with median scores ranging from 1.0-1.8. Caregivers rated saying no to their son when he asks for food because of his DMD as a situation of moderate difficulty (median score 2.0).

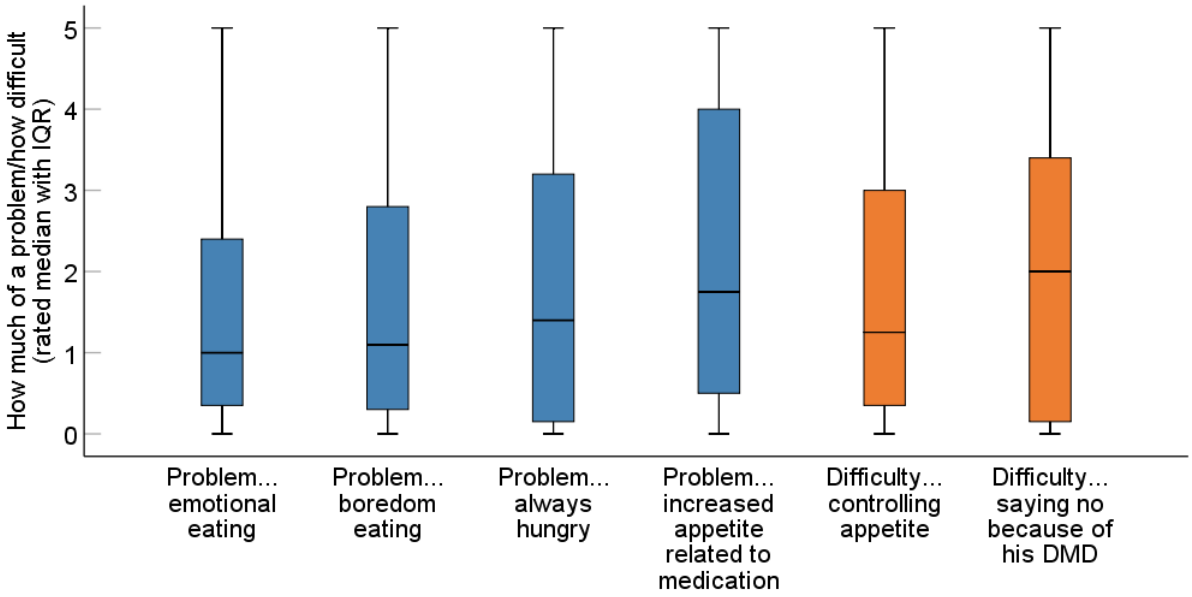


Figure 45

Problems and Difficulties Related to Food, Emotion and Appetite

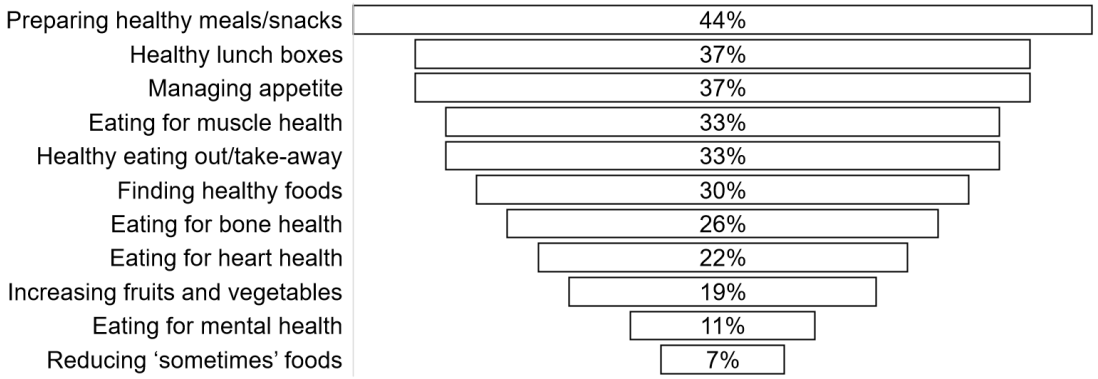
Caregivers were asked to record in a free text box which emotions, if any, made their son(s) want to eat. Responses are summarised in Supplementary Table 27. Eight caregivers reported negative emotions such as depression, anger and anxiety. Two caregivers commented that feeling hungry or certain occasions or days of the week triggered their son to eat different, rather than emotions.

5.5 Results: Caregiver Consultation on a Healthy Lifestyle Program

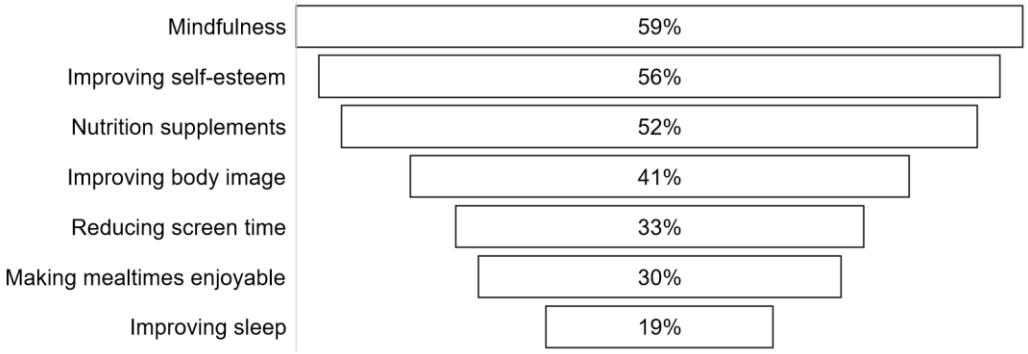
The majority of caregivers thought the focus of the program should be improving the whole lifestyle (n=15, 56%) rather than improving healthy eating (n=6, 22%) or focusing on weight management/loss (n=2, 7%). Caregiver preferences for aspects of the program design are reported below.

5.5.1 Topics Covered in the Program

The most frequently selected nutrition-related topics to be covered in the program were: preparing and cooking healthy meals and snacks, healthy lunch boxes and managing appetite (Figures 46a and b, Supplementary Table 28 and Supplementary Table 29). Other topics selected mindfulness, improving self-esteem and nutrition supplements.



a. Nutrition Topics



b. Other Topics

Figures 46a and b

Caregiver Preferences for Nutrition and Other Topics to be Covered in the Program

5.5.2 Resources

The most frequently selected preferences for resources were written information, meal plans and recipe and snack ideas (78-82% selected, see Supplementary Table 30). Supermarket tours to learn where to find healthy foods was the least popular resources with one caregiver selecting this.

5.5.3 Program Delivery

The majority of caregivers preferred the program to be delivered through individual (n=15, 56%) rather than group (n=9, 33%) sessions. In person and over video call were the most popular first preferences for delivery mode (63% and 22% selected as their first preference, respectively), see Supplementary Table 31.

The majority (n=21, 78%) of caregivers selected six weeks for length of duration which was the shortest option provided. Other options selected were 12 weeks (n=1), 24 weeks (n=3), one day (n=1, selected as other option) and one participant did not answer. Selections for frequency of visits were: monthly (n=9, 33%), weekly or fortnightly (both n=6, 22%), one visit at the beginning and at the end of the program (n=3, 11%) or once only (n=1 3.7%, selected as other option). Delivery on weekdays was mostly preferred (n=19, 70%) compared to weekends (n=8, 30%). Most preferred visits in the middle of the day (n=16, 59%) compared to evenings (n=7, 26%), after school or mornings (both n=2, 7%).

For additional support from the dietitian during the program 13 (48%) caregivers wanted to be able to text/SMS, 22 (82%) wanted to email, 21 (78%) wanted online support and, 13 (48%) wanted an online support group/forum with other families.

5.5.4 Outcome Measures

Caregivers preferences for outcome measures were: quality of life (n=15, 56%), weight (n=14, 52%) and, the amount of healthy foods (n=11, 41%), see Figure 47 and Supplementary Table 32.

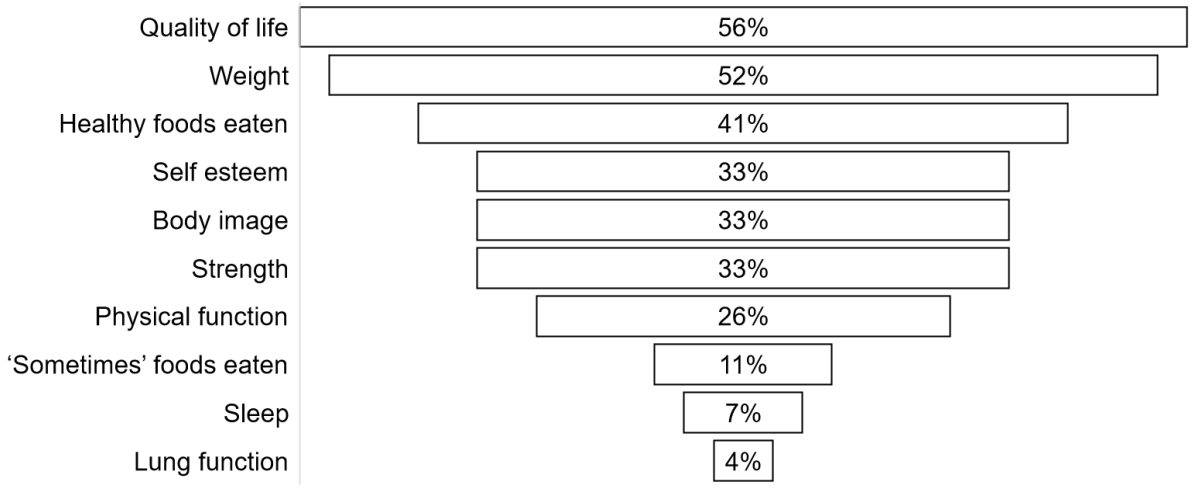


Figure 47

Parent Preferences for Outcome Measures

5.5.5 Additional Comments

Caregivers were given an opportunity to leave additional comments they had about the factors related to nutrition or weight or the development of a weight management program for DMD (Table 53). Due to a low number of caregivers recording additional comments, qualitative analysis of data was not conducted.

Table 53
Additional Comments Left by Caregivers
He likes to plan what he's having for dinner the next day, makes sure we have all the ingredients, and helps me cook. He loves to grow vegetables and eats straight from the garden.
My son is not extremely overweight like some of the DMD boys and doesn't eat huge amounts but it is extremely difficult to maintain or reduce his weight given he is in a wheelchair full time and can't undertake any sort of exercise to help lose weight. The steroids have impacted hugely on his weight as he was always a slim kid prior to moving into a wheel chair and taking steroids.
My son is not your usual Duchenne muscular dystrophy teenager, as he is underweight and has not real put on much weight in the last 2 years.
Not enough information is provided in clinic to keep your child in a healthy weight range. How many calories he should be eating per day or even suggestions of foods that will keep him feeling full for longer. We need to research and work it out ourselves.
Information is always appreciated hopefully this become a real thing and not only a survey.
Best type of diet to follow when on steroids.

5.6 Further Consultation with Caregivers and Healthcare Professionals

Following the completion of the online survey, caregiver responses from RCH were analysed descriptively. The program design features most frequently selected by caregivers in the survey informed the draft program. The available evidence for typically developing young people (see section 1.7.2 and Appendix A) and those with chronic healthcare needs (Chapter 4) also underpinned the draft program design. The draft program was then designed and disseminated to caregivers and healthcare professionals (Figure 48). Of the 27 caregivers who completed the survey, 21 (78%) indicated they were willing to provide further feedback by providing their name and email address and were sent the proposed program outline and a feedback questionnaire. Of these, two responded and completed the feedback form. Table 54 summarises the feedback provided by caregivers and healthcare professionals.

The Royal Children's Hospital Melbourne | MONASH University

SNOW-P

Supporting Nutrition and Optimising Wellbeing Program for DMD

Why are we running this program? Many young people with Duchenne muscular dystrophy find managing their weight difficult. The aim of *SNOW-P* is to support positive changes to lifestyle to help young people with DMD manage their weight.

Who can take part? Young people with DMD (under 18 years of age) who are above a healthy weight (97th BMI percentile or above). The young person will take part with their parent/guardian.

What does taking part involve? This is a 6 week program but we will also do measurements 6 weeks after the program ends. See below for more information about the proposed program.

What will participants get?

- ✓ Individual sessions with a dietitian
- ✓ Online or email support from the dietitian
- ✓ Report based on food diary
- ✓ Written information on all topics
- ✓ Recipe and snack ideas
- ✓ Suggestions for flexible meal plans

Initial consult topics:

- Nutrition for a healthy weight
- Based on food diaries
- Protein intake to help muscles and promote fullness

"Extra" topics (choose up to 2):

- Healthy lunchboxes
- Preparing & cooking healthy meals and snacks
- Mindfulness
- Reducing screen time
- Nutritional supplements

Program structure

Families complete pre-program forms and food diary

Initial (60-90 mins): Attend RCH for measurements + dietitian consult.
Topics covered: nutrition for a healthy weight + protein intake

Week 1: brief phone review (20 min)

Week 2 (45-60 mins): Attend RCH *or* phone/video dieititian consult.
Topics covered: "Extra" topic 1 + re-visit topics from initial consult

Week 3: brief phone review (20 min)

Week 4 (45-60 mins): Attend RCH *or* phone/video dieititian consult.
Topics covered: "Extra" topic 2 + re-visit topics from initial consult

Week 5: brief phone review (20 min)

Week 6: Families come to RCH for final review with the dietitian and measurements

Week 12: Measurements

To understand whether the program was successful we will measure:

- Weight
- Physical function
- Quality of life
- Dietary intake

DRAFT

Figure 48

Draft program outline developed for further consultation

Table 54

Further Consultation with Stakeholders (Caregivers and Healthcare Professionals)

Stakeholder	Mode	Summary of feedback
Caregivers		
Caregiver 1	Questionnaire	• Agreed with all aspects of the design and had no further comments or feedback.
Caregiver 2	Questionnaire	• Suggested shorter intervention and only including the phone reviews if required by individual families to optimise feasibility for families living regionally.
Healthcare professionals		
Physiotherapists x 2	Face-to-face meeting	• Intervention delivery: flexible mode of delivery is preferred. • Outcome measures: suggested to measure feasibility and acceptability, step count, global rating of change, quality of life, fatigue scale, timed 10m walk/run & times supine to stand (ambulant participants), timed can stacking exercise (non-ambulant participants). • Eligibility criteria: keep age criteria broad, include those with mental health co-morbidities.
Neurologist	Phone call	• Timing: have options for evening and after school sessions. Frequency of visits would likely be feasible and acceptable due to the flexible mode of delivery. • Nutrition topics: focus on all macronutrients including protein to optimise management of appetite. A website hub could include links to resources. • Outcome measures: ideally six-minute walk distance would be included as an outcome, however it's unlikely to be sensitive enough to see change over six weeks. Suggested to use a patient-reported measure of function.
Neurologist	Face-to-face meeting	• Outcome measures: suggested to also measure blood pressure
Dietitian	Face-to-face meeting	• Intervention delivery: flexibility of mode of delivery is a strength. Set meaningful and achievable goals with participants, avoid delivering too much content during sessions. • Outcome measures: food diary phone applications as an alternative to paper food diaries.
Dietitian	Face-to-face meeting	• Wording of intervention to families: emphasise point of difference between routine care, ensure families understand the frequency of visits (e.g. weekly)

5.7 Final Product: Supporting Nutrition and Optimising Wellbeing Program (SNOW-P) for Duchenne muscular dystrophy

5.7.1 Overall Design of SNOW-P

Following the consultation process, recommendations from caregivers and healthcare professionals were collated and informed the final program: The Supporting Nutrition and Optimising Wellbeing Program (SNOW-P) for DMD. SNOW-P is a six-week family-focussed lifestyle weight management intervention delivered by a dietitian. The content delivered throughout the program is semi-structured, that is, caregivers choose from set topics informed by the consultation process however dietary and lifestyle advice and goals related to each topic are individualised to each family. In addition, all families receive general weight management advice based on analysis of food diaries and exploration of appetite and the family mealtime environment. For each topic, the dietitian identifies the family's existing knowledge about the topic, provides education on the topic, answers any questions and then sets SMART (Specific, Measurable, Achievable, Relevant, Timely) goals together with the family. Motivational interviewing techniques are used such as; using open ended questions to explore barriers and enablers to healthy eating, affirmations of existing or new lifestyle choices, reflecting on progress during the fortnightly phone reviews and encouraging families to set their own goals. (235)

5.7.2 Adaptations Made Due to COVID-19

The COVID-19 pandemic resulted in a catastrophic number of lives lost, predominantly in adult populations. (236) In addition to the direct morbidity and mortality caused by the virus, many indirect health consequences of "lockdowns" (periods of staying at home to avoid risk of infection) and social isolation have emerged. While Australia was fortunate to have some of the lowest cases of the virus globally, residents in the state of Victoria endured some of the strictest lockdown measures in the world. Of Australian states, Victoria was the most hard-hit in terms of case numbers (case numbers=20944 in total as of 31st July 2021), time spent in lockdown (the longest lockdown was 112 days in 2020) and restrictions placed on daily living. (237,238) In young people including those with obesity, challenges related to lockdowns included less

structure, routine and physical activity, increased anxiety related to COVID-19, more snacking and screen time which was associated with an increase in reported weight gain. (239-242)

Due to these indirect negative health consequences of the pandemic on young people, the research team perceived a weight management program for DMD as important to continue. However, as with other healthcare organisations in Victoria in 2020-2021, patient-facing clinical activities at RCH were limited and restrictions were placed on all non-essential participant-facing research. Individuals with DMD are also a high infection risk due to reduced respiratory function and as steroids are immunocompromising. Therefore, to eliminate infection risk and adhere to local restrictions and regulations, adaptations were made to the program design. SNOW-P was transformed to enable an entirely virtual delivery via telehealth (video call) and phone. Table 55 describes the final design of the SNOW-P feasibility and acceptability pilot study which was delivered virtually via RCH.

Table 55

Design for SNOW-P Delivered in a Feasibility and Acceptability Pilot Study

Features of program design	Program design
Overall design	
Focus of program	Lifestyle weight management strategies
Components of the program	Multi-component including dietary and behaviour change (e.g. screen time, mindfulness)
Person delivering intervention	Accredited Practising Dietitian (APD)
Participant involvement	Individual, family-focussed sessions involving young person and caregivers
Mode of delivery	Virtual visits via telehealth (video call) and/or phone call.
Frequency of sessions	Weekly visits with alternating telehealth sessions of 45-60 minutes and phone reviews of 10-15 minutes
Timing	Flexible days of the week (both weekday or weekend) and time (morning, afternoon or evening)
Length of follow-up	Six-week intervention with six week post-intervention period (12 weeks total follow-up)

Typical structure of telehealth sessions (week 0, 2 and 4)
45-60 minutes via telehealth (video call) with both participant with DMD and caregiver Typical agenda: 1. Introduction to session and rapport building 2. Safety check of adverse events 3. Check prior knowledge of topic and discuss family's preferences for specific education/goal-setting related to topic 4. Education on topic 5. Mutual goal-setting with SMART goals (Specific, Measurable, Achievable, Relevant, Timely) 6. Motivational interviewing techniques used throughout sessions (e.g. open-ended questions, affirmations and encouraging families to set their own goals) 7. Confirmation of proceeding session
Typical structure of phone reviews (week 1, 3, 5)
10-15 minutes via phone with caregiver Typical agenda: 1. Introduction and rapport building 2. Safety check of adverse events 3. Check in on goal progress and motivational interviewing techniques (e.g. affirmations, reflecting on progress) 4. Troubleshoot any issues identified with goals
"Core topics" # 1 (provided to all participants) delivered in first (week 0) session:
1. Nutrition for a healthy weight: The 5 food groups 'Everyday' vs. 'sometimes' foods and drinks Healthy weight strategies during home isolation (if relevant at time of program delivery) 2. Managing appetite: Optimal carbohydrate, fat, protein and fibre intake to promote fullness Even distribution of protein across the day to promote fullness and optimise LM Increasing inter-meal intervals & normalising feelings of hunger Meal and snack ideas to promote fullness and feeling fuller for longer Distraction techniques to assist with hunger 3. Advice based on food diaries: Report based on food diaries provided to family Suggestions for meal/snack planning, incorporating education covered in "nutrition for a healthy weight" and "managing appetite"

“Extra” topic # 1 (participants select up to 2) delivered in weeks 2 and 4
1. Strategies for a healthy lunch box: Five food groups in the lunchbox, lunch and recess/morning tea ideas, after school snacks 2. Meal preparation and cooking: Overcoming barriers to meal preparation, meal and snack ideas and recipes 3. Mindfulness strategies: Mealtime environment e.g. avoiding screens, using a hunger rating scale (243) 4. Activities and interests: Screen-free activities, participating in community and social activities, participating in physiotherapy/hydrotherapy 5. Nutrition supplements
Additional resources
Additional support via email or text message from the dietitian, when required Written resources on topics Recipe and snack ideas to be included in resource pack Recommendations for meal planning incorporated into food diary feedback and goal setting

5.8 Discussion

To the authors' knowledge, this is the first study internationally to explore caregivers' perspectives on healthy eating and weight management in DMD. Potential barriers to healthy eating and weight management for young people with DMD identified in the survey included fussy eating, avoidance of foods due to their taste, texture or smell, time constraints to prepare meals and an increased appetite because of medication. There may also be a deficit in caregiver's general nutrition knowledge with approximately one third unable to identify foods belonging to core food groups and approximately one half unable to identify discretionary foods. Enablers to healthy eating that emerged were caregivers perceiving healthy eating as a high priority, high ratings of confidence in ability to prepare healthy foods for their families and perceived benefits of healthy eating practices. See Table 56 for summary of potential barriers and enablers. To our knowledge, a weight management program has not been developed in DMD and therefore consulting caregivers on the design and delivery of a lifestyle weight management program is unique. Caregivers responding to the survey indicated their preference for a holistic (lifestyle-focussed rather than weight-focussed), short (six week), face-to-face and individualised (rather than group) program.

Table 56

Key Findings for Each Domain with Summary of Potential Impact on Healthy Eating and Weight

Domain	Key findings	Potential impact [1]
Physiological factors related to nutrition and weight	• Caregivers reported moderate difficulty in achieving and maintaining a healthy weight for their son.	≈
	• Fussy eating and avoiding/choosing certain foods due to the texture, smell or taste is common in DMD.	-
Knowledge	• Approximately two thirds of caregivers could identify the Five Food Groups. • Just under half could identify 'sometimes' foods.	-
Skills, Beliefs about capabilities	• Caregivers are highly confident in their skills to choose and prepare/cook healthy foods median.	+
Beliefs about consequences	• It was widely accepted that healthy eating was highly beneficial to their family and son(s) with DMD and not following a healthy eating pattern could have adverse consequences.	+
Goals Reinforcement	• Healthy eating is a high priority and is almost always considered in food provision.	+
Intentions	• Most caregivers intended to help their son stay the same weight, majority thought their son wanted to lose weight.	≈
Environmental context and resources	• Time constraints and fussy eating or sensory preferences are barrier to providing healthy foods, meals are frequently rushed in households.	-
	• Many families frequently eat meals together at a table or bench.	+
	• Screens are frequently used during mealtimes.	-
Social influences	• Caregivers report giving 'sometimes' foods only on occasion, for example at celebrations or parties.	+
Emotion and behaviour regulation	• Some families may find an increased appetite because of medications problematic and saying no to their son when he asks for food because of his DMD difficult. • Some young people with DMD may experience emotional eating due to depression, anger and anxiety.	-

[1] + positive impact, - negative impact, ≈ neutral impact

This survey identified that weight is an important issue for families with a son with DMD. The most commonly reported reason caregivers provide healthy foods to their son was to prevent them from gaining too much weight. Approximately one third of caregivers reported their son wanted to lose weight and for those who were reported to be a above a healthy weight (n=11) the most commonly reported impact was making their son self-conscious. There was also a higher proportion of boys who intended to lose weight compared to caregivers who intended to help their lose weight. This suggests young people with DMD are aware of their weight and may have an intrinsic motivation to change. However, the topic of managing weight needs to be discussed sensitively with families and weight stigma and blame should be avoided. Weight stigma occurs frequently in healthcare settings (244) and may be in the form of language, bias and prejudice from healthcare professionals and lack of appropriate equipment, furniture or healthcare services. (245) Weight stigma can lead to negative emotional and psychological consequences, social isolation, disordered eating and further exacerbation of weight-promoting behaviours. (245) It is essential that healthcare professionals working with individuals with DMD understand how to sensitively approach and discuss the topic of weight to avoid psychological and physical harm.

Caregivers frequently reported their son with DMD was a fussy eater or avoided or chose certain foods due to the texture, smell or taste. There has been little exploration of the barrier of fussy eating in DMD. One investigation identified that boys with DMD had typical oral sensory processing, however the authors noted that this finding was contrary to anecdotal reports from caregivers. (246) We are unable to deduce from this survey whether fussy or avoidant eating behaviours are more prevalent in DMD compared to general populations as there is no universally accepted definition or assessment of fussy eating, it is subjective and, the prevalence amongst general populations greatly varies (approximately 10-60%). (247) Nevertheless, it does appear to be problematic for families as caregivers reported it was the second biggest barrier to providing healthy foods to their family (either their son with DMD or other family members). Neurodevelopmental disabilities (or traits without a definitive diagnosis) may play a role in the development of fussy eating in DMD. In our sample 28% were diagnosed or investigated for ASD, 13% for OCD and 10% for ADHD. Past studies have also reported high prevalence of features of autism, emotional and behavioural dysregulation and obsession and compulsion in boys with DMD. (142) To avoid nutritional deficiencies and optimise development, extreme fussy eating or sensory issues may require

referral to a speech pathologist or occupational therapist with expertise in feeding therapies e.g. trained in the Sequential-Oral-Sensory (SOS) approach.

There is an emerging theme from this study on the influence of their son's diagnosis on caregivers' food provision. Caregivers reported moderate difficulty in saying no to their son when asking for food because of his DMD. The interrelationship between diagnosis and parental behaviours around food provision has not been explored previously in DMD. In other populations of parents of a child with a chronic disease, perceived outlooks on a child's diagnosis can influence how parents promote weight-related behaviours. (248) In one study of parents of a child with spina bifida or Down syndrome a consistent theme was that a child's condition may have a positive impact on food provision as parents were wanting to empower their child. (248) However, parents also raised the notion of 'picking their battles' (e.g. with competing healthcare needs) and how this can impact on their ability to do what is ideal for their child's health. (248) Amongst caregivers of a child with cystic fibrosis, parental stress related to fears of the uncertainty of the outlook of their child's illness may influence adherence to recommended nutritional management. (249) While findings from the current study touch on this theme, further exploration using qualitative methods is required.

Barriers to healthy eating and weight management related to environmental context and resources were identified in this study. Family meals are associated with a higher consumption of nutrient-rich foods, lower intake of soft drink, reduce likelihood of overweight and improved psychosocial wellbeing. (250) In our sample, majority of families ate meals together at a table or bench. However, caregivers reported frequent screen use during mealtimes which can be associated with a higher consumption of energy-dense nutrient-poor foods and make it difficult for young people to recognise satiety signals. (250,251) Promoting screen-free, family meals that support healthy weight behaviours should form part of dietary counselling for families with a son with DMD. Other barriers to healthy eating identified were time constraints and rushed mealtimes. Amongst multiple healthcare appointments, school, work and social commitments, this finding is not surprising. The impact of multiple healthcare needs on day-to-day family routine has also been identified in other populations of young people with disabilities. (248) The time pressures felt by families should be respected by dietitians working with families and nutrition advice should be practical, specific, and include time-saving strategies.

From the survey of caregivers, a gap in general nutrition knowledge was identified. Approximately two thirds of caregivers identified all of the five good groups according to the Australian Guide to Healthy Eating (155) and just under half could correctly identify 'sometimes' foods. Approximately two thirds of caregivers reported to have accessed a dietitian within the neuromuscular clinic, which falls short of care guidelines (see section 1.2.1). (24) Nutrition professionals have a role in working with families to understand these basic nutrition principals, which form the foundation of management of both under- and overnutrition; and how these nutrition principles are applied in DMD. There is potential for improvement in nutrition knowledge and access to dietitians to assist in preventing excessive weight gain and optimising nutritional status in young people with DMD. There is emerging evidence from the comments left in the survey that caregivers would like further information on nutrition and weight management in DMD.

For a lifestyle weight management program for DMD majority of survey respondents wanted individual sessions delivered over six weeks. Almost all caregivers preferred face-to-face sessions, however as this survey was delivered prior to the COVID-19 pandemic when telehealth services increased it would be important to re-consult caregivers on this preference. Quality of life and weight were preferred outcome measures. There has been little exploration of the link between quality of life and weight, or the potential to improve quality of life with weight management. One qualitative study found that adults with DMD and their caregivers would like healthcare providers to "highlight the link between weight gain and quality of life while also trying to help Duchenne families find practical solutions to logistical challenges they face daily". (108) A multidisciplinary team approach is an important consideration for future research and clinical practice for weight management in DMD. Psychologists hold the expertise to work on topics such as mindfulness, improving self-esteem, and appetite management which were identified as important to caregivers. Emotional eating related to emotions such as depression, anger and anxiety was also identified in approximately one third of our sample. Psychological management can address these underlying causes of potentially excessive food intake as well as optimising overall wellbeing and managing mental health comorbidities. In Australia access to adequate and appropriate mental health services and clinicians with expertise in DMD is a barrier. (27) Physiotherapists are an integral member of the multidisciplinary team to support safe and

effective participation in physical activities for young people with DMD. Speech pathologists and occupational therapists can also advise on strategies to assist with sensory issues and food aversions.

Strengths of this study include exploring multiple areas related to nutrition and weight from a range of domains affecting behaviour change using the TDF. Using the TDF has enabled identification of specific areas to target behaviour change or availability and access to services. For example, it was identified that caregivers may have a knowledge deficit regarding general nutrition principals. This identifies a potential need to change the behaviour of healthcare professionals (e.g. dietitians increasing time spent educating on these nutrition basics) or increase access to services that support weight management. Conversely, for the beliefs about consequences domain it was widely accepted by caregivers that healthy eating was highly beneficial to their family and their son with DMD. Educating families about the benefits and consequences of healthy eating may be 'preaching to the converted' and dietetic consultation time can be spent discussing practical strategies. A limitation of using the TDF for this study was that several factors relevant to DMD, such as steroid-related increase in appetite, do not relate to behaviour but rather physiological factors that influence weight. However, these physiological factors are well documented in DMD (see section 1.5.2) whilst there has been very little prior exploration of the behavioural influences on weight. The TDF may be useful in future studies, which could consider employing qualitative methods, to further explore influences on complex behaviours that relate to multiple domains (e.g. a child's diagnosis of DMD influencing parental food provision). Another strength of this study was that families were consulted twice for the development of a weight management program, however uptake of the second consultation process was low (n=2). Limitations of the study were a small sample size of caregivers from a single site and that we did not obtain young peoples' perspectives directly. Future research should consider exploring the perspectives of young people with DMD, to gain further insight into factors such as appetite, emotions and food preferences. There is also a potential of response bias in this study, for example, caregivers may have reported nutrition to be a high priority due to an unconscious influence from researchers. Caregivers who completed the survey may also had an interested in nutrition which influenced their responses.

5.9 Conclusions

This was a novel exploration of the barriers and enablers to healthy eating and weight management as reported by a caregiver of a young person with DMD (see Box 23 for what this study contributes). Weight management appears to be an important issue for families. Potential barriers to healthy eating and weight management include young people with DMD avoiding or choosing certain foods due to sensory preferences, time pressures felt by families and knowledge deficits in general nutrition principals. Enablers include nutrition being a high priority for families, caregivers having high confidence in their skills to prepare healthy foods and a sound understanding of the consequences (positive or negative) of healthy eating. This is the first study internationally to consult caregivers on their preferences for a weight management program in DMD. Caregivers wanted individual sessions delivered over six weeks and topics such as healthy lunchboxes, managing appetite and mindfulness. Findings from this study have informed the design of a lifestyle weight management program which will be tested in a feasibility and acceptability pilot study.

Box 23

Contribution to Knowledge Gaps (Chapter 5)

This study contributes knowledge that…

- Nutrition knowledge, environmental context and resources (e.g. mealtime environment or time constraints) and physiological factors (e.g. appetite) were barriers to healthy eating for weight management in DMD.
- Enablers for change: caregivers' beliefs about consequences of healthy eating, confidence in meal preparation skills and nutrition being perceived as a high priority.
- Caregivers would like individual, face-to-face sessions delivered over a shorter time frame with topics such as healthy lunchboxes, managing appetite and mindfulness.

Chapter 6.

Supporting Nutrition and Optimising Wellbeing Program (SNOW-P) for DMD Feasibility and Acceptability Pilot Study

Peer reviewed journal article:

Ethics Reference: HREC/58876/RCHM-2019

Peer-Reviewed Journal Article:

Title: Supporting Nutrition and Optimising Wellbeing Program (SNOW-P) for DMD Feasibility and Acceptability Pilot Study

Authors: Natassja Billich, Paula Bray, Helen Truby, Maureen Evans, Kate Carroll, Katy de Valle, Justine Adams, Rachel Kennedy, Andrew Kornberg, Daniella Villano, Eppie Yiu, Monique Ryan, Zoe Davidson

In Preparation

6.1 Preamble

This thesis chapter describes the comprehensive pilot study in which we implemented a weight management program for young people with DMD. Two case studies (one including one participant, the other including three) exist in the literature, these have been described in detail in section 1.7.1. These case studies provide useful proof of concept data. However; as up to one in two young people with DMD have obesity there is a compelling need to understand optimal weight management strategies. Box 24 summarises the identified gaps in the literature regarding weight management in DMD.

Chapter 5 described the development of the Supporting Nutrition and Optimising Wellbeing Program (SNOW-P) informed by co-design with families and neuromuscular and nutrition healthcare professionals (see Table 55 for details an overview of SNOW-P). This chapter describes a feasibility and acceptability pilot study of SNOW-P. As this is a novel program and a weight management program has never been implemented in DMD, a feasibility and acceptability study will help determine whether the program is recommended for efficacy testing. (252) This pilot study is ongoing and the results presented here are a preliminary analysis of seven participants, the target sample size is 10.

As previously described (see section 5.7.2), in light of the COVID-19 pandemic the SNOW-P protocol was adapted to be delivered entirely virtually via telehealth (video call) and phone calls. All sessions and outcomes measured were conducted within participants' homes to eliminate the risk of infection associated with study visits to a tertiary hospital during the pandemic. Caregivers were also asked additional questions at baseline and in the post-program feedback questionnaire related to the impact of the COVID-19 pandemic on weight management and ability to participate in SNOW-P. While two versions of the program were available – a virtual and face-to-face version – the persistent nature of the pandemic meant the virtual program was delivered to all participants. Herein describes the virtual version of SNOW-P.

Box 24

Identified Knowledge Gaps (Chapter 6)

Regarding weight management interventions in DMD…

- Only two case studies (n=1 and n=3 participants, respectively) have explored weight management interventions in DMD, therefore little is known about optimal management of obesity.
- It is unknown whether a lifestyle weight management program is feasible and acceptable for families with a son with DMD.

6.2 Aims

The aims of this study were to:

1. Determine the feasibility and acceptability of a lifestyle weight management program (SNOW-P) for young people with DMD who have obesity, which was informed by co-design with families and healthcare professionals.
2. Determine the impact of the SNOW-P nutrition intervention on weight, waist circumference, physical function, quality of life, self-reported fatigue levels, dietary intake and adverse events for young people with DMD who have obesity.

6.3 Methods

6.3.1 Study design

This was a single-arm, open-label, feasibility and acceptability pilot study for SNOW-P. As previously described in detail in Chapter 5, the design of SNOW-P was informed by co-design with 27 families with a son with DMD as well as neuromuscular and nutrition healthcare professionals. SNOW-P is a lifestyle weight management program delivered intensively over six weeks with 12 weeks total follow-up. All study procedures were approved by the RCH Research and Governance office (HREC/58876/RCHM-2019). The study protocol was prospectively registered (ACTRN12620000167965 available from: www.anzctr.org.au).

6.3.2 Setting

SNOW-P was delivered through a single paediatric neuromuscular clinic at the RCH in Melbourne, Australia. This is one of Australia's largest paediatric neuromuscular clinics and services all children with a neuromuscular disease within Victoria and Tasmania. The neuromuscular clinic also services young people with neuromuscular disorders from the Northern Territory. All recruitment and documentation processes were conducted through RCH. However, as this program was delivered entirely virtually, the intervention was delivered and outcomes were measured in the participants' home. All study visits were conducted outside of routine neuromuscular clinic visits.

6.3.3 Participants

Young people attending RCH who were 18 years or younger with a diagnosis of DMD confirmed by genetic testing or muscle biopsy and who had obesity were eligible to participate. Criteria for obesity was a BMI z-score ≥1.64 (equivalent to BMI ≥97th percentile) according to the CDC BMI-for-age male growth charts at the most recent measure available within electronic medical records. (40) Access to a device with internet connection to enable telehealth and/or a phone was a requirement. Exclusion criteria for this study were: enrolment in any other interventional study; documented significant illness that may contraindicate participation in a weight management program e.g. inpatient admission

for acute illness; currently undergoing treatment for a clinical eating disorder; participant or caregiver with poor level of spoken English such that the intervention program cannot be delivered; enrolment in another formal weight management program; or attending a specialist weight management clinic. Participants with neurodevelopmental co-morbidities such as such as autism spectrum disorder, intellectual disabilities and obsessive-compulsive disorder were eligible for inclusion provided they met all other eligibility criteria. A pre-program phone call explored eating behaviours to screen for any characteristics that may contraindicate participation in a weight management program e.g. for a young person with obsessive-compulsive disorder, an obsession with counting kilojoules/calories may contraindicate participation. Taking metformin was not an exclusion criterion.

Potential participants were identified through neuromuscular patient lists or by referrals from treating clinicians. Additionally, 16 (59% of total survey participants) caregivers who expressed interest in participating in the program during the co-design process were sent information and invited to discuss eligibility with a member of the research team. Potential participants were assessed against the eligible criteria through review of electronic medical records and a screening phone call with one researcher and APD (NB). During the screening phone call any questions about the program were answered. Caregivers of eligible participants were then contacted approximately one week after the screening phone call to determine willingness to participate. Informed consent was obtained from a legal guardian and participants with DMD if appropriate depending on cognition and maturity.

6.3.4 Pre-program Procedures

Once enrolled and consent obtained, one researcher and APD (NB) reviewed the participant's electronic medical record and collected data for social, medical and medication history. The APD conducted a second pre-program phone call (separate to the screening phone call) with caregivers to collect further medical and psychosocial history which was used to both report baseline participant characteristics and to inform appropriate and tailored advice during the program. For example, any sensory preferences were explored during the pre-program phone call to ensure dietary strategies were tailored to participants' needs. Information on family structure, type of schooling (e.g. mainstream or special development school), barriers to nutrition (e.g. financial, environmental, food preferences of other family members), activity interests and abilities were collected. Three-day food and hunger dairies

(see Appendix F) were then sent by email to caregivers for completion prior to the first (baseline) session. Food and hunger diaries asked caregivers to record what was eaten, how much, where and with whom foods were eaten and level of participant self-reported hunger (if able) using the Bennet *et al.* children's hunger rating scale. (243)

6.3.5 Intervention Delivery

Figure 49 provides an overview of SNOW-P delivery and examples of the goals set for one participant, see Table 55 in Chapter 5 for further details of the intervention design and delivery. SNOW-P was delivered by one APD (NB) over eight virtual (telehealth video calls or phone) visits across 12 weeks; this included six weeks of intensive intervention delivery and an addition six weeks follow-up. The telehealth sessions involved education and goal setting and both participants with DMD and their caregivers were encouraged to attend, other siblings or dependants within the household were welcome to listen. In the first telehealth session (week 0) families were also provided a report with detailed written suggestions based on a food and hunger diary (see Appendix F). Motivational interviewing techniques were used throughout telehealth and phone sessions (see Table 55 for further details). The final two visits delivered at weeks 6 and 12 involved planning for goals and weight management strategies for the proceeding six weeks and post-program periods, respectively. The final session included recommendations for future support such as re-engagement with the neuromuscular clinic dietitian and/or community clinicians.

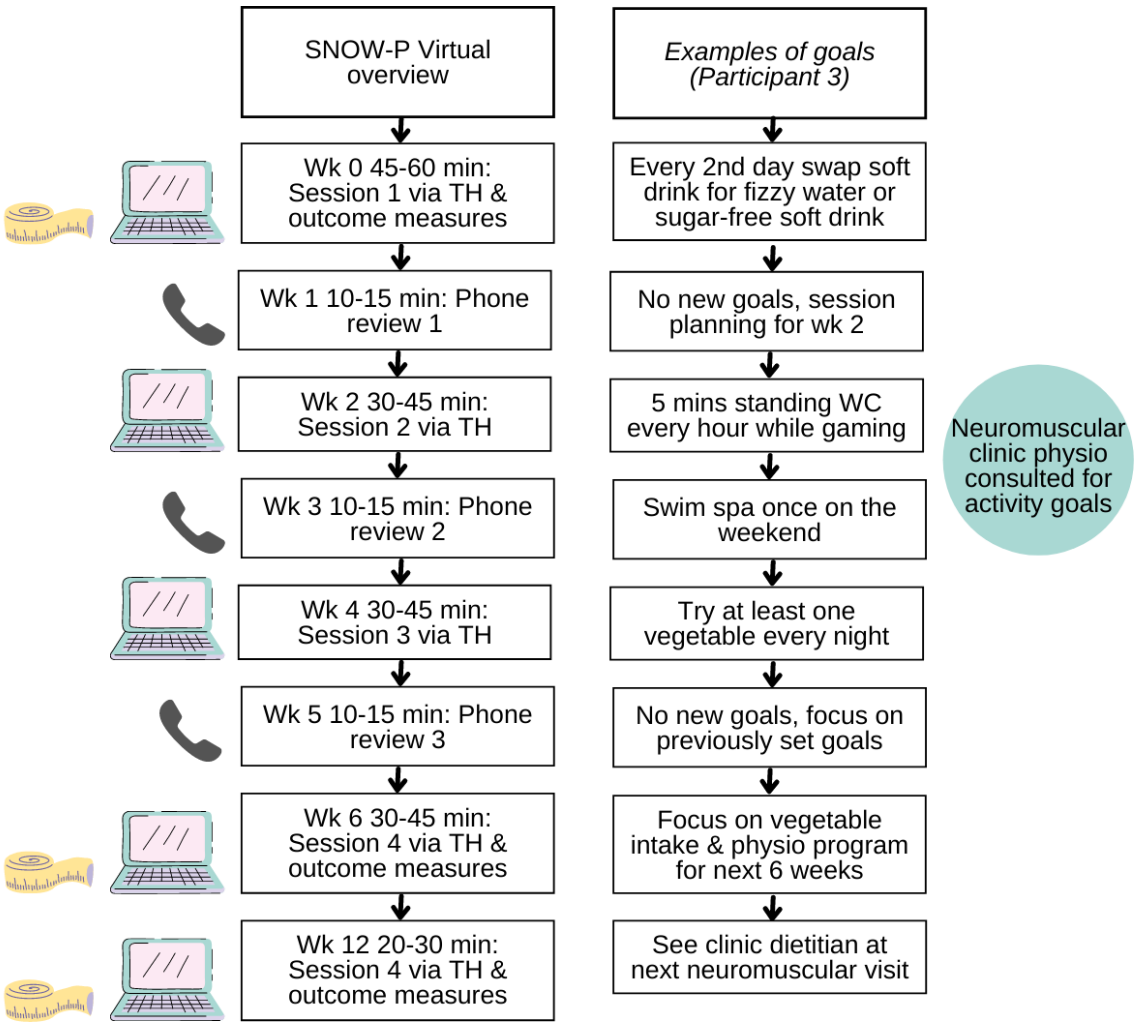


Figure 49

SNOW-P Delivery Process and Examples of Goals

6.3.6 Primary outcome measures

The primary outcomes were feasibility and acceptability of the SNOW-P in young people DMD. Feasibility and acceptability were measured with attrition and program uptake data including: the number of participants referred, approached or that expressed interest in the program; reason for ineligibility; number of participants enrolled; number of withdrawals and reasons; number of program completers; and number lost to follow up. Caregivers who completed the program were asked to complete a feedback questionnaire via REDCap which included: overall satisfaction with the program; likelihood of recommending the program; perceived success of the program; ease and feasibility of participating; best aspects and recommendations for changes to the program; and the impact of the COVID-19 pandemic on

the feasibility of participating. A simplified version of the feedback questionnaire was provided to some participants with DMD depending on maturity and level of cognition. For those who withdrew from the program, caregivers were asked to complete a questionnaire including: reason for withdrawal; barriers to participating in the program; and recommended changes to the program to improve acceptability or feasibility. To minimise bias, families were also offered an additional opportunity to provide feedback independent to the APD delivering SNOW-P; this was provided to the Principal Investigator (ZD) who phoned all participants who completed the program. Adverse events were also recorded.

6.3.7 Secondary outcome measures

While a single arm study cannot determine true effectiveness of an intervention, nor was this pilot study powered to determine efficacy, weight and clinical measures were included as secondary exploratory outcomes to inform future controlled trials. Secondary outcomes were change in weight, waist circumference, physical function, quality of life, self-reported fatigue levels and dietary intake across the six week intervention and 12 weeks follow up. All secondary outcomes were measured within participants' homes.

Anthropometry:

Weight was measured in ambulatory participants using their own standing scales at home and was recorded to the nearest 0.1 kg. It was requested that families use the same set of scales at each timepoint. The research team offered scales to those who did not already own them. Weight z-scores were determined using the LMS method with CDC growth chart data. (40,131) For non-ambulatory participants, weight was not measured as it was not feasible to obtain appropriate equipment within the participants' home.

Waist circumference for both ambulatory and non-ambulatory participants was measured by caregivers using a flexible measuring tape and recorded to the nearest centimetre. Caregivers were instructed to measure at the point of the umbilicus.

Physical function:

Change in physical function was measured using two timed function tests: a timed supine-to-stand for ambulatory participants and a timed can stacking exercise for non-ambulatory participants. Timed function tests were instructed and assessed by an appropriately trained physiotherapist (KC, JA, RK or KdV) over telehealth. The timed supine-to-stand is recommended by the DMD Care Considerations to be routinely assessed in clinical practice to measure physical function in ambulant individuals with DMD. (24) For non-ambulatory participants, the 'can stacking' exercise assessed the time taken to stack 5 x 400g cans. The 'can stacking' exercise is a sub-section of the Performance of the Upper Limb (PUL) version 1.2. (253) The PUL is recommended by the DMD Care Considerations to assess upper-limb function in non-ambulant individuals with DMD. (24) A sub-section of the PUL was used to minimise participant burden, rather than completing the entire assessment which takes approximately 20-30 minutes. Both the supine-to-stand and can stacking exercise were administered according to standardised instructions. To overcome potential time delays due to poor internet connections over telehealth, caregivers recorded the assessment on their mobile phone and emailed the recordings to the research team for assessment by a physiotherapist.

For all participants whom who had access to their own (or a family members') activity tracker were encouraged to wear it during the study period. The purpose of this outcome was to assess the feasibility of measuring step count for ambulant participants and upper limb movements as a proxy for step count for non-ambulant participants. To assess feasibility, the number of participants who have access to their own activity tracker and the number of days the activity tracker was worn across the study period was recorded.

Quality of life:

Change in quality of life was measured using the Paediatric Quality of Life Inventory DMD module (PedsQL DMD). (254) PedsQL DMD surveys were administered electronically using REDCap, and electronic versions were validated by Mapi Research Trust. The PedsQL DMD Young Child version was administered to caregivers as a proxy for participants aged five to seven years. For those aged eight to 12 years and 13-18 years the PedsQL DMD Child Report and Teen Report was self-administered by participants, respectively.

Global rating of change:

A global rating of change question about fatigue was asked end of the intervention period (week 6) and the end of follow-up (week 12) (Appendix F). The single question about perceived change in fatigue across the duration of the intervention (administered at week 6) and follow-up (administered at week 12) periods was self-administered by participants using an electronic survey in REDCap. For participants who were unable to answer the question due to immaturity or level of cognition, caregivers recorded their perceived change in their son's fatigue levels.

Dietary intake:

Dietary intake was measured using a three-day food diary over two weekdays and one weekend day (Appendix F). Diet was analysed by one APD (NB) and analysis included: energy, macronutrients (protein, carbohydrate, fat, saturated fat, fibre), micronutrients (calcium, iron, folate, zinc, vitamin C, vitamin B12 and vitamin A) serves of core food groups (grains, fruit, vegetables, proteins and dairy) and discretionary foods. Energy, macro- and micro-nutrients analysis was conducted using Foodworks nutrient analysis software (FoodWorks 10 Professional, v10.0. Brisbane: Xyris Pty Ltd, 2019). Core food groups and discretionary foods were analysed by the APD guided by the Australian Guide to Healthy Eating. (155)

Adverse events e.g. acute illness' that occurred during the study were also recorded, their severity and whether they were related to the intervention.

6.3.8 Data analysis

Participant-level and descriptive data are reported where appropriate. Participant-level data was reported due to the small sample size and due to the feasibility and acceptability study design. Continuous descriptive data were analysed using SPSS statistical software (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp) and are reported as median and IQR. The PedsQL DMD module scores were transformed according to standardised procedures and the mean total score for all 18 items was determined for each participant. (255)

6.4 Results

6.4.1 Participant Characteristics

There were 19 participants identified from clinic lists, referred by clinicians or who expressed interest during the co-design process that were screened for eligibility. Of these, 10 families did not respond whether they were willing to participate, one declined participation and one is a planned enrolment for later in 2021. Included in this preliminary analysis were seven participants who were enrolled as of July 2021, see Table 57. The median age of participants was 11.0 (IQR 7.9, 12.3) and majority (6/7) were treated with steroids. One participant was already taking metformin to assist with weight management. Of enrolled participants six resided in Victoria and one interstate (Northern Territory).

Table 57

SNOW-P Participant Characteristics

No.	Age (years) at enrolment	Ambulant	Steroid treated: type	Other medications/ supplements	Comorbidities [1]	Completed program
1	11.0	Yes	No	SSRI, antipsychotic, metformin, calcium, vitamin D	ASD, ADHD, anxiety, OSA on CPAP	Yes
2	15.8	No	Yes: DFZ	Vitamin D	ASD, ID, anxiety, OSA on CPAP	Withdrew
3	12.3	No	Yes: PNL	Vitamin D, multivitamin	ASD, other DD, OCD, anxiety, ODD, OSA on CPAP	Yes
4	8.9	Yes	Yes: DFZ	Vitamin D, creatine	None	Yes
5	4.9	Yes	Yes: PNL	Creatine	ASD, other DD	Yes
6	11.7	Yes	Yes: PNL	Vitamin C, multivitamin	None	Ongoing
7	7.9	Yes	Yes: Other [2]	Vitamin C, multivitamin	None	Ongoing
All	Median 11.0 (IQR 7.9, 12.3)	Ambulant: 5/7	Steroid treated: 6/7		ASD: 4/7, ID: 1/7, ADHD: 1/7, Other DD: 2/7, OCD: 1/7, Anxiety: 3/7, OSA/CPAP: 3/7	

[1] Abbreviations: ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; DFZ, deflazacort; ID, intellectual disability; IQR, interquartile range; No., participant number; OCD, obsessive-compulsive disorder; ODD, oppositional defiance disorder; OSA/CPAP, obstructive sleep apnoea requiring continuous positive airway pressure; Other DD, other developmental disability; PNL, prednisolone

[2] In the extension, post-trial period for a drug trial

6.4.2 Feasibility and acceptability

Of the seven participants enrolled, one withdrew and six completed the intervention and follow-up period. Of the six participants who completed the program, four attended 100% of the scheduled visits and two attended 88% of the scheduled visits (only one phone review was not attended). The extra topics selected by parents were meal preparation and cooking (n=4), followed by activities and interests, nutrition supplements (both n=2), strategies for a healthy lunchbox and mindfulness (both n=1).

Four parents and two participants with DMD completed the post-program questionnaire, see Table 58 for responses and Table 59 for further feedback recorded as comments. Across participants and parents there was a high level of satisfaction with the program and all recorded they would recommend it to another family with a son with DMD. In regards to feasibility, all parents and participants rated ease of participating as either a four or five (with five being the highest rating of easiness). All respondent liked participating in the program from home and the acceptability of telehealth visits emerged as a theme in the open-response feedback. Only one suggested change to the program was made by one parent who thought face-to-face sessions would be preferable after the COVID-19 pandemic. The weekly visits emerged as a beneficial aspect of the program from the feedback left by participants and parents.

One participant withdrew after enrolment and collection of baseline data but prior to the first session due to changing their mind about participating. Using the withdrawal questionnaire, the caregiver reported COVID-19 made it difficult to participate in the program, but there were no other barriers to participating nor did they have any other suggestions to improve feasibility or acceptability of the program.

Table 58

Findings from the Parent and Participant Post-Program Questionnaire

Respondent [1]	Satisfaction with the program	Recommend to another family/ person with DMD?	Beneficial to participant	Beneficial to parent	Ease of participating	Should the program be offered through the Neuromuscular Clinic?	Did you like doing program all from home?
Parents							
Parent 1	5/5	Yes	Yes	Yes	4/5	Yes	Yes
Parent 3	5/5	Yes	Yes	Yes	5/5	Yes	Yes
Parent 4	5/5	Yes	Yes	Yes	5/5	Yes	Yes
Participants with DMD							
Participant 3	5/5	Yes	Yes	-	5/5	Yes	Yes
Participant 4	3/5	Yes	I don't know	-	4/5	I don't know	Yes

[1] Parent and participant numbers correspond to participant numbers in Table 57

Table 59

Comments Recorded by Participants and Parents

Topic	Comments
Feedback provided in post-program questionnaires	
Beneficial aspects of the program for son	*It is (sic) hard to get (son) to engage in anything so seeing (dietitian) was very helpful for him.* (Parent 1) *My son was able to stick to the small weekly changes and was happy to do it each week as they were one thing at a time.* (Parent 3) *Provided better/different alternatives to food. provided better portion sizes for food.* (Parent 3)
Beneficial aspects of the program for parent/family/household	*For the same reason above it was nice to work with him towards something positive.* (Parent 1) *The whole family benefited from small easy changes for the better.* (Parent 3) *I liked how we had weekly check ins and that made us ultimately stick to changes that were made and that made us feel good as a family.* (Participant 3, aged 12 years) *Better understanding of food requirements for DMD with steroids (sic).* (Parent 5)
Barriers to participating	*(Son) is very resistant to doing anything that he does not want to do so without him engaging with (dietitian) it would be hard. I think when Covid is over it would be much better to have face to face sessions.* (Parent 1) *Distance.* (Parent 5)
Best parts of the program	*The visualization of hunger and the regular catch-ups.* (Parent 1) *The weekly check ins made it easier to stick to the program.* (Parent 3) *All* (Parent 5) *Just making small changes each week and having them followed up and discussed each week.* (Participant 3, aged 12 years)

Table 59

Comments Recorded by Participants and Parents

Topic	Comments
Should the program be offered through the neuromuscular clinic, why/why not	*I found it very easy and helpful to stick to some changes in my son's lifestyle for the better, in the way of diet and exercise.* (Parent 3) *Yes, not many people would understand the portion sizes or alternatives for food, particularly if autism is also a factor. Sometimes its (sic) also too hard to find alternatives just by researching on your own, better to talk to someone who knows, especially specifically for DMD.* (Parent 5)
Other comments	*I really liked that it was done via Telehealth, it made it very easy and fast.* (Parent 3) *THANKYOU so much, (dietitian), for putting your time and energy into this program. It is Very much appreciated.* (Parent 4) *I really liked that the program was done via Telehealth, as the sessions were generally quite quick so the fact we didn't have to travel to the hospital for short appointments made a big difference.* (Participant 3, aged 12 years)
Feedback provided in follow-up phone call	
Additional feedback provided to Principal Investigator (independent of study dietitian)	• No negative feedback. Appreciated the simple and clear explanations especially around mindfulness. • No additional feedback. • No negative feedback. Only positive things to say. Weekly was good – but really only achievable because of telehealth. Short sharp appointments were good. The 6 weeks was an appropriate time because it helped make the changes to habit. • Videoconference – face-to-face over telehealth is preferred over phone. Suggested additions/changes to the program: - Consider expense of trying to find the right food, consider budget, food for storage and freezer options - Strategies to deal with wastage when a child won't eat certain foods. - Knowing the environment, climate and relevant food options (family from Northern Territory) - Strategies/ideas for cooking large batches of a preferred dinner that can be frozen. - Ideas for supports that can be included in National Disability Insurance Scheme packages e.g. freezers to allow more bulk cooking of preferred foods in the context of autism spectrum disorder.

6.4.3 Secondary outcome measures

There were five participants with self-reported weight measurements available at baseline, week 6 and week 12, see Table 60. The median baseline weight was 37.8 kg (IQR 29.5, 50.9) which slightly increase by 0.4 kg (IQR -1.0, 1.7) at week 6 and remained stable at week 12 (n=3 available for preliminary analysis). Weight z-score slightly decreased at week 6 and 12 by -0.01 (IQR -0.15, 0.15) and -0.10 (n=3), respectively. Waist circumference decreased by -1 cm (IQR -4, 0.5) and -2 at week 6 and 12 (n=3), respectively.

At baseline, dietary energy intake was 7137kJ (IQR 6797, 8383) of which 18.5 % (16.1, 36.7) was contributed to by discretionary foods and drink (see Supplementary Table 33). For weeks 6 and 12 only two families completed food diaries respectively (n=2 have also not completed follow-up), the change in dietary intake was therefore not conducted.

Table 60

Anthropometric Measures at Baseline, Week 6 and Week 12

	Weight (kg)			Weight z-score			Waist circumference (cm)		
No	**Baseline (wk 0)**	**△ wk 0-6**	**△ wk 0-12**	**Baseline (wk 0)**	**△ wk 0-6**	**△ wk 0- 12**	**Baseline (wk 0)**	**△ wk 0-6**	**△ wk 0-12**
1 [1]	52.2	+0.4	+0.4	1.66	-0.01	-0.10	83	-	-
2	Withdrew	-	-	-	-	-	-	-	-
3	NA	-	-	NA	-	-	101	-2	-1
4	33.8	-0.1	-0.3	0.93	-0.06	-0.21	74	-1	-2
5	25.1	+1.9	+1.9	2.17	+0.25	+0.11	67	+1	-3
6	49.6	+1.5	Ongoing	1.14	+0.04	Ongoing	90	-6	Ongoing
7	37.8	-1.8	Ongoing	1.96	-0.24	Ongoing	69	0	Ongoing
All	**37.8 (29.5, 50.9)**	**+0.4 (-1.0, 1.7)**	**+0.4**	**1.66 (1.04, 2.07)**	**-0.01 (-0.15, 0.15)**	**-0.10**	**79 (69, 93)**	**-1 (-4, 0.5)**	**-2**

[1] Self-reported waist circumference excluded from analysis due to implausible change (-11cm change at week 6 and +9cm change at week 12)
Abbreviations: Abbreviations: △, change; NA, non-ambulatory; wk, week

Timed function tests were completed by five participants of which three completed a timed supine-to-stand and two the timed can stacking exercise, see Table 61. One participant was unable to complete either assessments due to young age and a neurodevelopmental disability and difficulty following the instructions. Compared to baseline, times for all participants except one increased at week 6.

Table 61

Timed Function Tests

Ambulatory participants – supine to stand					
Participant (age)	**Baseline**	**Wk 6**	**△ wk 0-6**	**Week 12**	**△ wk 0-12**
1 (11.0)	6	8	+2	10	+4
4 (8.9)	8	11	+3	8	0
5 (4.9)	Not able	-	-	-	-
7 (7.9)	4	4	0	Ongoing	-
Non-ambulatory participants – can stacking [1]					
Participant (age)	**Baseline**	**Wk 6**	**△ wk 0-6**	**Week 12**	**△ wk 0-12**
2 (15.8)	Withdrew	-	-	-	-
3 (12.3)	11	9	-3	9	-3
6 (11.7)	**7**	8	+1	Ongoing	**-**

[1] One participant was able to walk independently but was not able to complete a supine-to-stand, therefore the can stacking exercise was completed instead
Abbreviations: △, change; wk, week

The global rating of change in fatigue question was only completed by two participants at week 6 and week 12. At week 6 one participant recorded they felt a “lot better” and one “the same” in regards to fatigue since baseline. At week 12 one participant recorded their levels of fatigue was “a little bit better” and one “the same” since baseline.

There were also low completion rates for the PedsQL DMD electronic survey, see Supplementary Table 34. Five participants completed the survey at baseline and two at weeks 6 and 12. For two participants PedsQL DMD scores increased (n=1 baseline 49 vs. 81 at week 6 and n=1 baseline 56 vs. 63 at week 12) and for one participant scores declined from 53 at baseline, 46 at week 6 and 36 at week 12.

Step count measured by a wrist worn activity tracker was only recorded by one participant. Two participants wore an activity tracker but steps were not able to be recorded; one was not able to obtain a record of the steps; for the other participant who was non-ambulatory the activity tracker did not detect upper limb movements as “steps”. The remaining three participants did not wear an activity tracker.

Three mild adverse events were recorded across two participants all of which were assessed to be unrelated to the intervention by the study Principal Investigator (ZD). One participant experienced an unwell episode with headaches, mild fever, pain and fatigue with some symptoms likely related to change in steroid regimen. The second participant had two unwell episodes both due to a respiratory tract infection with symptoms including loss of appetite.

6.4.4 Impact of the COVID-19 Pandemic on Lifestyle Factors and Participation

At baseline, 4/7 caregivers said the COVID-19 had a negative impact on their son’s weight (options were yes, no, I don’t know). Amongst lifestyle factors, physical activity was most negatively impacted with 6/7 caregivers reporting at least a moderate (at least three out of five) negative impact, see Table 62.

Following the completion of the program, all participants recorded that COVID-19 was not a barrier to participating and that it was a good thing to do during the pandemic.

Table 62

Caregivers Perceptions on the Impact of the COVID-19 Pandemic on Lifestyle Factors for Their Son [1]

Factor	0 (no negative impact)	1	2	3	4	5 (very negative impact)
Diet	4	0	2	0	0	1
Activity	1	0	0	1	4	1
Sleep	3	0	0	3	1	0
Routine	1	0	3	2	1	0
Screen time	3	0	1	1	1	1
Mental health	1	0	0	3	2	1

[1] Number of caregivers (n) selecting each option is reported

6.4.5 Additional Researcher Observations

There were several observations made by the APD who delivered the intervention (NB) which provide further insight into the complexity of managing weight in DMD, but which were not able to be captured in outcome measures. These observations were captured in research notes and are summarised here.

Low mood, anxiety and emotional dysregulation were a common theme amongst participants. One participant experienced bullying at school which led to emotional eating, but the family reported difficulty in finding a psychologist with appropriate expertise and were seeking recommendations from the APD. Another participant experienced significant mood swings after a change in steroid regimen which significantly impacted his ability to engage with the lifestyle goals during the program. Three participants were reported to have been diagnosed with anxiety at baseline.

Features of neurodevelopmental disabilities (e.g. autism spectrum disorder) also complicated the implementation of weight management strategies for families. Of the seven participants, four had at least one neurodevelopmental comorbidity (e.g. autism spectrum disorder, attention deficit hyperactivity disorder, obsessive-compulsive disorder, intellectual disability). One participant with multiple neurodevelopmental comorbidities was finding it

difficult to adjust to a change in school environment and refused to eat at school, implementing regular meals (and regular protein intake) was therefore challenging. Sensory preferences, food aversions and neophobia were also common such as aversions to strong smells, distress around fruits and vegetables and difficulty deviating away from preferred foods.

6.5 Discussion

In this preliminary analysis of this feasibility and acceptability study, we have shown that a co-designed, six-week, intensive lifestyle weight management program delivered virtually is both feasible and acceptable for young people with DMD and their families. There was a high level of satisfaction with the program and all participants reported they would recommend it to other individuals with DMD and their families. Families reported it was easy to participate in the program and the virtual mode of delivery using telehealth was acceptable. There were high rates of attendance for the scheduled sessions and low withdrawal rates. Overall, participants demonstrated weight and/or waist circumference stability for the duration of the program. However, most families did not complete the secondary outcome measures. Outcomes with incomplete data were those requested to be completed outside of schedule visits including: food diaries, electronic surveys for the PedsQL DMD and global rating of change in fatigue questionnaire.

Family-centred interventions delivered weekly that utilise goal-setting and motivational interviewing techniques are emerging as a feasible and acceptable solution to improving weight status, dietary intake and physical activity in DMD. There has been one prior study that identified a solution-focussed coaching intervention (SFC-Peds), delivered using a combination of face-to-face and video call visits, may be a feasible and acceptable approach for diet and physical activity goal setting in young people with DMD (n=5). (112) In SNOW-P the APD delivering the intervention in some aspects also assumed the role of a coach. For example, by prompting participants and/or parents to identify their own goals, using affirmation and in some instances encouraged participation in activities guided by other healthcare professionals (e.g. activities recommended by a neuromuscular physiotherapist). Evidence from the prior SFC-Peds study and from the current SNOW-P study have been consistent in demonstrating: a high completion and attendance rate; young people with DMD would recommend the intervention to others with DMD; and young people with DMD and/or their parents believed the intervention was beneficial. (112) For SFC-Peds, two participants reported the video calls conducted remotely (within participants' homes) were acceptable while three would have preferred face-to-face. (112) The acceptability and feasibility of telehealth visits was clearly demonstrated in the SNOW-P post-program questionnaire (albeit one parent suggested face-to-face visits following the COVID-19 pandemic). During the time of the delivery of SNOW-P throughout the COVID-

19 pandemic, telehealth was the status quo for many healthcare appointments which may have contributed to the ease of utilising this service. Telehealth weight management interventions have also shown to be acceptable, feasible and efficacious in typically developing young people with overweight or obesity. (256,257) One unique benefit of conducting weight management or nutrition programs or consults over telehealth is the insights it can provide into the home food environment, for example families can share food brands and labels, portion sizes and cooking utensils over the video call. However, this study demonstrates that outcome measures conducted within the participants homes may lead to incomplete data. To understand the efficacy on weight and health outcomes in DMD a hybrid model should be considered in the future with flexible telehealth delivery of the intervention but with face-to-face outcome measures.

In addition to virtual delivery over telehealth, the regular weekly visits and "check-ins" emerged as an accepted aspect of SNOW-P. As one participant reported the best aspect of the program was "*just making small changes each week and having them followed up and discussed each week.".* In our recent systematic literature review (see Chapter 4) weekly visits were a key aspect of efficacious weight management programs for young people with chronic healthcare needs. Additionally, higher intensity, multi-component interventions are supported in the literature for typically developing children with overweight and obesity. (119) Interventions delivered at a higher intensity allow time for small, achievable goals to be set without compromising on effectiveness, and this model has been utilised by up-scaled community-based weight management programs. (220)

Secondary outcome measures for this study included the change in weight, waist circumference, physical function, dietary intake, self-reported fatigue and quality of life. At both week 6 and week 12 the median change in weight from baseline was relatively stable (slight increase of 0.4kg at week 6 which remained stable at week 12). Typically for young people with overweight or obesity, weight maintenance is recommended during linear growth while gradual weight loss may be indicated for older post-pubertal adolescents. (258) Weight maintenance is therefore appropriate for the young (≤12 years) cohort of boys with DMD completing our program. Although height growth may be slow in DMD (see sections 1.3.2 and 2.4.3), weight maintenance is preferred than an increasing weight trajectory. We observed a slight reduction in waist circumference across participants, this is a promising finding considering the positive association between waist circumference and metabolic risk factors observed in DMD (see Table 7). (61) In the clinical setting if measuring weight is not

feasible, measuring waist circumference may be a simple way of identify metabolic risk for non-ambulatory individuals with DMD. With the current sample size in this preliminary analysis we are unable to determine median change in time function tests as two different assessments were conducted for ambulatory (n=3) and non-ambulatory (n=2) and individual changes in times were variable.

We identified that secondary outcome measures that were requested to be completed outside of scheduled visit times may not be feasible for families. Outcomes included dietary intake using food diaries, change in self-reported fatigue and quality of life using electronic questionnaires. As such, we had a high amount of missing data and were not able to assess change in some outcome measures (e.g. dietary intake and quality of life). This was an unexpected finding regarding the feasibility of delivering a virtual weight management program in DMD. Despite evidence of validity (90) anecdotally participants of research studies (and patients within clinical settings) find food diaries burdensome. In future research, it is worth considering quicker methods of dietary assessment that can be completed in a single phone call or visit (such as a food frequency questionnaire or 24-hour recall). Delivering a similar program using a combination of telehealth delivery of content but with face-to-face visits for outcomes measures may prevent missing data and overcome the limitations associated with self-reported anthropometric measures and availability of equipment for non-ambulatory boys. While the research team attempted to overcome the impact of COVID-19 by delivering an entirely virtual program, limitations such as self-reported weight and low response rate for online surveys were unable to be overcome. In future, if self-reported anthropometric outcome measures are collected, participants should be guided by researchers with a demonstration to ensure measurements are correctly taken (e.g. waist circumference measurements) and photos or videos could be used to confirm measurements. For timed function tests the physiotherapists instructed participants for the assessments over telehealth while videos were taken on parent's mobile phones to overcome inaccurate times due to poor internet connections. There is emerging evidence that validates functional outcome measures conducted over telehealth in other conditions such as Friedreich's Ataxia, however there is not yet any evidence specific to DMD. (259) This study also identified that using participants own activity trackers is not feasible, as they are either not commonly owned by participants or upper limb movement are not detected. Future studies should consider using standardised, validated wrist accelerometers (e.g. Actigraph) to monitor physical activity in both ambulatory and non-ambulatory patients with DMD. (81)

As identified in the researcher observations, there are several psychosocial factors that contribute to the complexity of managing weight in DMD. As previously discussed (see section 5.8), weight can be a sensitive topic and many young people with DMD also experience issues such as low mood and anxiety. It is essential that those involved in weight management in DMD provide a safe space and build rapport so families feel comfortable discussing sensitive issues (e.g. emotional eating). Clinicians working in DMD should be aware of appropriate referral pathways (e.g. to psychologists or social workers) within or external to their organisation when psychosocial issues arise. For boys with neurodevelopmental disabilities, the researcher observations further support the need for multidisciplinary input, for example from an occupational therapist (Chapter 5 also highlights this), to address feeding and sensory issues that may inhibit weight management strategies.

A major strength of this study was the co-design processes that informed the intervention design and delivery which likely optimised families' acceptance of the intervention. Internationally, this is also the first study for young people with DMD to adopt an evidence-based weight management program that includes multiple components, is family-focussed and delivered by a dietitian. (124) However, an intervention delivered by a multidisciplinary team, such as a dietitian, physiotherapist and mental health clinician, would strengthen this program in the future. The program was also available to all young people with DMD and obesity regardless of ambulatory status or comorbidities (e.g. autism spectrum disorder), however creativity is required to overcome this when assessing outcomes such as using different measures of upper limb function. As previously mentioned there was a high amount of missing data which limited our analysis of secondary outcome measures. Weight and waist circumference measurements were also self-reported which may have implications for reliability, however we attempted to somewhat overcome this by requesting families to use the same scales at each time point. Due to measurements being self-reported we also did not include height and as a result BMI as outcome measures. BMI will be essential to include in future studies as it has shown to impact clinical outcomes in DMD. Future directions for a larger controlled trial, including further co-design with families, are discussed in detail in the discussion chapter of this thesis (see section 7.1).

6.6 Conclusion

Preliminary analysis of SNOW-P suggests that this co-designed, virtual, family-centred, lifestyle weight management program provides a feasible and acceptable solution for weight management in young people with DMD. The virtual delivery and the regular (weekly) visits were key components which contributed to the acceptability of this program. SNOW-P may also lead to weight stability in young people with DMD, efficacy needs to be further tested in a controlled trial. However, the virtual delivery of the program limited the reliability and completion rates for secondary outcome measures. This program is recommended for further co-design with families and healthcare professionals and for efficacy testing in a controlled trial. Box 25 summarises what this chapter contributes regarding weight management in young people with DMD.

Box 25

Contribution to Knowledge (Chapter 5)

For young people with DMD…

- This is the largest weight management program implemented internationally and the first in Australia.
- A co-designed, virtual, family-centred, lifestyle weight management program is a feasible and acceptable solution to managing obesity and may lead to weight stability.
- Efficacy testing is recommended for a similar program.

Chapter 7.

Recommendations for Future Research and Clinical Practice

This thesis provides several recommendations and directions for future research to further develop understanding of the impact and management of body weight in young people with DMD. This thesis also provides key recommendations for clinical practice to help guide nutrition and weight management in DMD.

7.1 Future Research Directions

Following the completion of the feasibility and acceptability study for SNOW-P (Chapter 6), families will be further consulted to refine and develop a DMD weight management program. Iterations of SNOW-P are already underway with healthcare professionals and neuromuscular experts. It has been identified that a specific physical activity component delivered by a physiotherapist would be an important addition in future programs. The refined program will therefore be the Supporting Nutrition And Physical activity in NeuroMuscular Disease (SNAP-NMD) program which incorporates nutrition, physical activity guidance and psychological support. This future program will be scaled-up from SNOW-P to include participants with any neuromuscular disorder (not just DMD), be delivered across multiple sites and have a longer intervention (12 weeks) delivered by a multidisciplinary team. SNAP-NMD will be conducted across four sites: the Melbourne Children's Campus incorporating the Royal Children's Hospital and Murdoch Children's Research Institute; Sydney Children's Hospital; The Children's Hospital at Westmead; and Queensland Children's Hospital. SNAP-NMD will continue to use co-design methodologies by conducting workshops with young people with neuromuscular disorders, caregivers and healthcare professionals. Co-design will inform: nutrition and physical activity topics; an understanding of barriers and enablers to participating in the intervention; preference for delivery of nutrition and physical activity sessions (together or separately); and preferences for resources, session times and engagement between sessions. A Medical Research Future Fund Clinician Researchers grant was submitted for the SNAP-NMD RCT, outcomes for which are expected in late 2021.

In addition to testing the efficacy of the SNAP-NMD program, there are several other areas of need for research regarding nutrition and weight management in DMD, see Table 63. These recommendations for research may also be applied to other rarer, neuromuscular disorders in which nutritional status (both underweight and obesity) may be problematic, such as spinal muscular atrophy and Charcot-Marie Tooth disease.

Table 63

Recommendations for Future Nutrition and Obesity Research in DMD

Regarding the potential contributing factors of excessive weight gain in young people with DMD, future research could consider…

- Measurement of resting and total energy expenditure using gold-standard methodology (indirect calorimetry for resting and doubly labelled water for total energy expenditure) in both ambulatory and non-ambulatory individuals with exploration of differences across nutritional status (e.g. underweight vs. obesity).
- Using qualitative methods, explore the impact of the caregiver's outlook on their son's condition on weight-related behaviours and food provision.
- Exploring the perspectives of young people with DMD regarding weight-related behaviours such as appetite and emotional eating.
- Understanding the role of dystrophin mutations in weight gain.
- The dietary intake of non-ambulatory, steroid-treated males with DMD and the changes in dietary intake as boys transition from the ambulatory to non-ambulatory phase.

For individuals with DMD, future research could consider the impact of BMI status and body composition on…

- Upper limb function in non-ambulatory individuals.
- Clinical outcomes such as cardiomyopathy, dysphagia, lung function and survival.
- Activities of daily living such as toileting, dressing and transfers.
- Quality of life, self- and body-esteem, particularly from the perspectives of young people with DMD as opposed to caregivers as a proxy.

The impact of BMI status and body composition has never been explored for many of these factors in DMD. Researchers should consult with the MDT, individuals with DMD and their families when designing research to ensure outcomes are relevant and meaningful.

Regarding the design and delivery of a weight management intervention for DMD, future research could consider…

- Re-consultation with families on virtual (telehealth) vs. face-to-face delivery of a weight management program following the COVID-19 pandemic.
- Obtaining the perspectives of individuals with DMD, for the design and delivery of a weight management program.
- Involving key healthcare professionals, such as physiotherapists and psychologists in intervention design and delivery.
- To understand the efficacy on clinical outcomes, it will be essential that a weight management program for DMD be tested in a controlled trial.

Regarding weight management interventions for young people with chronic healthcare needs…

- There is a concerning lack of evidence available for weight management for young people with chronic healthcare needs, particularly those with physical disabilities. This should be made a priority in relevant research centres and funding schemes.

7.2 Future Research Design Considerations

There is a need for a contemporary, prospective analysis of growth and weight in DMD (see section 1.3). A large, multi-site, prospective study will enable analysis such as exploring the effect of dystrophin mutation on BMI status. Prospective data would also allow for systematic screening of clinical milestones (e.g. loss of independent ambulation) and would improve accuracy and consistency in anthropometric data. The relationship between BMI status and clinical outcomes in DMD is complex, prospective studies will therefore allow for systematic screening and data collection for covariates mediating these relationships. For example, dietary calcium intake and overall diet quality as a potential mediatory between obesity and earlier fractures could be explored. A large, multi-site sample size would enable stratification by minority BMI categories (e.g. underweight and severe obesity) to explore their effect on clinical outcomes and disease progression. It should also be considered in future research design that consistency is key when exploring the role of nutritional status in DMD. While there are limitations to using BMI, by using consistent, standard measures such as BMI and exploring its effect on clinical outcomes it will become clearer what is considered a ‘heathy weight range’ in DMD. That is, a weight that is associated with the least additional health risks.

7.3 Recommendations for Clinical Practice

Dietitians are skilled at managing nutrition and weight in DMD, although there are few that specifically work with this population. The role of the dietitian working with a young person with DMD and their family may include: assessment of growth and weight, identification and management of nutritional deficiencies and other nutrition-related issues (e.g. constipation), weight management advice (both nutrition/food alongside behavioural strategies such as reducing screen time) and coordinating or advising on broader weight management care involving other healthcare specialties. For the latter, the dietitian should refer to other healthcare professionals which may include (but not limited to): physiotherapists for physical activity advice, medical professionals (e.g. neurologists, endocrinologists, paediatricians or general practitioners) for assessment of metabolic complications, psychologists, social workers or other mental health clinicians to support psychosocial wellbeing (e.g. supporting a young person experiencing bullying, low self-esteem or vulnerability). Specific recommendations for clinical practice that stem from this thesis are listed in Table 64.

Table 64

Recommendations for Clinical Practice for Nutrition and Weight Management in DMD

Monitoring and follow-up:

- High rates of obesity start from as young as five years of age in DMD (section 2.4.4). Weight should be measured and height measured or estimated for non-ambulatory boys and BMI values plotted on CDC growth charts biannually from diagnosis until 20 years of age. (27) This will enable early identification and management of both under- and over-nutrition.
- There is evidence that a higher BMI on the CDC growth charts is associated with adverse clinical outcomes such as OSA, fractures and metabolic risk factors (sections 1.6 and 2.5). This therefore supports monitoring BMI in the clinical setting.
- Monitor for weight loss and implement appropriate nutritional management strategies following scoliosis or other major surgery to prevent malnutrition (section 2.4.7).
- As both obesity and underweight can occur in later adolescence and adulthood (section 2.4.4), transition to adult services should also include dietetic follow-up.
- Routinely screening for metabolic risk factors in young people with DMD and obesity. Routine measurement of waist circumference may indicate metabolic risk factors, and may be particularly useful for non-ambulatory individuals when a weight or height measurement cannot be obtained (section 1.6). Assessment of acanthosis nigricans may be another quick and practical way of identifying metabolic complications (section 1.6). If obesity, a high waist circumference or acanthosis nigricans are present, blood tests may be required (e.g. lipids, fasting glucose, glycated haemoglobin A1c and liver function tests).

General nutritional management:

- All individuals with DMD, but particularly those who are steroid-treated and/or have obesity are at risk of earlier fractures (section 2.5.6). It is therefore recommended to regularly monitor vitamin D levels and calcium intake. Implement strategies if deficient/inadequate including: supplementation, increase dietary calcium intake and safe sun exposure (for vitamin D). (27)
- Nutritional professionals should address fussy eating and avoidance of foods due to their taste, texture or smell with families (Chapter 5). If fussy eating or sensory issues are problematic (e.g. they are causing nutritional deficiencies or are hindering weight management strategies) referral and partnership with an appropriately trained speech pathologist, occupational therapist or specialist feeding clinic may be required. In Australia, the National Disability Insurance Scheme may be an option for some families to support feeding therapy.
- Nutrition advice should respect the time constraints felt by families (Chapter 5). Dietitians should help families identify practical ways to reduce time spent on meal purchasing, preparation and cooking. For example, nutritious meal ideas that can be frozen or quick meals as an alternative to take-away.
- Support families to improve dietary quality (section 3.4.4), such as increasing vegetables and decreasing discretionary foods, to help prevent or assist in the management of diet- or obesity-related co-morbidities such as hypertension and constipation.

Table 64

Recommendations for Clinical Practice for Nutrition and Weight Management in DMD

Specific recommendations for weight management in DMD:

- Preventative weight management strategies should be implemented during the early ambulatory period shortly after diagnosis (Chapter 2). Input from the dietitian early in the disease course will help build trust and rapport between the clinician and families. Focussing on dietary quality early will optimise acceptance of foods such as vegetables which are important for assisting with weight management and diet-related issues such as constipation.
- Dietary education and management should focus on protein sources to promote satiety, help lower total energy intake and to optimise muscle mass (Chapter 3). Dietary protein-sources should be evenly distributed across the day and be included in each meal and snack. Of particular importance is high biological value protein sources such as chicken, eggs, lean meat, fish, dairy foods and legumes over protein derived from discretionary foods (e.g. processed coated meat).
- Clinicians should consider specific DMD-related factors when estimating energy requirements and work with families to adjust energy intakes accordingly, while also implementing strategies to assist with appetite management. Energy output should also be increased by engaging in physical activities where possible as guided by a physiotherapist. Careful estimation of energy balance is required when boys transition to a wheelchair full time which will reduce total energy requirements considerably, or when steroids are commenced as steroid treatment may increase muscle mass (and therefore increase resting energy expenditure) but also increase appetite (see Chapters 1-3).
- If fussy or avoidant eating or sensory issues are barriers to implementing weight management strategies, refer as soon as possible to a feeding specialist (Chapter 5).
- Promote screen-free family meals to support overall wellbeing and development and enable young people with DMD to recognise hunger and satiety cues (Chapter 5).
- Weight should be discussed sensitively, and stigmatising language or blame should be avoided to prevent further psychological burden for young people with DMD and their families (Chapter 5). Healthcare professionals should upskill in approaches to discussing weight sensitively.
- The dietitian should spend time building trust and rapport with families to facilitate open and productive discussions around weight and weight management strategies.
- For young people with DMD who are experiencing psychological distress, bullying, poor-self-esteem, body image concerns or emotional eating (Chapter 5) refer to a psychologist. Psychological support should also be encouraged by the MDT.

Recommendations for healthcare organisations:

- As well as the impact on individuals with DMD and their families, healthcare organisations should consider the costs associated earlier comorbidities such as fractures, OSA or metabolic complications related to a higher BMI. There needs to be adequate staffing and resources in neuromuscular clinics to support preventative weight management strategies and effective obesity treatment.

Thesis Conclusions

This thesis provides a novel understanding of the impact and management of a higher body weight in DMD. Young people with DMD are at high risk of excessive weight gain which can lead to poorer health outcomes. Half of boys aged 11 years have obesity which is six times the rate of typically developing children and adolescents. (6) Historically, the rate of obesity in DMD diminishes throughout adolescence, (5) however it now tracks into adulthood. A higher BMI compromises metabolic health, physical and respiratory function and is associated with earlier risk of comorbidities such as OSA and bone fractures in DMD. Severe physical disability and physical activity limitations, long term steroid treatment, sleep disturbances and reduced resting energy expenditure contribute to obesity in DMD. Dietary risk factors for excessive weight gain may occur in younger ages in boys with better motor function when energy intakes are above estimated requirements. Poor dietary quality and a propensity for a high intake of discretionary foods and low intake of vegetables, fruits, wholegrains and lean protein sources are also dietary risk factors for weight gain in DMD. Barriers to healthy eating and weight management include fussy or avoidant eating behaviours, emotional eating, increased appetite due to steroids and time constraints felt by families. However, enablers of optimal nutrition and effective weight management include caregiver's perceptions that healthy eating is important, beneficial and is a high priority for their family. There is limited evidence for weight management interventions in young people with DMD and other chronic healthcare needs. This thesis provides preliminary evidence that supports the feasibility and acceptability of a co-designed, family-centred, intensive, short (six week) lifestyle weight management program delivered via telehealth for young people with DMD and their caregivers. However, there are limitations of assessing outcome measures via telehealth in this population. Analysis of secondary outcome measures suggests this co-designed intervention may lead to weight and waist circumference stabilisation in DMD. Future directions include further co-developing a weight management program and testing its efficacy in a randomised trial.

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Appendix A.

Supplementary Data for Chapter 1

Supplementary Table 1

Summary of Clinical Practice Guidelines from Australia, USA and UK for Lifestyle Weight Management Interventions for Children and Young People

Source (Country)	**Recommendations for lifestyle weight management interventions:**
*NHMRC [112] * (Aus.)* **Rescinded*	• *Use the 5A's framework: Ask, Assess, Advise, Agree, Assist* • *Focus lifestyle programs on parents, carers and families (C grade of evidence)* • *Plan weight management programs that involve frequent contact with healthcare professional (B grade of evidence)* • *Weight maintenance is an acceptable approach in most situations (D grade of evidence)* • *Recommend lifestyle change— including reduced energy intake and sedentary behaviour, increased physical activity and measures to support behavioural change. (B grade of evidence)*
Academy of Nutrition and Dietetics (USA) [110]	• Registered/accredited dietitians should be part of multicomponent weight management interventions (Strong) • Interventions should be multicomponent and include diet/nutrition, physical activity, and behavioural components (Strong) • Family participation as an integral part of weight management interventions for children of all ages, including teens (Strong) • Interventions should be at least 6 months in duration (Weak) • Interventions can be either within or outside the clinic setting (Weak) • Interventions can include either individual or group sessions (involving family) (Weak)
National Institute for Health and Care Excellence (UK) [111]	Ensure all lifestyle weight management programmes for overweight and obese children and young people are multi-component, including: • diet and healthy eating habits • physical activity • reducing the amount of time spent being sedentary • strategies for changing the behaviour of the child or young person and all close family members

Supplementary Table 1

Summary of Clinical Practice Guidelines from Australia, USA and UK for Lifestyle Weight Management Interventions for Children and Young People

Source (Country)	Recommendations for lifestyle weight management interventions:
	Ensure the following core components, developed with the input of a multidisciplinary team are included: • Behaviour-change techniques to increase motivation and confidence in the ability to change. This includes strategies to help the family identify how changes can be implemented and sustained at home. • Positive parenting skills training, including problem-solving skills, to support changes in behaviour. • An emphasis on the importance of encouraging all family members to eat healthily and to be physically active, regardless of their weight. • A tailored plan to meet individual needs, appropriate to the child or young person's age, gender, ethnicity, cultural background, economic and family circumstances, any special needs and how obese or overweight they are. This should include helping them and their family to set goals, monitor progress against them and provide feedback. • Information and help to master skills in, for example, how to interpret nutritional labelling and how to modify culturally appropriate recipes on a budget. • Help to identify opportunities to become less sedentary and to build physical activity into their daily life • A range of physical activities that the children or young people enjoy and that can help them gradually become more active. • Information for family members who may not attend the programme itself to explain the programme's aims and objectives and how they can provide support. • Ongoing support and follow-up for participants who have completed the programme.

Appendix B.

Supplementary Data for Chapter 2

ETHICS APPROVAL &
GOVERNANCE AUTHORISATION

The Royal Children's Hospital Melbourne

1 June 2018

Dr Z Davidson
Neuroscience Research
Murdoch Children's Research Institute

Dear Dr Davidson,

Project Title: **A retrospective chart review to determine the relationship between weight status and clinical, functional and strength outcomes in patients with Duchenne muscular dystrophy**

HREC Reference Number: **LNR/18/RCHM/233**

I am pleased to advise that the above clinical audit project has received ethical approval from The Royal Children's Hospital Melbourne Human Research Ethics Committee (HREC).

The HREC confirms that your proposal meets the requirements of the National Statement on Ethical Conduct in Human Research (2007). This HREC is organised and operates in accordance with the National Health and Medical Research Council's (NHRMC) National Statement on Ethical Conduct in Human Research (2007), and all subsequent updates, and in accordance with the Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95), the Health Privacy Principles described in the Health Records Act 2001 (Vic) and Section 95A of the Privacy Act 1988 (and subsequent Guidelines).

The project has also received governance authorisation at the Melbourne Children's Campus (incorporating The Royal Children's Hospital, Murdoch Children's Research Institute and the University of Melbourne Department of Paediatrics).

HREC Approval Date: 1 June 2018*
Please note that approval is ongoing until the completion of the project. Annual and final reports are not required for clinical audits.

Participating Sites:
Ethical approval for this project applies at the following sites:

Site Name
• Melbourne Children's Campus (incorporating The Royal Children's Hospital, Murdoch Children's Research Institute and the University of Melbourne Department of Paediatrics).

Approved Documents:
The following documents have been reviewed and approved:

Document	Version	Date
Protocol	-	10 May 2018

Conditions of Ethics Approval:
- Notify the reviewing HREC of your inability to continue as Coordinating Principal Investigator.
- Notify the reviewing HREC of any matters which may impact the conduct of the project.
- The HREC, authorising institution and/or their delegate/s may conduct an audit of the project at any time.

Yours sincerely

Deeptika Chauhan
Research Ethics and Governance Officer
Research Ethics and Governance
The Royal Children's Hospital Melbourne
Phone : (03) 9345 5044
Email : rch.ethics@rch.org.au
Web : www.rch.org.au

Supplementary Table 2

Anthropometric Measures and Z-Score Values Across Age Groups (Observations n=1123) [1]

Age group **(year), n (%)**	**Height (m)**	**Height z-score**	**Weight (kg)**	**Weight z-score**	**BMI (kg/m^2)**	**BMI z-score**	**BMI z-score change, *n***
2, 17 (1.5)	0.90 (0.85, 0.94)	-0.73 (-1.29, 0.65)	14.3 (13.2, 16.0)	0.54 (-0.30, 1.09)	17.22 (16.08, 18.90)	0.53 (-0.03, 1.88)	0.20 (0.15, 0.70) *n=6*
3, 40 (3.6)	0.97 (0.93, 0.99)	-0.48 (-1.22, 0.24)	16.4 (14.9, 17.4)	0.84 (-0.11, 1.10)	17.52 (16.55, 18.40)	1.30 (0.52, 1.89)	0.05 (-0.26, 0.47) *n=18*
4, 61 (5.4)	1.03 (0.99, 1.05)	-0.71 (-1.30, -0.20)	17.9 (16.7, 19.5)	0.40 (-0.22, 0.98)	17.11 (16.33, 18.02)	1.21 (0.66, 1.76)	-0.04 (-0.29, 0.19) *n=34*
5, 78 (7.0)	1.08 (1.04, 1.12)	-0.75 (-1.42, 0.03)	19.5 (18.1, 21.1)	0.21 (-0.35, 0.72)	17.02 (15.71, 17.89)	1.09 (0.24, 1.56)	0.21 (-0.20, 0.58) *n=49*
6, 88 (7.8)	1.12 (1.10, 1.17)	-0.82 (-1.41, -0.04)	21.8 (20.2, 24.9)	0.01 (-0.36, 0.92)	17.18 (15.94, 18.46)	1.13 (0.35, 1.62)	0.02 (-0.26, 0.25) *n=55*
7, 97 (8.6)	1.18 (1.14, 1.22)	-0.99 (-1.64, -0.12)	24.4 (22.5, 28.0)	0.27 (-0.33,1.07)	17.94 (16.59, 19.58)	1.23 (0.64, 1.68)	0.02 (-0.16, 0.33) *n=76*
8, 97 (8.6)	1.23 (1.18, 1.26)	-1.17 (-1.89, -0.46)	28.0 (25.0, 32.3)	0.40 (-0.36, 1.17)	18.83 (16.42, 21.97)	1.28 (0.38, 1.94)	0.01 (-0.17, 0.17) *n=66*
9, 95 (8.5)	1.27 (1.23, 1.31)	-1.27 (-2.01, -0.60)	32.6 (27.8, 38.7)	0.57 (-0.28, 1.34)	20.32 (17.61, 23.81)	1.45 (0.61, 2.05)	0.03 (-0.17, 0.21) *n=80*
10, 91 (8.1)	1.31 (1.26, 1.36)	-1.30 (-2.13, -0.50)	37.5 (30.5, 45.5)	0.63 (-0.39, 1.59)	21.89 (18.81, 25.39)	1.56 (0.79, 2.07)	0.05 (-0.11, 0.16) *n=67*
11, 81 (7.2)	1.35 (1.30, 1.44)	-1.53 (-2.21, -0.23)	44.0 (32.4, 53.2)	0.81 (-0.66, 1.46)	23.44 (18.81, 28.73)	1.67 (0.63, 2.24)	-0.01 (-0.08, 0.14) *n=53*

12, 73 (6.5)	1.37 (1.30, 1.46)	-1.75 (-2.97, -0.86)	46.7 (34.7, 54.0)	0.50 (-0.88, 1.16)	24.12 (18.73, 29.59)	1.64 (0.34, 2.18)	-0.02 (-0.15, 0.12) *n=42*
13, 67 (6.0)	1.40 (1.34, 1.54)	-2.31 (-3.05, -0.56)	50.0 (39.4, 60.0)	0.31 (-0.86, 0.98)	24.82 (21.02, 28.84)	1.56 (0.80, 2.06)	-0.02 (-0.15, 0.14) *n=41*
14, 57 (5.1)	1.47 (1.38, 1.57)	-2.20 (-3.18, -1.04)	55.0 (45.5, 60.0)	0.19 (-0.82, 0.68)	25.63 (20.96, 28.55)	1.49 (0.55, 1.95)	0.00 (-0.13, 0.16) *n=40*
15, 60 (5.3)	1.50 (1.40, 1.63)	-2.58 (-3.68, -1.06)	56.7 (41.7, 64.9)	-0.10 (-1.97, 0.58)	26.01 (20.55, 29.46)	1.45 (0.22, 1.94)	-0.06 (-0.22, 0.04) *n=36*
16, 43 (3.8)	1.55 (1.47, 1.65)	-2.33 (-3.33, -1.25)	57.3 (47.6, 81.0)	-0.45 (-1.60, 1.37)	26.22 (19.53, 30.12)	1.44 (-0.62, 1.96)	-0.04 (-0.21, 0.21) *n=23*
17, 36 (3.2)	1.53 (1.42, 1.65)	-3.03 (-4.28, -1.55)	56.9 (43.4, 65.7)	-0.89 (-2.97, 0.04)	26.92 (19.43, 29.80)	1.41 (-0.80, 1.84)	-0.30 (-0.73, -0.05) *n=26*
18, 25 (2.2)	1.63 (1.50, 1.68)	-1.89 (-3.61, -1.20)	66.0 (51.2, 75.0)	-0.20 (-2.10, 0.53)	26.51 (20.96, 29.00)	1.14 (-0.42, 1.63)	-0.09 (-0.23, 0.24) *n=9*
19, 12 (1.1)	1.56 (1.38, 1.71)	-2.92 (-5.30, -0.86)	71.0 (51.4, 80.8)	0.14 (-2.22, 0.88)	29.22 (23.03, 30.24)	1.54 (0.04, 1.72)	0.35 (-0.39, 0.41) *n=3*
20, 4 (0.4)	1.55 (1.39, 1.72)	-2.98 (-5.27, -0.64)	64.1 (51.8, 75.6)	-0.82 (-2.22, 0.41)	25.93 (24.62, 28.01)	0.78 (0.47, 1.21)	*n=0*
21, 1 (0.1)	-	-	56	-1.6	-	-	*n=0*

[1] Values are median (IQR), z-scores computed from CDC growth chart data
Observations are one measure per patient for each age group, measures closest to patient's birthday were selected if both height and weight values were available
BMI z-score change is the difference in z-score between first and last BMI measure within each year of age, *n* varies as only patients with ≥2 BMI z-score observations for each age group were included

Supplementary Table 3

Body Composition Measures Derived from DXA Across Age Groups (Observations N=232) [1]

Age (n)	Fat Mass (kg)	Fat mass (%)	Truncal fat (kg)	Truncal fat (%)	Lean Mass (kg)	Lean Mass (%)
5 (n=7)	4.5 (4.0, 6.2)	23.4 (21.3, 24.4)	2.1 (1.8, 2.8)	21.0 (19.5, 23.5)	15.6 (14.7, 16.4)	73.7 (72.4, 76.9)
6 (n=11)	5.8 (4.4, 8.0)	27.9 (20.0, 29.8)	2.4 (1.8, 3.5)	24.9 (21.1, 29.5)	18.0 (15.3, 19.8)	69.4 (68.7, 77.2)
7 (n=19)	8.0 (6.0, 10.4)	30.2 (25.3, 34.7)	3.1 (2.4, 4.4)	27.6 (25.3, 32.8)	17.8 (16.0, 19.1)	67.2 (62.8, 71.4)
8 (n=22)	10.3 (7.6, 12.4)	34.9 (27.7, 42.6)	4.5 (3.0, 5.5)	32.6 (25.3, 39.6)	20.0 (17.6, 22.4)	62.8 (55.6, 70.2)
9 (n=22)	13.9 (9.6, 18.8)	40.9 (31.4, 45.2)	6.7 (4.0, 9.0)	39.4 (31.6, 44.4)	21.3 (17.8, 22.5)	56.8 (53.3, 68.6)
10 (n=17)	15.0 (12.0, 20.5)	40.8 (37.9, 45.7)	6.5 (5.2, 8.9)	40.0 (34.8, 45.3)	20.9 (19.6, 23.5)	57.1 (52.2, 60.0)
11 (n=20)	22.6 (12.1, 27.9)	47.5 (34.8, 51.2)	9.5 (4.6, 14.0)	44.8 (30.5, 52.4)	24.6 (20.1, 26.5)	51.7 (47.4, 62.7)
12 (n=14)	20.3 (15.1, 26.9)	44.8 (40.1, 51.3)	8.9 (6.1, 13.1)	43.5 (39.6, 52.9)	24.8 (20.9, 27.1)	53.4 (47.1, 58.3)
13 (n=19)	25.9 (18.1, 30.3)	49.3 (46.4, 54.0)	13.1 (9.5, 17.5)	51.6 (43.7, 55.3)	24.4 (19.7, 29.4)	49.1 (44.2, 51.7)
14 (n=14)	23.9 (17.7, 27.0)	48.6 (46.1, 54.5)	10.9 (7.9, 14.0)	48.4 (44.6, 54.8)	22.7 (21.0, 26.6)	49.4 (44.3, 52.4)
15 (n=21)	26.9 (24.6, 32.5)	49.3 (46.0, 56.7)	12.8 (11.7, 13.8)	50.5 (46.5, 57.8)	26.8 (23.7, 28.1)	49.2 (41.9, 52.3)
16 (n=12)	32.1 (25.4, 36.5)	52.9 (45.6, 55.9)	15.1 (13.1, 18.7)	55.2 (49.6, 60.5)	28.3 (25.8, 29.3)	44.6 (41.2, 51.6)
17 (n=11)	33.2 (22.7, 35.8)	54.3 (49.1, 55.6)	15.8 (10.6, 18.6)	55.5 (52.6, 57.2)	27.8 (22.0, 28.0)	44.6 (42.5, 49.2)
18 (n=7)	35.9 (19.3, 41.7)	53.4 (43.6, 56.8)	17.3 (9.1, 20.6)	55.2 (45.0, 59.6)	28.3 (20.5, 29.8)	44.9 (39.9, 51.2)
19 (n=5)	29.7 (19.6, 30.6)	51.1 (42.0, 57.6)	15.2 (9.2, 15.4)	58.6 (46.0, 58.8)	23.3 (21.7, 27.5)	43.1 (40.8, 50.6)
20 (n=3)	31.1 (22.0, 46.0)	51.0 (43.2, 59.3)	17.3 (11.3, 25.2)	63.6 (45.5, 64.1)	27.6 (21.0, 29.7)	39.6 (38.8, 54.6)

[1] Values are reported as median (IQR)
One additional measure of fat and truncal fat mass % available for ages: 5 (n=8), 16 (n=13), 18 (n=8), 19 (n=6) and 20 years (n=4)
Abbreviations: DXA, dual energy x-ray absorptiometry

Supplementary Table 4

Proportion of Patients Across BMI Status Categories Including Obesity Severity

Age group (year)	Healthy weight	Underweight	Overweight	Moderate obesity [1]	Severe obesity class 1	Severe obesity class 2
2	9 (52.9)	0	3 (17.6)	5 (29.4)	0	0
3	16 (40.0)	0	10 (25.0)	14 (35.0)	0	0
4	26 (42.6)	1 (1.6)	17 (27.9)	16 (26.2)	1 (1.6)	0
5	32 (41.0)	2 (2.6)	31 (39.7)	12 (15.4)	1 (1.3)	0
6	40 (45.5)	1 (1.1)	25 (28.4)	18 (20.5)	4 (4.5)	0
7	41 (42.3)	1 (1.0)	29 (29.9)	18 (18.6)	8 (8.2)	0
8	34 (35.1)	4 (4.1)	26 (26.8)	17 (17.5)	13 (13.4)	3 (3.1)
9	31 (32.6)	3 (3.2)	21 (22.1)	22 (23.2)	12 (12.6)	6 (6.3)
10	21 (23.1)	5 (5.5)	23 (25.3)	26 (28.6)	9 (9.9)	7 (7.7)
11	20 (24.7)	7 (8.6)	13 (16.0)	18 (22.2)	16 (19.8)	7 (8.6)
12	17 (23.3)	7 (9.6)	14 (19.2)	16 (21.9)	13 (17.8)	6 (8.2)
13	19 (28.4)	4 (6.0)	12 (17.9)	19 (28.4)	10 (14.9)	3 (4.5)
14	15 (26.3)	5 (8.8)	13 (22.8)	17 (29.8)	5 (8.8)	2 (3.5)
15	17 (28.3)	8 (13.3)	9 (15.0)	18 (30.0)	5 (8.3)	3 (5.0)
16	13 (30.2)	5 (11.6)	8 (18.6)	13 (30.2)	3 (7.0)	1 (2.3)
17	8 (22.2)	7 (19.4)	10 (27.8)	10 (27.8)	1 (2.8)	0 (0.0)
18	6 (24.0)	5 (20.0)	8 (32.0)	5 (20.0)	1 (4.0)	0 (0.0)
19	5 (41.70)	0 (0)	4 (33.3)	3 (25.0)	0	0
20	3 (75.0)	0	1 (25.0)	0	0	0

[1] Moderate obesity BMI%95 100-120; severe obesity class 1 BMI%95 120-140; severe obesity class 2 BMI%95 >140

Supplementary Table 5

BMI Z-Score Across Ambulatory Status Stratified by Age Groups [1]

	Ambulant		Non-ambulant		
Age group (year)	**n (N%)**	**Median (IQR)**	**n (N%)**	**Median (IQR)**	**P-value**
7	91 (94.8)	1.23 (0.64, 1.68)	5 (5.2)	1.47 (0.86, 2.43)	0.387
8	91 (94.8)	1.33 (0.50, 2.04)	5 (5.2)	0.24 (-4.48, 1.10)	**0.024***
9	82 (88.2)	1.45 (0.78, 2.04)	11 (11.8)	0.61 (-1.15, 2.19)	0.284
10	68 (75.6)	1.54 (0.85, 1.95)	22 (24.4)	1.93 (0.62, 2.21)	0.256
11	50 (64.9)	1.54 (0.63, 2.24)	27 (35.1)	1.93 (1.48, 2.28)	0.216
12	30 (44.1)	1.66 (0.84, 2.05)	38 (55.9)	1.65 (0.34, 2.27)	0.882
13	25 (39.7)	1.66 (1.06, 2.18)	38 (60.3)	1.17 (0.69, 1.96)	0.216
14	16 (29.6)	1.70 (0.95, 2.16)	38 (70.4)	1.27 (0.53, 1.84)	0.256
15	13 (22.8)	1.73 (0.91, 2.27)	44 (77.2)	1.39 (0.14, 1.89)	0.148
16	2 (5.0)	0.90 (0.08, 1.72)	38 (95.0)	1.44 (-0.76, 2.03)	0.974
17	2 (5.9)	1.88 (1.55, 2.21)	32 (94.1)	1.41 (-1.17, 1.84)	0.257
18	2 (8.7)	0.25 (-0.64, 1.14)	21 (91.3)	1.20 (-0.42, 1.66)	0.506
19	2 (16.7)	0.04 (-0.48, 0.57)	10 (83.3)	1.61 (0.68, 1.80)	0.273
20	1 (25.0)	0.57 (0.57, 0.57)	3 (75.0)	0.99 (0.36, 1.43)	1.000

[1] All patients were ambulant between the ages of 2-6

Supplementary Table 6

Fat Mass % Across Ambulatory Status Stratified by Age Groups [1]

	Ambulant		Non-ambulant		
Age group (year)	**n (N%)**	**Median (IQR)**	**n (N%)**	**Median (IQR)**	**P-value**
10	15 (88.2)	40.2 (36.7, 45.7)	2 (11.8)	48.0 (44.9, 51.0)	0.132
11	14 (73.7)	46.1 (33.9, 48.2)	5 (26.3)	55.8 (45.4, 60.5)	0.186
12	6 (46.2)	41.5 (35.3, 48.0)	7 (53.8)	46.7 (41.8, 54.7)	0.295
13	10 (55.6)	48.1 (42.6, 54.4)	8 (44.4)	52.9 (46.6, 53.7)	0.633
14	5 (35.7)	46.1 (42.1, 46.3)	9 (64.3)	50.0 (48.0, 55.1)	0.083
15	8 (40.0)	47.6 (46.0, 50.1)	12 (60.0)	50.6 (46.7, 57.1)	0.343
16	2 (16.7)	43.9 (43.2, 44.6)	10 (83.3)	54.2 (47.9, 55.9)	0.121
17	1 (9.1)	44.3 (44.3, 44.3)	10 (90.9)	54.5 (49.5, 55.6)	0.364
19	1 (16.7)	41.0 (41.0, 41.0)	5 (83.3)	55.0 (47.1, 57.6)	0.333
20	1 (25.0)	43.5 (43.5, 43.5)	3 (75.0)	58.4 (42.9, 60.1)	1.000

[1] All patients were ambulant between the ages of 2-9 years

Supplementary Table 7

Lean Mass % Across Ambulatory Status Stratified by Age Groups [1]

	Ambulant		Non-ambulant		
Age group (year)	**n (N%)**	**Median (IQR)**	**n (N%)**	**Median (IQR)**	**P-value**
10	15 (88.2)	57.5 (52.2, 60.7)	2 (11.8)	50.1 (47.0, 53.1)	0.132
11	14 (73.7)	52.3 (50.0, 63.7)	5 (26.3)	42.8 (38.3, 53.2)	0.219
12	6 (46.2)	56.9 (50.1, 62.0)	7 (53.8)	51.2 (44.2, 56.2)	0.295
13	10 (55.6)	50.2 (44.2, 55.8)	8 (44.4)	45.6 (44.4, 51.3)	0.573
14	5 (35.7)	52.4 (51.6, 56.1)	9 (64.3)	48.5 (43.7, 50.1)	0.112
15	8 (40.0)	50.6 (48.2, 52.5)	12 (60.0)	47.9 (41.5, 51.4)	0.384
16	2 (16.7)	54.2 (53.9, 54.5)	10 (83.3)	43.2 (42.6, 47.5)	**0.036**
17	1 (9.1)	54.2 (54.2, 54.2)	10 (90.9)	43.9 (42.5, 48.8)	0.364
19	1 (16.7)	57.3 (57.3, 57.3)	5 (83.3)	41.9 (40.8, 46.8)	0.400
20	1 (25.0)	54.6 (54.6, 54.6)	3 (75.0)	39.2 (38.8, 39.6)	1.000

[1] All patients were ambulant between the ages of 2-9 years

Supplementary Table 8

BMI Status Across New and Old Era Young People With DMD

Age group n (N%)		Underweight		Healthy weight		Overweight		Obese	
New	**Old**	**New**	**Old**	**New**	**Old**	**New**	**Old**	**New**	**Old**
2 (10)	-	0 (0.0)	-	4 (40.0)	-	1 (10.0)	-	5 (50.0)	-
3 (23)	18 (3.6)	0 (0.0)	0 (0.0)	7 (30.4)	9 (50.0)	5 (21.7)	1 (5.6)	11 (47.8)	8 (44.4)
4 (41)	28 (5.6)	1 (2.4)	0 (0.0)	16 (39.0)	9 (32.1)	11 (26.8)	9 (32.1)	13 (31.7)	10 (35.7)
5 (52)	39 (7.8)	0 (0.0)	1 (2.6)	23 (44.2)	17 (43.6)	18 (34.6)	10 (25.6)	11 (21.2)	11 (28.2)
6 (58)	54 (10.7)	0 (0.0)	1 (1.9)	24 (41.4)	28 (51.9)	20 (34.5)	9 (16.7)	14 (24.1)	16 (29.6)
7 (65)	56 (11.1)	0 (0.0)	1 (1.8)	26 (40.0)	23 (41.1)	20 (30.8)	15 (26.8)	19 (29.2)	17 (30.4)
8 (63)	53 (10.5)	2 (3.2)	2 (3.8)	13 (20.6)	15 (28.3)	19 (30.2)	19 (35.8)	29 (46.0)	17 (32.1)
9 (66)	55 (10.9)	2 (3.0)	3 (5.5)	18 (27.3)	22 (40.4)	13 (19.7)	10 (18.2)	33 (50.0)	20 (36.4)
10 (63)	48 (9.5)	2 (3.2)	4 (8.3)	13 (20.6)	14 (29.2)	16 (25.4)	7 (14.6)	32 (50.8)	23 (47.9)
11 (59)	43 (8.5)	2 (3.4)	5 (11.6)	16 (27.1)	11 (25.6)	10 (16.9)	7 (16.3)	31 (52.5)	20 (46.5)
12 (55)	30 (6.0)	4 (7.3)	3 (10.0)	13 (23.6)	10 (33.3)	12 (21.8)	4 (13.3)	26 (47.3)	13 (43.3)
13 (54)	30 (6.0)	3 (5.6)	4 (13.3)	14 (25.9)	15 (50.0)	10 (18.5)	5 (16.7)	27 (50.0)	6 (20.0)
14 (44)	25 (5.0)	5 (11.4)	3 (12.0)	9 (20.5)	9 (36.0)	9 (20.5)	8 (32.0)	21 (47.7)	5 (20.0)
15 (53)	22 (4.4)	7 (13.2)	5 (22.7)	13 (24.5)	8 (36.4)	9 (17.0)	3 (13.6)	24 (45.3)	6 (27.3)
16 (40)	2 (0.4)	4 (10.0)	4 (26.7)	11 (27.5)	4 (53.3)	8 (20.0)	1 (6.7)	17 (42.5)	2 (13.3)
17 (36)	-	7 (19.4)	-	8 (22.2)	-	10 (27.8)	-	11 (30.6)	-
18 (25)	-	5 (20.0)	-	6 (24.0)	-	8 (32.0)	-	6 (24.0)	-
19 (12)	-	0 (0.0)	-	5 (41.7)	-	4 (33.3)	-	3 (25.0)	-
20 (4)	-	0 (0.0)	-	3 (75.0)	-	1 (25.0)	-	0 (0.0)	-

Supplementary Table 9

BMI Status at Ages Five to Nine Years as A Predictor of Time to Loss of Ambulation Using A Cox Proportional Hazards Model [1]

Age at BMI measure	BMI status	Hazard Ratio	95% CI lower	95% CI upper	P-value
Five years	*Overweight*	1.237	0.572	2.675	0.590
	Obese	0.644	0.178	2.338	0.504
Six years	*Overweight*	0.602	0.242	1.499	0.276
	Obesity	0.771	0.357	1.662	0.507
Seven years	*Overweight*	0.930	0.470	1.839	0.834
	Obese	0.737	0.351	1.546	0.419
Eight years	*Overweight*	0.820	0.406	1.658	0.581
	Obese	0.714	0.368	1.383	0.317
Nine years	*Overweight*	1.211	0.608	2.410	0.587
	Obese	0.919	0.458	1.844	0.812

[1] *Five years*: event n=30, censored n=45, missing n=80, censored cases before the earliest event in a stratum n=3. *Six years*: event n=37, censored n=49, missing n=71, censored cases before the earliest event in a stratum n=1. *Seven years*: event n=46, censored n=48, missing n=61, excluded loss of ambulation prior to seven years n=3. *Eight years*: event n=52, censored n=41, missing n=56, excluded loss of ambulation prior to eight years n=9. *Nine years*: event n=48, censored n=35, missing n=57, excluded loss of ambulation prior to nine years n=18
Reference category is no overweight or obesity

Supplementary Table 10

BMI Status at Earliest Measure as A Predictor of a Time Function Tests Using a Cox Proportional Hazards Model

BMI status	Hazard Ratio	95% CI lower	95% CI upper	P-value
10m walk/run completed in 7-10 seconds [1]				
Overweight	1.151	0.636	2.084	0.642
Obese	0.762	0.372	1.562	0.459
10m walk/run completed in >10 seconds[2]				
Overweight	1.123	0.504	2.502	0.777
Obese	1.181	0.524	2.663	0.688
four stair climb completed in >8 seconds [3]				
Overweight	0.951	0.494	1.830	0.881
Obese	0.808	0.356	1.830	0.609
Supine-to-stand completed in >7 seconds[4]				
Overweight	1.190	0.659	2.149	0.564
Obese	0.848	0.423	1.698	0.641

[1] Event n=56, censored n=35, missing n=66, censored cases before the earliest event in a stratum n=1
[2] Event n=35, censored n=47, missing n=75, censored cases before the earliest event in a stratum n=1
[3] Event n=45, censored n=41, missing n=71, censored cases before the earliest event in a stratum n=1
[4] Event n=57, censored n=33, missing n=64, excluded event prior to first BMI measure n=3 censored cases before the earliest event in a stratum n=1
Reference category is no overweight or obesity

Supplementary Table 11

BMI Status at Ages Five to Nine Years as a Predictor of Time to a 10m Walk/Run Completed in >10 Seconds Using a Cox Proportional Hazards Model [1]

Age at BMI measure	BMI status	Hazard Ratio	95% CI lower	95% CI upper	P-value
Five years	*Overweight*	1.655	0.598	4.581	0.332
	Obese	0.869	0.179	4.219	0.862
Six years	*Overweight*	0.849	0.261	2.763	0.786
	Obese	1.236	0.420	3.633	0.700
Seven years	*Overweight*	1.451	0.624	3.375	0.387
	Obese	1.302	0.503	3.373	0.587
Eight years	*Overweight*	0.648	0.251	1.675	0.371
	Obese	0.776	0.330	1.826	0.561
Nine years	*Overweight*	1.561	0.614	3.967	0.349
	Obese	1.363	0.549	3.386	0.505

[1] *Five years*: event n=17, censored n=31, missing n=103, censored cases before the earliest event in a stratum n=7. *Six years*: event n=19, censored n=42, missing n=97. *Seven years*: event n=29, censored n=43, missing n=86. *Eight years*: event n=30, censored n=36, missing n=90, excluded10m walk/run completed in >10 seconds occurred prior to eight years n=2. *Nine years*: event n=28, censored n=30, missing n=95, excluded 10m walk/run completed in >10 seconds occurred prior to nine years n=5
Reference category is no overweight or obesity

Supplementary Table 12

BMI Status at Ages Five to Nine Years of as a Predictor of a Four Stair Climb Completed in >8 Seconds Using a Cox Proportional Hazards Model [1]

Age at BMI measure	BMI status	Hazard Ratio	95% CI lower	95% CI upper	P-value
Five years					
	Overweight	0.515	0.216	1.231	0.136
	Obese	0.537	0.149	1.941	0.343
Six years	*Overweight*	0.895	0.357	2.245	0.813
	Obese	0.701	0.269	1.823	0.466
Seven years	*Overweight*	0.842	0.404	1.758	0.647
	Obese	0.682	0.291	1.602	0.380
Eight years	*Overweight*	0.632	0.279	1.432	0.272
	Obese	0.507	0.225	1.142	0.101
Nine years	*Overweight*	0.718	0.279	1.844	0.718
	Obese	0.619	0.263	1.454	0.619

[1] *Five years*: event n=25, censored n=28, missing n=101, censored cases before the earliest event in a stratum n=4. *Six years*: event n=28, censored n=36, missing n=94. *Seven years*: event n=37, censored n=37, missing n=84. *Eight years*: event n=35, censored n=30, missing n=84, excluded four stair climb completed in >8 seconds occurred prior to eight years n=9. *Nine years*: event n=29, censored n=26, missing n=89, excluded four stair climb completed in >8 seconds occurred prior to nine years n=14
Reference category is no overweight or obesity

Supplementary Table 13

BMI Status at Ages Five to Nine Years of a Predictor of a Supine-To-Stand Completed in >7 Seconds Using a Cox Proportional Hazards Model [1]

Age at BMI measure	BMI status	Hazard Ratio	95% CI lower	95% CI upper	P-value
Five years	*Overweight*	0.909	0.449	1.843	0.792
	Obese	0.658	0.219	1.976	0.456
	Overweight	1.075	0.494	2.339	0.855
Six years	*Obese*	0.770	0.339	1.750	0.532
	Overweight	1.198	0.612	2.345	0.599
Seven years	*Obese*	0.776	0.369	1.632	0.504
	Overweight	0.723	0.334	1.565	0.410
Eight years	*Obese*	0.620	0.301	1.276	0.194
Nine years	*Overweight*	0.885	0.355	2.209	0.794
	Obese	0.638	0.299	1.361	0.245

[1] *Five years*: event n=35, censored n=24, missing n=98, censored cases before the earliest event in a stratum n=1. *Six years*: event n=38 censored n=31, missing n=89. *Seven* years: event n=46, censored n=31, missing n=81. *Eight years*: event n=41, censored n=26, missing n=81, excluded supine-to-stand completed in >7 seconds occurred prior to eight years n=10. *Nine years*: event n=34, censored n=20, missing n=81, excluded supine-to-stand completed in >7 seconds occurred prior to nine years n=23
Reference category is no overweight or obesity

Supplementary Table 14

BMI Status at Ages Five to Nine Years as a Predictor of a NSAA Score ⩽9 Using a Cox Proportional Hazards Model [1]

Age at BMI measure	BMI status	Hazard Ratio	95% CI lower	95% CI upper	P-value
Five years	*Overweight*	1.317	0.505	3.436	0.573
	Obesity	0.751	0.158	3.578	0.719
Six years	*Overweight*	1.894	0.694	5.167	0.212
	Obesity	1.516	0.491	4.678	0.469
Seven years	*Overweight*	2.082	0.846	5.124	0.110
	Obesity	1.089	0.326	3.642	0.889
Eight years	*Overweight*	0.747	0.260	2.147	0.588
	Obesity	1.080	0.450	2.593	0.863
Nine years	*Overweight*	1.076	0.386	3.003	0.889
	Obesity	1.461	0.582	3.665	0.419

[1] *Five years*: event n=19, censored n=32, missing n=104, censored cases before the earliest event in a stratum n=3. *Six years*: event n=21 censored n=39, missing n=98. *Seven years*: event n=24, censored n=42, missing n=92. *Eight years*: event n=27, censored n=35, missing n=94, excluded NSAA score ≤ 9 occurred prior to eight years n=2. *Nine years*: event n=27, censored n=29, missing n=98, excluded NSAA score ≤ 9 occurred prior to nine years n=4
Reference category is no overweight or obesity

Supplementary Table 15

BMI Status at Ages Five to Nine Years as a Predictor of a 6MWD <325m Using a Cox Proportional Hazards Model [1]

Age at BMI measure	BMI status	Hazard Ratio	95% CI lower	95% CI upper	P-value
Five years	*Overweight*	0.411	0.088	1.912	0.257
	Obesity	0.205	0.021	2.023	0.175
Six years	*Overweight*	1.049	0.267	4.122	0.945
	Obesity	0.487	0.091	2.611	0.401
Seven years	*Overweight*	0.752	0.230	2.464	0.638
	Obesity	0.523	0.130	2.107	0.362
Eight years	*Overweight*	0.864	0.254	2.943	0.815
	Obesity	0.567	0.185	1.742	0.322
Nine years	*Overweight*	1.248	0.360	4.333	0.727
	Obesity	0.876	0.293	2.614	0.812

[1] *Five years*: event n=9, censored n=13, missing n=126, censored cases before the earliest event in a stratum n=10. *Six years*: event n=11 censored n=14, missing n=123, censored cases before the earliest event in a stratum n=10. *Seven years*: event n=15, censored n=23, missing n=118, censored cases before the earliest event in a stratum n=2. *Eight years*: event n=17, censored n=24, missing n=117. *Nine years*: event n=17, censored n=17, missing n=122, excluded 6MWD <325m occuured prior to nine years n=2
Reference category is no overweight or obesity

Supplementary Table 16

BMI Status at Ages Five to Nine Years as a Predictor of Scoliosis Using a Cox Proportional Hazards Model [1]

Age at BMI measure	BMI status	Hazard Ratio	95% CI lower	95% CI upper	P-value
Five years	*Overweight*	0.572	0.167	1.959	0.374
	Obesity	0.536	0.065	4.394	0.561
Seven years	*Overweight*	0.310	0.090	1.074	0.065
	Obesity	0.735	0.267	2.025	0.552
Eight years	*Overweight*	1.077	0.441	2.630	0.870
	Obesity	0.544	0.181	1.636	0.279
Nine years	*Overweight*	0.472	0.165	1.345	0.160
	Obesity	0.828	0.348	1.970	0.669

[1] *Five years*: event n=12, censored n=53, missing n=80, censored cases before the earliest event in a stratum n=13. *Six years*: not able to be performed as coefficients did not converge. *Seven years*: event n=23, censored n=73, missing n=61, censored cases before the earliest event in a stratum n=1. *Eight years*: event n=27, censored n=65, missing n=61, censored cases before the earliest event in a stratum n=3, excluded scoliosis diagnosis before eight years n=2. *Nine years*: event n=26, censored n=65, missing n=61, censored cases before the earliest event in a stratum n=1, excluded scoliosis diagnosis prior to nine years n=5
Reference category is no overweight or obesity

Supplementary Table 17

BMI Status at Ages Five to Nine Years of as a Predictor Of FVC <1L Using a Cox Proportional Hazards Model [1]

Age at BMI measure	BMI status	Hazard Ratio	95% CI lower	95% CI upper	P-value
Six years	*Overweight*	1.046	0.270	4.045	0.948
	Obesity	0.919	0.243	3.480	0.901
Seven years	*Overweight*	1.194	0.412	3.458	0.744
	Obesity	0.762	0.202	2.881	0.689
Eight years	*Overweight*	0.623	0.113	3.429	0.586
	Obesity	2.716	0.773	9.547	0.119

[1] *Five* and *eight years*: Not able to be performed as coefficients did not converge. *Six years*: event n=14, censored n=59, missing n=85. *Seven years*: event n=17, censored n=71, missing n=70. *Nine years*: event n=13, censored n=62, missing n=72, censored cases before the earliest event in a stratum n=11
Reference category is no overweight or obesity

Supplementary Table 18

Descriptive Statistics for Right and Left Hand Grip Strength Observations Stratified by BMI Status and Age Groups

Age group (years)	Underweight		Healthy weight		Overweight		Obese	
	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD	n	Mean ± SD
Right hand grip								
6-8	0		4	29 ± 10	6	43 ± 18	1	44
8-10	0		4	44 ± 27	1	42	14	48 ± 16
10-12	0		5	46 ± 32	9	39 ± 21	15	46 ± 30
12-14	2	22 ± 8	10	45 ± 14	5	34 ± 20	21	45 ± 23
14-16	7	20 ± 13	9	37 ± 15	11	23 ± 9	13	31 ± 24
16-20	7	30 ± 12	7	31 ± 10	11	36 ± 11	18	37 ± 24
Left hand grip								
6-8	0		4	28 ± 9	6	36 ± 17	1	14
8-10	0		4	39 ± 17	1	38	14	46 ± 12
10-12	0		5	52 ± 33	9	41 ± 24	15	45 ± 29
12-14	2	20 ± 0	10	49 ± 22	5	39 ± 18	21	43 ± 26
14-16	7	25 ± 18	9	35 ± 15	11	20 ± 8	13	31 ± 23
16-20	7	39 ± 19	7	34 ± 10	11	35 ± 12	18	33 ± 17

Appendix C.

Supplementary Data for Chapter 3

Supplementary Table 19

Intake of the Five Food Groups and Discretionary Foods Compared to the Australian Guide to Healthy Eating Recommendations.

	Healthy weight (mean age 7.7 years)			Above a healthy weight (mean age 9.1 years)			Total	
	AGHE [cxii] recommended serves 4-8 years	**Serves/day**	**Below target %**	**AGHE recommended serves 9-11 years**	**Serves/day**	**Below target %**	**Serves/day**	**Below target %**
Vegetables	4.5	0.8 [0.1, 1.3]	100	5	0.9 [0.5, 1.8]	100	0.8 [0.4, 1.4]	100
Fruit, total (including pure fruit juice)	1.5	1.8 [0.7, 2.3]	45.5	2	1.9 [0.8, 3.4]	46.2	1.8 [0.8, 3.2]	46.0
Fruit, fresh fruit only	1.5	0.8 [0.5, 1.4]	81.8	2	0.8 [0.3, 1.5]	80.8	0.8 [0.3, 1.5]	81.1
Grain (cereal) foods	4	4.1 [3.0, 5.8]	54.6	5	4.0 [3.0, 4.5]	69.2	4 [3.0, 4.5]	64.9
Lean meat and poultry, fish, eggs, nuts and seeds, and legumes/beans	1.5	1.4 [0.7, 1.8]	54.6	2.5	1.4 [1.0, 1.9]	76.9	1.4 [0.9, 1.8]	70.3
Milk, yoghurt, cheese and/or alternatives	2	1.4 [0.8, 2.8]	72.7	2.5	1.7 [1.1, 2.1]	84.6	1.7 [1.1, 2.1]	81.1
Discretionary foods	0-2.5	3.5 [2.6, 6.2]	72.7	0-3	3.2 [2.0, 3.7]	53.8	3.3 [2.0, 4.7]	59.5

[cxii] Abbreviations: AGHE, Australian Guide to Health Eating

Appendix D.

Supplementary Data for Chapter 4

Search strategy

#1 MeSH descriptor: [Child] explode all trees

#2 MeSH descriptor: [Adolescent] this term only

#3 child*:ti,ab

#4 adolescen*:ti,ab

#5 MeSH descriptor: [Pediatrics] explode all trees

#6 pediatric*:ti,ab (Word variations have been searched)

#7 teen*:ti,ab

#8 MeSH descriptor: [Minors] explode all trees

#9 youth*:ti,ab

#10 (under near/1 "18 years"):ti,ab

#11 "young people":ti,ab

#12 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11

#13 MeSH descriptor: [Chronic Disease] explode all trees

#14 disease*:ti,ab

#15 disab*:ti,ab

#16 syndrome*:ti,ab

#17 disorder*:ti,ab

#18 autis*:ti,ab

#19 cancer*:ti,ab

#20 aspergers:ti,ab

#21 asthma*:ti,ab

#22 neuromuscular:ti,ab

#23 injur*:ti,ab

#24 (muscular next dystrophy):ti,ab

#25 neurodevelopmental:ti,ab

#26 (special next need*):ti,ab

#27 (spina next bifida):ti,ab

#28 (prader next willi):ti,ab

#29 epilep*:ti,ab

#30 illness*:ti,ab

#31 retard*:ti,ab

#32 (non next ambulant):ti,ab

#33 (restrict* next mobil*):ti,ab

#34 (brain next damage*):ti,ab

#35 (mental next health):ti,ab

#36 (birth next defect*):ti,ab

#37 (Spinal next dysraphism):ti,ab

#38 Hypopituitarism:ti,ab

#39 diabet*:ti,ab

#40 disorder*:ti,ab

#41 (multiple next sclerosis):ti,ab

#42 arthrit*:ti,ab

#43 (cerebral next palsy):ti,ab

#44 leukemia:ti,ab

#45 (chronic next health next condition*):ti,ab

#46 (chronic next condition*):ti,ab

#47 (birth next defect*):ti,ab

#48 #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47

#49 weight:ti,ab

#50 "body mass index":ti,ab

#51 BMI:ti,ab

#52 MeSH descriptor: [Weight Loss] explode all trees

#53 #49 or #50 or #51 or #52

#54 nutrition*:ti,ab

#55 diet*:ti,ab

#56 lifestyle*:ti,ab

#57 behaviour*:ti,ab

#58 (weight next reduc*):ti,ab

#59 (weight next loss):ti,ab

#60 obesity:ti,ab

#61 (weight next maintenance):ti,ab

#62 (energy next restrict*):ti,ab

#63 (calor* next restrict*):ti,ab

#64 (weight next management):ti,ab

#65 #54 or #55 or #56 or #57 or #58 or #59 or #60 or #61 or #62 or #63 or #64

#66 intervention*:ti,ab

#67 program*:ti,ab

#68 clinic:ti,ab

#69 trial:ti,ab

#70 therap*:ti,ab

#71 treatment*:ti,ab

#72 prescription*:ti,ab

#73 regime*:ti,ab

#74 management:ti,ab

#75 strateg*:ti,ab

#76 #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73 or #74 or #75

#77 #65 near/2 #76

#78 MeSH descriptor: [Healthy Lifestyle] explode all trees

#79 MeSH descriptor: [Caloric Restriction] explode all trees

#80 MeSH descriptor: [Diet, Reducing] explode all trees

#81 MeSH descriptor: [Diet, Carbohydrate-Restricted] this term only

#82 MeSH descriptor: [Diet, Fat-Restricted] this term only

#83 MeSH descriptor: [Diet, Mediterranean] this term only

#84 MeSH descriptor: [Fasting] this term only

#85 MeSH descriptor: [Ketogenic Diet] this term only

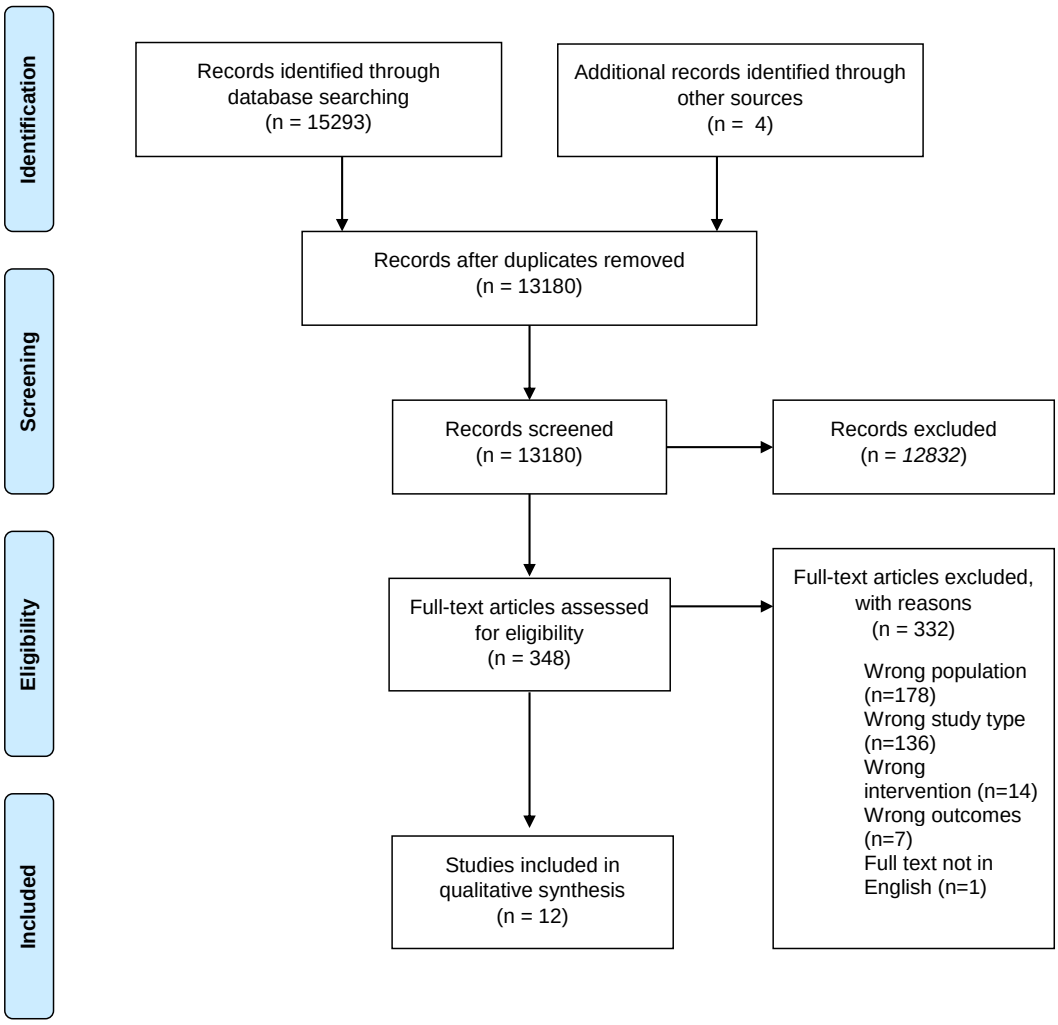
#86 MeSH descriptor: [Weight Reduction Programs] explode all trees

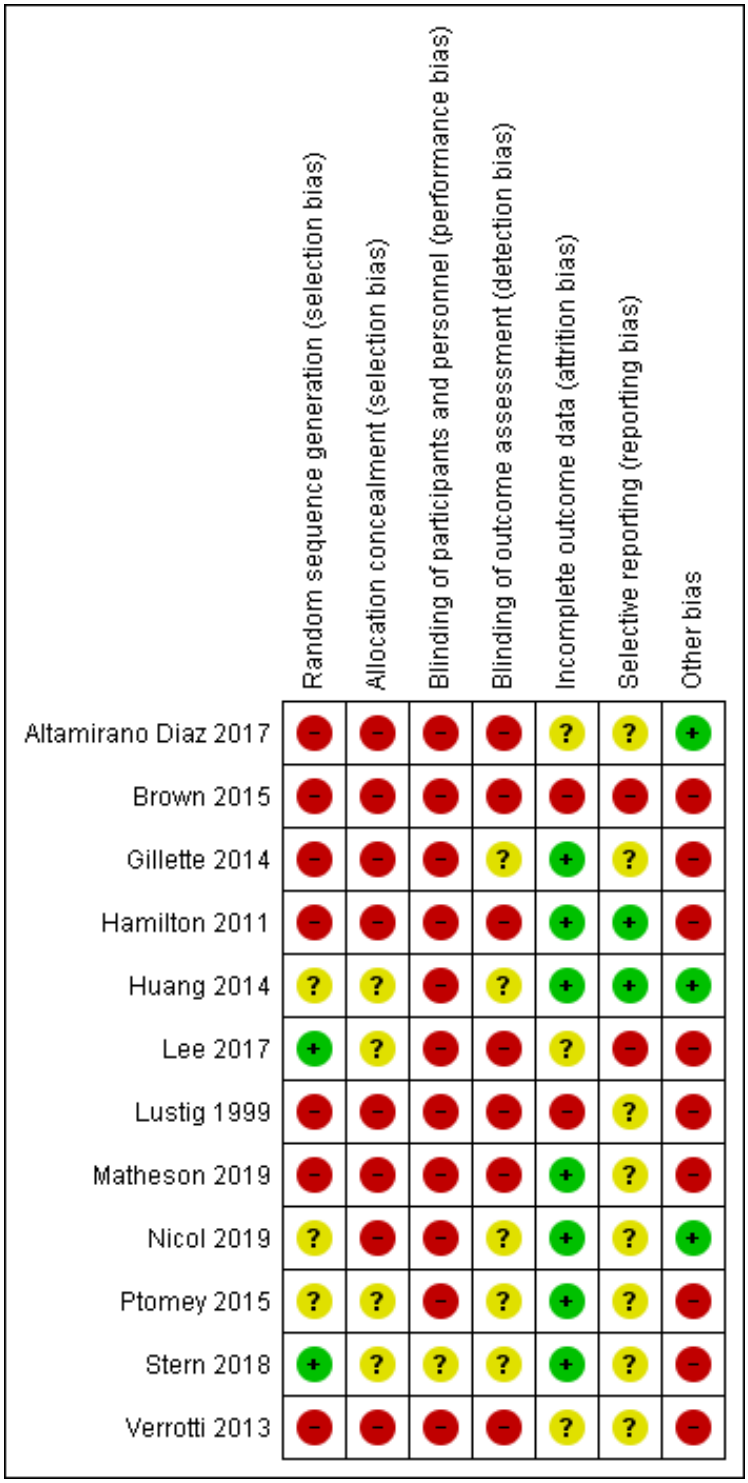
#87 #78 or #79 or #80 or #81 or #82 or #83 or #84 or #85 or #86

#88 #77 or #87

#89 #12 and #48 and #53 and #88

PRISMA 2009 Flow Diagram





Supplementary Figure 1

Summary of the risk of bias for each study included in the systematic review assessed using the Cochrane Risk of Bias tool.

Appendix E.

Supplementary Data for Chapter 5

ETHICS APPROVAL

The Royal Children's Hospital Melbourne

17 May 2019

Professor M Ryan
Neurology Department
The Royal Children's Hospital Melbourne

Dear Professor Ryan,

Project Title: **EAT-DMD**

HREC Reference Number: **HREC/51070/RCHM-2019**
RCH HREC Reference Number: **2019.067**

I am pleased to advise that the above project has received ethical approval from The Royal Children's Hospital Melbourne Human Research Ethics Committee (HREC).

The HREC confirms that your proposal meets the requirements of the National Statement on Ethical Conduct in Human Research (2007). This HREC is organised and operates in accordance with the National Health and Medical Research Council's (NHRMC) National Statement on Ethical Conduct in Human Research (2007), and all subsequent updates, and in accordance with the Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95), the Health Privacy Principles described in the Health Records Act 2001 (Vic) and Section 95A of the Privacy Act 1988 (and subsequent Guidelines).

HREC Approval Date: 17 May 2019*
Please note the HREC are no longer issuing pre-determined approval periods. Ethical approval is now ongoing, subject to the submission of an annual report on the anniversary of approval.

Participating Sites:
Ethical approval for this project applies at the following sites:

Site Name
• Melbourne Children's Campus (incorporating The Royal Children's Hospital, Murdoch Children's Research Institute and the University of Melbourne Department of Paediatrics)
• Monash University
• Sydney Children's Hospital
• The Children's Hospital at Westmead

Approved Documents:
The following documents have been reviewed and approved:

Document	Version	Date
Protocol	4.0	13 May 2019
Master Email invitation to participate	2.0	6 May 2019
Master Participant Information Statement	2.0	6 May 2019
Survey	1.0	8 March 2019

Site Specific Assessment:

Site-specific governance authorisation must be obtained by each participating site before the study can commence at that site.

You are required to provide a copy of this HREC approval letter to the principal investigator at each site covered by this ethics approval to assist each site PI with obtaining governance approval to commence the project at that site.

Conditions of Ethics Approval:

- You are required to submit to the HREC:
  - An Annual Progress Report (that covers all sites listed on approval) for the duration of the project. This report is due on the anniversary of HREC approval. Continuation of ethics approval is contingent on submission of an annual report, due within one month of the approval anniversary. Failure to comply with this requirement may result in suspension of the project by the HREC.
  - A comprehensive Final Report upon completion of the project.
- Submit to the reviewing HREC for approval any proposed amendments to the project including any proposed changes to the Protocol, Participant Information and Consent Form/s and the Investigator Brochure.
- Notify the reviewing HREC of any adverse events that have a material impact on the conduct of the research in accordance with the NHMRC Position Statement: *Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016*.
- Notify the reviewing HREC of your inability to continue as Coordinating Principal Investigator.
- Notify the reviewing HREC of the failure to commence the study within 12 months of the HREC approval date or if a decision is taken to end the study at any of the sites prior to the expected date of completion.
- Notify the reviewing HREC of any matters which may impact the conduct of the project.
- If your project involves radiation, you are legally obliged to conduct your research in accordance with the Australian Radiation Protection and Nuclear Safety Agency Code of Practice 'Exposure of Humans to Ionizing Radiation for Research Purposes' Radiation Protection series Publication No.8 (May 2005)(ARPANSA Code).
- The HREC, authorising institution and/or their delegate/s may conduct an audit of the project at any time.

Yours sincerely

Deeptika Chauhan
Research Ethics and Governance Officer
Research Ethics and Governance
The Royal Children's Hospital Melbourne
Phone : (03) 9345 5044
Email : rch.ethics@rch.org.au
Web : www.rch.org.au

GOVERNANCE AUTHORISATION

The Royal Children's Hospital Melbourne

17 May 2019

Professor M Ryan
Neurology Department
The Royal Children's Hospital Melbourne

Dear Professor Ryan,

Project Title: EAT-DMD

HREC Reference Number: HREC/51070/RCHM-2019
SSA Reference Number: SSA/51070/RCHM-2019
RCH HREC Reference Number: 2019.067

I am pleased to advise that the above project has received governance authorisation at the Melbourne Children's Campus (incorporating The Royal Children's Hospital, Murdoch Childrens Research Institute and the University of Melbourne Department of Paediatrics).

HREC Approval Date: 17 May 2019

Governance Authorisation Date: 17 May 2019*
**Please note that governance authorisation is ongoing, subject to the submission of an annual report on the anniversary of HREC approval.*

Authorised Documents:
The following documents have been authorised for use at the Melbourne Children's Campus:

Document	Version	Date
Protocol	4.0	13 May 2019
RCH Email invitation to participate	2.0	6 May 2019
RCH Participant Information Statement	2.0	6 May 2019
Survey	1.0	8 March 2019

Conditions of Governance Authorisation

As Principal Investigator, you are required to:

1. Comply with the Investigator's responsibilities as outlined in the *Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95).*
2. Submit a copy of this letter to the person responsible for radiation safety at this site. **This condition only applies if** the project involves exposure to ionising radiation that exceeds dose constraints, and the Medical Physicist's report has advised that the project needs to be added to the site's *Licence for Research Involving Human Volunteers* issued by the Department of Health Radiation Safety Section (for more information, visit http://www.health.vic.gov.au/radiation/). *Note: If the Medical Physicist's report has advised that the project needs to be added to the site's licence, the project cannot commence at site until you have confirmed that the project has been added to the site's licence.*
3. Notify the RGO of:
    - The actual start date of the project.

- Any amendments to the project after these have been approved by the reviewing HREC.
- Any adverse events involving patients at this site, in accordance with the NHMRC Position Statement: *Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016*.
- Any changes to the indemnity, insurance arrangements or Clinical Trial Research Agreement for this project. This includes changes to the project budget or other changes which may have financial or other resource implications at this site.
- Your inability to continue as Principal Investigator or any other change in research personnel involved in this project.
- Failure to commence the study within 12 months of the Reviewing HREC approval date or if a decision is taken to end the study at this site.
- Any other unforeseen events.
- Any other matters which may impact the conduct of the project at this site.

4. Ensure that HREC approval remains current for the entire duration of the project. Investigators undertaking projects without current Reviewing HREC approval risk their indemnity, funding and publication rights.
5. Submit an annual progress report every 12 months for the duration of the project. This report is due on the anniversary of HREC approval (data above). Continued Governance Authorisation is contingent on receipt of an annual report by the RGO. In addition, a comprehensive final report should be submitted to the RGO upon completion of the project.

You must also abide by the following requirements:

1. Where applicable, ensure that the CTN has been electronically lodged to the TGA by the sponsor.
2. For clinical trials where the site is the Sponsor, you are required to contact MCTC to organise submission of the electronic Clinical Trial Notification (e-CTN) to the TGA. This must be completed before commencement of your project.
3. It is the Principal Investigator's responsibility to ensure that copies of the complete submitted e-CTN and TGA issued acknowledgement are included in the study Site File for the project at this site.
4. Ensure that the Clinical Trial Research Agreement (CTRA) and Indemnities (or other research agreements as applicable) are fully executed, i.e. signed by all parties; and an original version (or copy) placed in the study file.

The RGO may conduct an audit of the project at any time.

If you have any matters that arise regarding conduct of the research at this site, please ensure you contact the Research Governance Manager on 03 9345 5044.

I wish you and your colleagues every success in your research.

Yours sincerely

Deeptika Chauhan
Research Ethics and Governance Officer
Research Ethics and Governance
The Royal Children's Hospital Melbourne
Phone : (03) 9345 5044
Email : rch.ethics@rch.org.au
Web : www.rch.org.au

HREC Project Number:	RCH HREC 2019.067		
Short Name of Project:	*EAT-DMD*		
Full Name of Project:	*Exploring attitudes and beliefs about healthy eating, weight and a healthy lifestyle program for Duchenne muscular dystrophy: A parents perspective*		
Principal Researcher:	Professor Monique Ryan, Director Department of Neurology, The Royal Children's Hospital		
Version Number:	v. 4	**Version Date:**	14/9/2020

Dear Parent/Guardian,

We are inviting you to take part in this research project, *EAT-DMD*, which is a survey for parents/guardians who have a son with Duchenne muscular dystrophy (DMD). As part of this project we want to:

- Explore the attitudes and beliefs that parents/guardians with a child with DMD have about healthy eating and weight
- Identify the barriers families face when trying to follow a healthy eating pattern
- Identify what parents/guardians believe influences their sons' eating behaviour
- Involve parents/guardians in the design of a healthy lifestyle program for children with DMD

We are doing this research study because many young people with DMD find it hard to stay in a healthy weight range and we would like to find out more about this. By doing this research study it **does not** mean your son is above a healthy weight. We would like to get information from all different families who have a son with DMD. By finding out this information we hope to manage weight and nutrition more confidently.

Study team:

This is a joint project between The Royal Children's Hospital (RCH), Sydney Children's Hospital Randwick (SCH), The Children's Hospital at Westmead (CHW), Queensland Children's Health (QCH)

and Monash University (MU). This study is being conducted by Natassja Billich from RCH and MU and will be submitted as part of her PhD thesis. The study team for this project are:

- Professor Monique Ryan (Principal Investigator RCH)
- Associate Professor Michelle Farrar (Principal Investigator SCH)
- Dr Manoj Menezes (Principal Investigator CHW)
- Dr Anita Cairns (Principal Investigator QCH)
- Ms Natassja Billich (Associate Investigator/Study Contact)

About the survey:

To be eligible to participate in this project you:

- Are a parent/guardian of a son with DMD
- Are responsible for providing food in your household (or you share this role with somebody else)
- Can read and understand English

This study involves completing a survey, which will take approximately 30-45 minutes. It does not have to be completed all at one time. In this survey you will be asked about the following topics:

- Health and basic information about your son (e.g. medications)
- Your knowledge and beliefs about healthy eating (e.g. benefits of healthy eating)
- The skills you have to provide healthy foods (e.g. your cooking skills)
- What meals are like in your household (e.g. whether the TV is on during meals)
- The types of food your provide to your family and son (e.g. 'sometimes' foods)
- Your beliefs about your son's weight (e.g. whether he is in a healthy weight range)
- Your input into a healthy lifestyle program for young people with DMD

You will also be asked if you would like to receive more information and/or provide further input into the healthy lifestyle program in the future. If you would like to do this, you can leave your name and email address.

How we will store the survey responses:

Your survey data will not contain any identifiable information and will be stored electronically on secure drives at RCH and MU for 10 years. If you choose to provide your name and email address, these will **not** be linked to your survey responses and will be stored on a secure drive at RCH in a password protected file.

Benefits and risks of this project:

This project may benefit healthcare professionals, researchers and people with DMD in the future as it may help us learn more about nutrition and weight in DMD. This knowledge may then help us manage nutrition and weight more confidently.

We do not expect that you will be exposed to any physical or psychological risks if you participate in this project. However, eating and questions around food behaviors and weight has potential to cause distress to families. It is also possible that thinking about your son's diagnosis of DMD and its effects may elicit worry, concern or distress. Should this arise, there are existing supports that can be accessed through the neuromuscular clinic. If you have any thoughts or questions about the survey or research project, especially if any part caused distress, please contact the study contact below.

Participating in this research:

Participation in any research project is voluntary. If you decide to take part in the survey and later change your mind, you are free to withdraw **during** the survey. You can do this by exiting the survey if you are completing it online or by telling the researcher if you are doing the survey in person. **Because the survey is anonymous, you will not be able to withdraw your survey after it has been submitted.** Your decision whether you can or cannot take part, or take part and then withdraw, will not affect your sons' routine treatment, your relationship with those treating them or relationship with RCH, SCH, CHW and/or QCH.

If you decide you want to take part in the research project, please select "Yes I consent to taking part in this research" below. By selecting this you are telling us that you:

- Understand what you have read
- Consent to taking part in the research project
- Consent to providing information about your family including your son(s) with DMD
- Consent to the information you provide to be used for this project and future research projects

Once you have consented to taking part, you <may click next to (delete if paper survey)> continue taking the survey.

If you have any questions about the project, you can contact Natassja Billich on <insert phone number> or Natassja.billich@rch.org.au.

Thank you very much for your time.

Yours sincerely

Natassja Billich

PhD student

Department of Neurology

The Royal Children's Hospital

Supplementary Table 20

Caregivers' Perceived Consequences of Not Following a Healthy Eating Pattern

	Consequences for Their Family n (N%)	**Consequences for Someone with DMD n (N%)**
Weight gain	26 (96.3)	26 (96.3)
Heart disease/problems	24 (88.9)	23 (85.2)
Type 2 diabetes	23 (85.2)	22 (81.5)
Affect behaviour	22 (81.5)	19 (70.4)
It can make concentrating harder	22 (81.5)	22 (81.5)
It can affect mood and mental health	22 (81.5)	19 (70.4)
It can make sleeping harder	19 (70.4)	18 (66.7)
Affect the bones and joints	18 (66.7)	19 (70.4)
It can increase the risk of some cancers	17 (63.0)	-
It increases the risk of poor height growth	16 (59.3)	-
It can affect muscle health	-	21 (77.8)
It has no impact on health and wellbeing	0 (0.0)	0 (0.0)

Standard: Consent (2 Questions)

Branch: New Branch
If
If Do you consent to taking part in this research? No I do not consent to taking part in this research Is Selected

EndSurvey: Advanced

Standard: Screening questions (3 Questions)

Branch: New Branch
If
If Are you the parent or a guardian of a child or teenager with Duchenne muscular dystrophy? No Is Selected

EndSurvey: Advanced

Branch: New Branch
If
If Are you the parent or guardian mainly responsible for providing (buying, preparing or cooking) fo... No Is Selected

EndSurvey: Advanced

Block: Demographic and family characteristics (9 Questions)

Branch: New Branch
If
If How many sons do you have with Duchenne muscular dystrophy? Please choose one answer. 1 Is Selected

Block: About your son (11 Questions)
Block: Your knowledge about food (5 Questions)
Block: Your skills to choose, prepare and cook foods (6 Questions)
Block: Meals in your household (3 Questions)
Block: Barriers to healthy eating (2 Questions)
Block: Attitudes and beliefs about healthy eating (19 Questions)
Block: Sometimes foods Son 1 (5 Questions)
Block: Your son's food choices (4 Questions)
Block: Your beliefs about your son's weight (10 Questions)
Block: Parent and guardian input into a nutrition program (18 Questions)

Branch: New Branch
If
If How many sons do you have with Duchenne muscular dystrophy? Please choose one answer. 2 Is Selected

Block: Your two sons (12 Questions)
Block: Your knowledge about food (5 Questions)
Block: Your skills to choose, prepare and cook foods (6 Questions)
Block: Meals in your household (3 Questions)
Block: Barriers to healthy eating (2 Questions)
Block: Attitudes and beliefs about healthy eating (19 Questions)
Block: Sometimes foods Son 2 (13 Questions)

Caregivers Survey

Start of Block: Consent

Q237 Please click here to view the participant information statement

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Q1.2
Do you consent to taking part in this research?

- ○ Yes I consent to taking part in this research (1)
- ○ No I do not consent to taking part in this research (0)

End of Block: Consent

Start of Block: Screening questions

Q2.1 Thank you for agreeing to participate in this survey.
This survey is for parents or guardians of a son with Duchenne muscular dystrophy. The person who usually provides (buys, prepares or cooks) food in your household should complete this survey. If more than one parent/guardian provides food in your household, you can choose who completes the survey or you can do it together.
In this survey "your son" refers to your child or teenager with Duchenne muscular dystrophy. In this survey "your family" refers to everyone in your household.
There are two sections in this survey. The first section asks a number or questions about food, eating and weight. The second section asks about what you think would be important to include in a healthy lifestyle program for young people with Duchenne muscular dystrophy.
It's expected that this survey will take you 30-45 minutes. You do not need to complete this survey all at once. If you would like to leave the survey and come back to it, you can do this if you use the same computer or device (phone or tablet) each time. If you use a different computer or device it will take you back to the beginning of the survey.

Q2.2 Are you the parent or a guardian of a child or teenager with Duchenne muscular dystrophy?

- ○ Yes (1)
- ○ No (2)

Q2.3 Are you the parent or guardian mainly responsible for providing (buying, preparing or cooking) food in your household? This includes if you share this responsibility equally with someone else.

- ○ Yes (4)
- ○ No (5)

End of Block: Screening questions

Start of Block: Demographic and family characteristics

Q3.1 How many children or teenagers (aged 18 years or less) live in your household?
Please choose one answer.

- ○ 1 (1)
- ○ 2 (2)
- ○ 3 (3)
- ○ 4 (4)
- ○ 5 (5)
- ○ 6 (6)
- ○ Other: (7) _____

Q3.2 How often do your children stay with you in your household?

Please choose one answer.

- ○ Most or all of the time (5-7 days per week) (1)
- ○ Around half of the time (3-4 days per week) (2)
- ○ Less than half of the time (1-2 days per week) (3)
- ○ Other: (4) _____

Q3.3 How many sons do you have with Duchenne muscular dystrophy?

Please choose one answer.

- ○ 1 (1)
- ○ 2 (2)
- ○ 3 (3)

Display This Question:

If Q3.3 = 1

Q3.4 You have selected that you have one son with Duchenne muscular dystrophy. If this is incorrect, please click back and change your answer.

If you have one son with Duchenne muscular dystrophy, you may continue taking the survey.

Display This Question:

If Q3.3 = 2

Q3.5 You have selected that you have two sons with Duchenne muscular dystrophy. If this is incorrect, please click back and change your answer.

For this survey we will ask some questions twice for each of your sons. To make this easy to follow we will call your sons "Son 1" and "Son 2". "Son 1" is your first born son with Duchenne muscular dystrophy and "Son 2" is your second born son with Duchenne muscular dystrophy.

This survey may take you an extra 5-10 minutes to complete. Thank you for your patience.

If you have two sons with Duchenne muscular dystrophy, you may continue taking the survey.

Display This Question:

If Q3.3 = 3

Q3.6 You have selected that you have three sons with Duchenne muscular dystrophy. If this is incorrect, please click back and change your answer.

For this survey we will ask some questions three times for each of your sons. To make this easy to follow we will call your sons "Son 1", "Son 2" and "Son 3". "Son 1" is your first born son with Duchenne muscular dystrophy, "Son 2" is your second born son with Duchenne muscular dystrophy and "Son 3" is your third born son with Duchenne muscular dystrophy.

This survey may take you an extra 5-10 minutes to complete. Thank you for your patience.

If you have three sons with Duchenne muscular dystrophy, you may continue taking the survey.

Q3.7 Do you access a dietitian for your son(s) with Duchenne muscular dystrophy?

Please choose one answer.

○ Yes, in the neuromuscular clinic (1)

○ Yes, outside of the neuromuscular clinic (e.g. a dietitian in a private clinic or community health centre) (2)

○ Yes, both in and outside the neuromuscular clinic (5)

○ No, we do not access a dietitian in the neuromuscular clinic or outside of the clinic (4)

○ I don't know if we access a dietitian (3)

Q3.8 Which cultural or ethnic group(s) does your family identify with? If you identify with more than one cultural or ethnic group, you may select multiple boxes.

Australian (1)

Indigenous Australian or Torres Strait Islander (2)

New Zealander (3)

South-East Asian (4)

North-East Asian (12)

Indian (5)

Middle Eastern (6)

European (7)

North American (8)

South American (9)

African (10)

Other, please specify: (11) _____

Q3.9 Please enter your postcode:

_____

End of Block: Demographic and family characteristics

Start of Block: About your son

Q4.1 The following nine (9) questions will ask for some health information about your son with Duchenne muscular dystrophy.

Q4.2 Please enter your son's age in years and months (e.g. 5 years and 2 months):

○ Years: (4) _____

○ Months: (5) _____

---

*

Q4.3 Please enter your son's current height in centimetres (cm):

If you do not know your son's height, leave this box blank.

_____

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*

Q4.4 Please enter your son's current weight in kilograms (kg):

If you do not know your son's weight, leave this box blank.

_____

Q4.5 Please select which option best answers the following sentence.

Before needing to stop and have a rest, my son can walk...

- ○ 500 metres (1)
- ○ 50 metres (2)
- ○ 5 metres (3)
- ○ He uses a wheelchair (4)
- ○ Other: (5) _____

Q4.6 Has your son ever taken steroids (prednisolone, deflazacourt or vamorolone) for Duchenne muscular dystrophy, even if they are no longer taking these?

- ○ Yes (1)
- ○ No (2)

Display This Question:

If Q4.6 = Yes

Q4.7 For how many years has your son taken steroids? If he has stopped taking them, enter the number of years he took them for.

_____

Q4.8 Has your son ever been diagnosed or tested for any of the following conditions?

Autism Spectrum Disorder (1)	▼ Diagnosed (by a doctor or psychologist) (1) ... I don't know (4)
Attention Deficit Hyperactivity Disorder (2)	▼ Diagnosed (by a doctor or psychologist) (1) ... I don't know (4)
Obsessive Compulsive Disorder (3)	▼ Diagnosed (by a doctor or psychologist) (1) ... I don't know (4)
Oppositional Defiant Disorder (4)	▼ Diagnosed (by a doctor or psychologist) (1) ... I don't know (4)

Q4.9 Please record the medications and/or supplements (nutritional, vitamin or mineral) your son regularly takes. This includes medications or supplements prescribed by a doctor and also ones you get over the counter (e.g. at a pharmacy or health food store).

_____

_____

_____

_____

_____

Q4.10 Do you think your son is a fussy/picky eater?

○ Yes (1)

○ No (2)

Q4.11 How often does your son avoid/choose certain foods due to the texture, smell or taste of the food?

- ○ Most or all of the time (1)
- ○ Some of the time (2)
- ○ Rarely or never (3)

End of Block: About your son

Start of Block: Your knowledge about food

Q5.1 The following four (4) questions are about what you *know* about food.

Q5.2 How much do you *know* about the following topics?

	I don't know anything				I know a lot	
	0	1	2	3	4	5
Foods that are healthy for my family ()						
Foods that are healthy for my son(s) with Duchenne muscular dystrophy ()						

Q5.3 Which of the following do you think best describes the *Five Food Groups*? You might have seen the *Five Food Groups* as a food plate or pyramid in the *Australian Guide to*

Healthy Eating.
Choose one answer.

- ○ Five foods that should never be eaten (1)
- ○ Five groups of food that are recommended to be eaten across the week (2)
- ○ Five groups of food that are recommended to be eaten every day (3)
- ○ Five groups of food that are sold in supermarkets/shops but don't make any difference to our health (4)
- ○ I have heard of the Five Food Groups but I don't know what they are (6)
- ○ I have never heard of the Five Food Groups (7)
- ○ Other: (5) _____

Q5.4 Which of the following types of food do you think belong to the *Five Food Groups*?

Select five (5) types of food or select "I don't know".

Hot foods such as pies, pizza and burgers (1)

Grain (cereal) foods (4)

Meat or poultry (e.g. chicken) that is crumbed and fried (5)

Cakes, desserts, muffins, biscuits and baked sweet foods (6)

Vegetables and legumes/beans (7)

Butter, margarine, oils and lard (8)

Milk, yoghurt cheese and/or non-dairy alternatives (9)

Fruit (10)

Lean meat and poultry (e.g. chicken), fish, eggs, tofu, nuts, seeds and legumes/beans (11)

⊗ I don't know which foods belong to the Five Food Groups (12)

Q5.5 Which of the following foods do you think are ‘sometimes’ foods? 'Sometimes' foods are recommended to only be eaten some of the time, rather than every day.
Select all that apply.

Grilled chicken breast (1)

Chocolate (2)

Fruit salad with yoghurt (3)

Pasta (4)

Yoghurt (5)

Chicken nuggets (6)

Bread (7)

Hot chips (8)

Apples (9)

McDonalds cheeseburger (10)

⊗ I don't know which of these are 'sometimes' foods (11)

End of Block: Your knowledge about food

Start of Block: Your skills to choose, prepare and cook foods

Q6.1 The following three (3) questions are about your skills to choose, prepare and cook foods.

Q6.2 How confident are you in the following skills?

	I'm not confident at all				I'm very confident	
	0	1	2	3	4	5
Choosing healthy foods (e.g. in the supermarket) ()						
Preparing and cooking healthy foods ()						

Q6.3 Would you like to improve your skills in choosing, preparing or cooking healthy foods?

○ Yes (4)

○ No (5)

Display This Question:

If Q6.3 = Yes

Q6.4 Which of the following skills would you like to improve? Number **only** three skills from 1 to 3, with 1 being the skill that you would like to improve the most.

_____ Finding where the healthy foods are in the supermarket/shops (1)
_____ Reading food labels (2)
_____ Preparing and cooking healthy meals (4)
_____ Preparing healthy snacks (6)
_____ Preparing healthy lunch boxes (7)
_____ Preparing and cooking vegetables (8)
_____ Buying and cooking healthy foods on a budget (9)
_____ Making healthy food taste nice (12)
_____ Finding healthy options on a take-away or restaurant menu when out (14)
_____ Learning which foods are healthy (18)
_____ Other (17)

Display This Question:

If Q6.3 = Yes

Q6.5 Would any of the following barriers get in the way when you are trying to learn these skills?

Select all that apply.

Finding time to learn them (1)

Being stressed about other things in my life (4)

Not knowing where or how to learn them (5)

The cost of healthy food (6)

Other: (7) _____

⊗ None of the above (8)

Display This Question:

If Q6.3 = No

Q6.6 Could you tell us why you don't want to improve your skills in choosing, preparing or cooking healthy foods? Number up to three reasons why, with 1 being the biggest reason.

_____ I don't need to improve these skills (1)
_____ Knowing these skills is not important to me (2)
_____ I do not have enough time (3)
_____ Learning new skills would be too stressful (4)
_____ I already have enough to worry about (5)
_____ Other: (6)

End of Block: Your skills to choose, prepare and cook foods

Start of Block: Meals in your household

Q7.1 The following question is about what mealtimes are like in your household.

Q7.2 How often do the following situations occur during meal times in your household? "Our son" may refer to more than one son with Duchenne muscular dystrophy, if you have more than one.

	Rarely or never (1 time or less per week) (1)	Some of the time (2-4 days per week) (2)	Most or all of the time (5-7 days per week) (3)
Our family eats meals together (1)	○	○	○
Meals in our household are rushed (3)	○	○	○
Our family eats meals at a table/bench (4)	○	○	○
Our son eats meals in the car (5)	○	○	○
Our son eats something different from other family members (6)	○	○	○
Our son eats meals sitting in front of a screen (e.g. a TV, phone or tablet) (10)	○	○	○
Someone in our household cooks the main meal (8)	○	○	○
The TV is on in the background during the main meal (11)	○	○	○
Meals occur later than expected or just before bed time (12)	○	○	○

Display This Question:

If Q7.2 = Our son eats something different from other family members [Some of the time (2-4 days per week)]

Or Q7.2 = Our son eats something different from other family members [Most or all of the time (5-7 days per week)]

*

Q7.3 Which of the following reasons best describes why your son eats something different at meals? Number up to three reasons why, with 1 being the main reason.

_____ He avoids/chooses certain foods due to the texture, smell or taste of the food (1)
_____ He is a fussy eater (2)
_____ Everyone in the family eats something different (8)
_____ He eats at a different time to everyone else (9)
_____ Other (10)

End of Block: Meals in your household

Start of Block: Barriers to healthy eating

Q8.1 The following question is about the barriers you face when trying to provide healthy foods to your family. A barrier is something that gets in the way and stops you being able to do something.

Q8.2 What are the three main barriers you face to provide healthy foods to your family? "Number 1 barrier" would be the biggest barrier.

If you don't think there are any barriers, please leave this box blank.

○ Number 1 barrier: (1) _____

○ Number 2 barrier: (2) _____

○ Number 3 barrier: (3) _____

End of Block: Barriers to healthy eating

Start of Block: Attitudes and beliefs about healthy eating

Q9.1 The following questions are about your attitudes and beliefs about healthy eating for your family.

Q9.2 Please select whether you believe the following statement is true or false:
I believe healthy eating is beneficial to my family.

- ○ True (1)
- ○ False (2)

Display This Question:

If Q9.2 = True

Q9.3 How beneficial do you think healthy eating is to your family?

	A little bit beneficial			Extremely beneficial		
	0	1	2	3	4	5
Healthy eating ()						

Q9.4 How often do you consider the healthiness of food when providing food to your family?

Choose one answer.

- ○ Most or all of the time (6)
- ○ Some of the time (7)
- ○ Rarely or never (8)

Display This Question:

If Q9.4 = Most or all of the time

Or Q9.4 = Some of the time

Q9.5 What goals do you try and achieve when thinking about the healthiness of the food you provide? Number up to three goals, with 1 being the goal you try and achieve the most.

_____ Eating a variety of foods from the Five Food Groups (2)
_____ Reducing the amount of sugar (3)
_____ Reducing the amount of unhealthy fat (4)
_____ Reducing the amount of salt (5)
_____ Reducing the amount of processed foods (6)
_____ Introducing new foods (7)
_____ Choosing foods that help us all be a healthy weight (9)
_____ Other: (8)

Q9.6 Besides the healthiness of food, what other things do you consider when making food choices for your family? Number up to three things you consider, with 1 being the thing you consider the most.

_____ Convenience (1)
_____ Taste (2)
_____ Cost (9)
_____ Storage (e.g. having a place to put food) (13)
_____ Having enough food for my family (14)
_____ Family preferences (15)
_____ Cooking ability (16)
_____ Other: (10)

Display This Question:

If Q9.4 = Rarely or never

Q9.7 Which of the following statements best describes your intentions to change the healthiness of the food you provide to your family?
Please choose one answer.

- ○ I don't intend to change the types of food I provide (1)
- ○ I intend to start making healthy changes in the next six months (2)
- ○ I intend to start making healthy changes in the next month (3)
- ○ I intend to make changes but I don't know when (6)
- ○ I have already started making some changes in the past six months (4)

Display This Question:

If Q9.7 = I don't intend to change the types of food I provide

Q9.8 Please write why you don't intend to change the types of food you provide:

_____

_____

_____

_____

_____

Display This Question:

If Q9.7 = I intend to start making healthy changes in the next six months

Or Q9.7 = I intend to start making healthy changes in the next month

Or Q9.7 = I have already started making some changes in the past six months

Q9.9 Please specify the changes you are planning to make or have already made:

_____

_____

_____

_____

_____

Q9.10 Considering everything going on in your family's life (e.g. school, work, hospital visits and health needs), how much of a priority is healthy eating?

	Not a priority at all				Highest priority	
	0	1	2	3	4	5
Healthy eating ()						

Q9.11 What do you believe the consequences of **not** following a healthy eating pattern are for your family?

Check all that apply.

It can increase the risk of weight gain (1)

It can increase the risk of heart disease (4)

It can increase the risk of type 2 diabetes (5)

It can increase the risk of some cancers (6)

It can affect the bones and joints (7)

It can make sleeping harder (8)

It can affect behaviour (9)

It can make concentrating harder (10)

It can affect mood and mental health (11)

It increases the risk of poor height growth (16)

Other: (13) _____

⊗ It has no impact on health and wellbeing (15)

Q9.12 The following questions are about your attitudes and beliefs about healthy eating for Duchenne muscular dystrophy.

Q9.13 Please select whether you believe the following statement is true or false.
I believe healthy eating is beneficial to our son(s) with Duchenne muscular dystrophy

○ True (1)

○ False (2)

Display This Question:

If Q9.13 = True

Q9.14 How beneficial do you think healthy eating is to your son(s) with Duchenne muscular dystrophy?

	A little bit beneficial				Extremely beneficial
	0	1	2	3	4	5
Healthy eating ()						

Q9.15 How often do you consider the healthiness of food when providing food to your son(s) with Duchenne muscular dystrophy?

Please choose one answer.

- ○ Most or all of the time (1)
- ○ Some of the time (2)
- ○ Rarely or never (3)

Display This Question:

If Q9.15 = Most or all of the time

Or Q9.15 = Some of the time

Q9.16 Why do you consider the healthiness of the food when providing food to your son(s)? Number **only** three reasons from 1 to 3, with 1 being the biggest reason.

_____ It's good for their mood (e.g. makes them happy) (1)
_____ It's good for their energy levels (2)
_____ It's good for their sleep (3)
_____ It's good for their heart (4)
_____ It's good for their mental health (5)
_____ To stop them gaining too much weight (6)
_____ It's good for their muscles (7)
_____ It's good for their bones (9)
_____ It's enjoyable for them to eat healthy foods (8)
_____ It's good for their height growth (11)
_____ Other: (10)

Q9.17 Besides the healthiness of food, what other things do you consider when making food choices for your son(s)? Number up to three things you consider, with 1 being the thing you consider most.

_____ Their food preferences (3)
_____ The enjoyment they get from eating food (4)
_____ Controlling their behaviour (5)
_____ The variety of textures, flavours and smells of the foods they eat (10)
_____ Other: (8)

Display This Question:

If Q9.15 = Rarely or never

Q9.18 Which of the following reasons best explains why you rarely or never consider the healthiness of the foods you provide to your son(s)? Number up to three reasons why, with 1 being the biggest reason.

_____ They do not like healthy foods (4)
_____ Our family does not like healthy foods (5)
_____ Healthy eating is not important to me and my family (7)
_____ I find it difficult to restrict the foods they eat because of their Duchenne muscular dystrophy (8)
_____ It's hard to say no when they ask for foods they like because of their Duchenne muscular dystrophy (10)
_____ Other: (9)

Q9.19 What do you believe the consequences of **not** following a healthy eating pattern are for someone with Duchenne muscular dystrophy?

Check all that apply.

It increases risk of weight gain (1)

It increases risk of heart problems (2)

It increases risk of type 2 diabetes (3)

It can affect behaviour (4)

It can make sleeping harder (5)

It can make concentrating harder (6)

It can affect mood and mental health (7)

It can affect bone health (8)

It can affect muscle health (9)

Other: (11) _____

⊗ It has no impact on their health or wellbeing (12)

End of Block: Attitudes and beliefs about healthy eating

Start of Block: Sometimes foods Son 1

Q10.1 The following questions are about when your son eats ‘sometimes’ foods (also known as ‘unhealthy’ or ‘junk’ foods).

Q10.2 How often do you give 'sometimes' foods to your son?

- ○ Most or all of the time (5-7 days per week) (1)
- ○ Some of the time (2-4 days per week) (2)
- ○ Rarely or never (1 day or less per week) (3)

Display This Question:

If Q10.2 = Most or all of the time (5-7 days per week)

Or Q10.2 = Some of the time (2-4 days per week)

Q10.3 For what reason do you give ‘sometimes’ foods to your son? Number **only** three reasons you give 'sometimes' foods from 1 to 3, with 1 being the most likely reason.

_____ To reward good behaviour (1)
_____ To celebrate an achievement (2)
_____ To celebrate a special occasion (3)
_____ To persuade him to do things (4)
_____ To make him happy (5)
_____ To make him be quiet (e.g. when in the car) (6)
_____ When he’s having a bad day (7)
_____ When he needs to go somewhere he doesn’t want to go (e.g. the hospital) (8)
_____ Because I feel sorry for him having Duchenne muscular dystrophy (13)
_____ I give 'sometimes' foods all the time, for no particular reason (12)
_____ Other: (9)

Q10.4 Do you think your son eats more 'sometimes' foods depending on what social situation he is in (e.g. with friends vs. alone)?

- ○ Yes he eats more (1)
- ○ No the amount doesn't change (4)
- ○ This doesn't apply, my son rarely or never eats 'sometimes' foods (5)

Display This Question:

If Q10.4 = Yes he eats more

Q10.5 In which of the following social situations is your son most likely to eat 'sometimes' foods? Number **only** three situations from 1 to 3, with 1 being the one where he is most likely to eat the most 'sometimes' foods.

_____ When at school (1)
_____ When at after school care (2)
_____ When at day care (3)
_____ When at other school-related events (4)
_____ When at home (5)
_____ When at parties (6)
_____ When at family celebrations (7)
_____ When on play dates or out with friends (8)
_____ When eating out (i.e. at restaurants or when having takeaway foods) (9)
_____ When alone (10)
_____ Other: (11)

End of Block: Sometimes foods Son 1

Start of Block: Your son's food choices

Q11.1 The following questions are about your beliefs about your son's eating behaviours.

Q11.2 Please rate how much of a problem each of the following situations are:

	This is not a problem at all					This is a big problem
	0	1	2	3	4	5
My son eats because of his feelings/emotions ()						
My son eats because he is bored ()						
My son is always asking for food because he is always hungry ()						
My son has an increased appetite because of the medication he takes for his Duchenne muscular dystrophy ()						

Q11.3 Please rate how difficult each of the following situations are for you:

	Not difficult at all					Extremely difficult
	0	1	2	3	4	5
Controlling my son's appetite ()						
Saying no to my son when he asks for food because of his Duchenne muscular dystrophy ()						

Q11.4 Please describe what feelings/emotions make your son want to eat, if any:

_____

_____

_____

_____

_____

End of Block: Your son's food choices

Start of Block: Your beliefs about your son's weight

Q12.1 The following questions are about your beliefs about your son's weight.

Q12.2 How do you perceive your son's current weight?

- ○ I believe he is below a healthy weight (1)
- ○ I believe he is a healthy weight (4)
- ○ I believe he is above a healthy weight (5)

Display This Question:

If Q4.6 = Yes

And Q12.2 = I believe he is above a healthy weight

Q12.3 Do you believe your son's weight gain is related to the steroids he takes or has taken in the past?

- ○ Yes, related to the steroids (6)
- ○ No, not related to the steroids (8)
- ○ I don't know (7)

Display This Question:

If Q12.3 = No, not related to the steroids

Q12.4 If his weight gain was not related to steroids, could you explain what you think it was related to?

_____

_____

_____

_____

_____

Q12.5 How easy is it for your son to achieve and maintain a healthy weight

	Not easy at all				Very easy	
	0	1	2	3	4	5
Achieve and maintain a healthy weight ()						

Q12.6 What are *your* intentions regarding your son's weight?

Please choose one answer.

- ○ Help him lose weight (1)
- ○ Help him gain weight (2)
- ○ Help him stay the same weight (3)
- ○ I don't intend to do anything about his weight (4)
- ○ I would prefer not to say (5)

Q12.7 What are *your son's* intentions for his weight?

Please choose one answer.

- ○ He wants to lose weight (1)
- ○ He wants to gain weight (4)
- ○ He wants to stay the same weight (5)
- ○ He doesn't intend to do anything about his weight (6)
- ○ I would prefer not to say (7)
- ○ I don't know what his intentions are (8)

Display This Question:

If Q12.2 = I believe he is above a healthy weight

Q12.8 What impact do you think being above a healthy weight has on *your son*?

Check all that apply.

It decreases his health (12)

It affects his self-esteem (1)

It affects his mood (i.e. low mood) (2)

It makes it harder for him to move around (3)

It makes him self-conscious (4)

It makes it harder for him to breathe (5)

It makes it harder for him to sleep (6)

It makes him less willing to socialise (7)

It makes him have low energy (8)

It improves his health (9)

Other: (11) _____

⊗ It has no impact on him (10)

Display This Question:

If Q12.2 = I believe he is above a healthy weight

Q12.9 What impact does your son being above a healthy weight have on *you*?

Check all that apply.

It makes caring for him more difficult (1)

It affects my mood (e.g. low mood) (2)

It makes me worried (3)

It makes me stressed (4)

Other: (6) _____

⊗ It has no impact on me (5)

Q12.10 Please write any other comments you have about anything covered in the survey so far:

_____

_____

_____

_____

_____

End of Block: Your beliefs about your son's weight

Start of Block: Parent and guardian input into a nutrition program

Q13.1 For this section we would like your help in designing a healthy lifestyle program for children or teenagers with Duchenne muscular dystrophy who are above a healthy weight. Even if you don't have a son who is above a healthy weight, you can still answer these questions.

The healthy lifestyle program would involve the whole family because we know these programs work the best for children and teenagers when the whole family takes part.

For the next part of the survey, imagine your family is going to take part in the healthy lifestyle program. How would you like it to be designed?

Q13.2 What do you think should be the main focus of the program?

○ Weight management (e.g. weight loss) (1)

○ Improving healthy eating (e.g. increasing vegetable intake) (2)

○ Improving the whole lifestyle (e.g. improving self-esteem as well as healthy eating) (4)

○ Other: (3) _____

Q13.3 What topics about nutrition would you like to learn about? Number **only** three topics from 1 to 3, with 1 being the one you would like to learn about the most.

_____ Healthy lunch boxes (5)
_____ Managing appetite (e.g. when on steroids) (6)
_____ Increasing fruits and vegetables (7)
_____ Reducing 'sometimes' foods (also known as 'unhealthy' or 'junk' foods) (8)
_____ Eating for muscle health (e.g. protein foods) (9)
_____ Eating for bone health (e.g. dairy foods) (10)
_____ Eating for mental health (e.g. fruits and vegetables) (11)
_____ Eating for heart health (e.g. reducing salt) (12)
_____ Finding healthy foods in the supermarket (15)
_____ Preparing and cooking healthy meals and snacks (16)
_____ Healthy meals when out/healthy take-away (19)
_____ Other: (21)

Q13.4 Besides nutrition topics, what other topics would you like to learn about? Number up to three topics, with 1 being the one you would like to learn about the most.

_____ Reducing screen time (1)
_____ Improving sleep (2)
_____ Mindfulness (3)
_____ Making mealtimes enjoyable (4)
_____ Improving self-esteem (7)
_____ Improving body image (8)
_____ Nutrition supplements (9)
_____ Other: (5)

Q13.5 What resources would you find the most helpful? Number up to three resources, with 1 being the one you would find the most helpful.

_____ Written information (e.g. booklet or information on a website) (1)
_____ Interactive activities to help your family learn about healthy eating and lifestyles (2)
_____ Supermarket tours to learn where to find healthy foods (3)
_____ Recipe and snack ideas (5)
_____ Meal plans for your family (6)
_____ Other: (7)

Q13.6 Would you prefer individual or group sessions?

- ○ Individual (one-on-one) (2)
- ○ Group (with other families) (3)
- ○ Other: (1) _____

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Q13.7 How would you like to do the program sessions? Number up to three preferences, with 1 being the one you would prefer the most.

_____ In person (e.g. in neuromuscular clinic) (1)
_____ Over the phone (2)
_____ Over a video call (e.g. using Skype or Zoom) (3)
_____ Social media- eg. Facebook group / chats / live videos (4)
_____ Other: (5)

Q13.8 How long would you like the program to go for?

- ○ 6 weeks (1)
- ○ 12 weeks (2)
- ○ 18 weeks (3)
- ○ 24 weeks (4)
- ○ Other: (5) _____

Q13.9 How frequently would you like to engage with the program (e.g. attend information sessions)?

- ○ Once per week (1)
- ○ Once per fortnight (2)
- ○ Once per month (3)
- ○ Only at the beginning and the end of the program (4)
- ○ Other : (5) _____

Q13.10 Would you prefer the sessions to be on weekdays or weekends?

- ○ Weekdays (1)
- ○ Weekends (2)

Q13.11 What time of day would be best to run the sessions?

- ○ In the middle of the day (1)
- ○ In the afternoon (e.g. after school) (2)
- ○ In the evening (e.g. after work) (3)
- ○ Other: (4) _____

Q13.12 What other type of support would be helpful?
Check all that apply.

Being able to text/SMS the dietitian (1)

Being able to email the dietitian (2)

Online support group/forum with other families (3)

Online support from the dietitian (5)

Other: (4) _____

Q13.13 What would you like measured at the start and end of the program? These measurements would help us see whether the program was successful or not. Number **only** three measurements from 1 to 3, with 1 being the most important measurement.

_____ The amount of healthy foods eaten (1)
_____ The amount of 'sometimes' foods eaten (2)
_____ Our son's weight (3)
_____ Our son's self-esteem (4)
_____ Our son's body image (11)
_____ Our son's strength (5)
_____ Our son's ability to move (e.g. ability to climb stairs or move arms) (6)
_____ Our son's lung function (7)
_____ Our son's quality of life (how good he perceives his life to be) (8)
_____ Our son's sleep (e.g. length and quality) (9)
_____ Other: (10)

Q13.14 Please write any other comments you have about a nutrition program for children and teens with Duchenne muscular dystrophy:

_____

_____

_____

_____

_____

Q13.15 Would you be interested in providing more feedback once the program is developed?

- ○ Yes (1)
- ○ No (2)

Q13.16 Would you and your family be interested in participating in the healthy lifestyle program?

By saying yes it does not mean you are participating in the program but you would receive more information at a later time.

- ○ Yes (1)
- ○ Maybe, I would need more information first (3)
- ○ No (2)

Display This Question:

If Q13.15 = Yes

Or Q13.16 = Yes

Or Q13.16 = Maybe, I would need more information first

Q13.17

Please note your name and email address is not linked to your survey responses so your answers will remain anonymous.

○ Please leave your first name: (6)

_____

○ Please leave your email address: (7)

_____

Q13.18 Did your son provide any input to this survey?

○ Yes (1)

○ No (2)

Supplementary Table 21

Nutrition Goals Caregivers Aim to Achieve When Providing Food to Their Family [1]

	# 1	# 2	# 3	Any
Eating from the five food groups	16 (59.3)	2 (7.4)	1 (3.7)	19 (70.4)
Reducing the amount of sugar	6 (22.2)	8 (29.6)	2 (7.4)	16 (59.3)
Reducing the amount of processed foods	3 (11.1)	6 (22.2)	9 (33.3)	18 (66.7)
Reducing the amount of unhealthy fat	2 (7.4)	5 (18.5)	3 (11.1)	10 (37.0)
Reducing the amount of salt	0	2 (7.4)	2 (7.4)	4 (14.8)
Introducing new foods	0	0	3 (11.1)	3 (11.1)
Choosing foods that help us be a healthy weight	0	4 (14.8)	7 (25.9)	11 (40.7)

[1] # 1, 2 and 3 indicating first, second and third goal selected respectively

Supplementary Table 22

Other Considerations Caregivers Make When Providing Food to Their Family [1]

	# 1	# 2	# 3	Any
Taste	9 (33.3)	7 (25.9)	5 (18.5)	21 (77.8)
Convenience	7 (25.9)	4 (14.8)	3 (11.1)	14 (51.9)
Family preferences	5 (18.5)	7 (25.9)	9 (33.3)	21 (77.8)
Having enough food for my family	4 (14.8)	1 (3.7)	1 (3.7)	6 (22.2)
Cost	2 (7.4)	4 (14.8)	5 (18.5)	11 (40.7)
Storage (having a place to put food)	0	0	1 (3.7)	1 (3.7)
Cooking ability	0	4 (14.8)	2 (7.4)	6 (22.2)
None selected	0	0	1 (3.7)	1 (3.7)

[1] # 1, 2 and 3 indicating first, second and third consideration selected respectively

Supplementary Table 23

Other considerations caregivers make when providing food to their son(s) with DMD [1]

	# 1	# 2	# 3	Any
Their food preferences	16 (59.3)	7 (25.9)	2 (7.4)	25 (92.6)
The enjoyment they get from eating food	8 (29.6)	6 (22.2)	6 (22.2)	20 (74.1)
Controlling their behaviour	0	2 (7.4)	4 (14.8)	6 (22.2)
The variety of textures, flavours and smells of the foods they eat	3 (11.1)	9 (33.3)	8 (29.6)	20 (74.1)
Their son makes healthy choices on their own (selected from other)	0	1 (3.7)	0	1 (3.7)
None selected	0	2 (7.4)	7 (25.9)	9 (33.3)

[1] # 1, 2 and 3 indicating first, second and third consideration selected respectively

Supplementary Table 24

Why Caregivers Consider the Healthiness of The Food When Providing Food to Their Son(S) [1]

It’s good for their mood	0	1 (3.7)	3 (11.1)	4 (14.8)
It’s good for their energy levels	2 (7.4)	6 (22.2)	8 (29.6)	16 (59.3)
It’s good for their sleep	0	1 (3.7)	1 (3.7)	2 (7.4)
It's good for their heart	0	4 (14.8)	2 (7.4)	6 (22.2)
It’s good for their mental health	0	1 (3.7)	4 (14.8)	5 (18.5)
To stop them gaining too much weight	17 (63.0)	3 (11.1)	5 (18.5)	25 (92.6)
It's good for their muscles	1 (3.7)	3 (11.1)	1 (3.7)	5 (18.5)
It's good for their bones	0	1 (3.7)	1 (3.7)	2 (7.4)
It's enjoyable for them to eat healthy foods	7 (25.9)	6 (22.2)	2 (7.4)	15 (55.6)
It's good for their height growth	0	1 (3.7)	0	1 (3.7)

[1] # 1, 2 and 3 indicating first, second and third reason respectively

Supplementary Table 25

Features of the Mealtime Environment in Households

	Rarely or never (≤1/week)	Some of the time (2-4 days/week)	Most or all of the time (5-7 days/week)
Our family eats meals together	2 (7.4)	5 (18.5)	20 (74.1)
Our family eats meals at a table/bench	2 (7.4)	5 (18.5)	20 (74.1)
Our son eats meals in the car	26 (96.3)	1 (3.7)	0
Meals in our household are rushed	14 (51.9)	12 (44.4)	1 (3.7)
Meals occur later than expected or just before bed time	25 (92.6)	2 (7.4)	0
Our son eats something different from other family members	20 (74.1)	4 (14.8)	3 (11.1)
Someone in our household cooks the main meal	0	2 (7.4)	25 (92.6)
Our son eats meals sitting in front of a screen (e.g. a TV, phone or tablet)	17 (63.0)	9 (33.3)	1 (3.7)
The TV is on in the background during the main meal	10 (37.0)	12 (44.4)	5 (18.5)

Supplementary Table 26

Problems and Difficulties Related to Eating, Emotions and Appetite

Rate how much of a problem each of the following situations are…	**Median (IQR)**
My son eats because of his feelings/emotions	1.0 (0.3, 2.6)
My son eats because he is bored	1.1 (0.3, 2.9)
My son is always asking for food because he is always hungry	1.4 (1.3, 3.3)
My son has an increased appetite because of the medication he takes for his Duchenne muscular dystrophy	1.8 (0.5, 4.0)
Rate how difficult each of the following situations are for you…	
Controlling my son's appetite	1.3 (0.3, 3.0)
Saying no to my son when he asks for food because of his Duchenne muscular dystrophy	2.0 (0.3, 3.6)

Supplementary Table 27

Emotions That Make Young People with DMD Want to Eat

Emotion(s) or situations	n
Sadness, depression, upset	2
Angry	2
Anxiety	1
Frustration	1
Boredom	1
Special occasions or only on certain days (e.g. weekends)	1
Only when hungry	1

Supplementary Table 28

Nutrition-Related Topics Selected by Caregivers to be Delivered in a Healthy Lifestyle Program [1]

	#1	#2	#3	Any
Preparing and cooking healthy meals and snacks	5 (18.5)	6 (22.2)	1 (3.7)	12 (44.4)
Healthy lunch boxes	4 (14.8)	2 (7.4)	4 (14.8)	10 (37.0)
Managing appetite (e.g. when on steroids)	8 (29.6)	2 (7.4)	0	10 (37.0)
Eating for muscle health (e.g. protein foods)	3 (11.1)	6 (22.2)	0	9 (33.3)
Healthy meals when out/healthy take-away	1 (3.7)	2 (7.4)	6 (22.2)	9 (33.3)
Finding healthy foods in the supermarket	2 (7.4)	4 (14.8)	2 (7.4)	8 (29.6)
Eating for bone health (e.g. dairy foods)	1 (3.7)	2 (7.4)	4 (14.8)	7 (25.9)
Eating for heart health (e.g. reducing salt)	0	2 (7.4)	4 (14.8)	6 (22.2)
Increasing fruits and vegetables	2 (7.4)	0	3 (11.1)	5 (18.5)
Eating for mental health (e.g. fruits and vegetables)	1 (3.7)	1 (3.7)	1 (3.7)	3 (11.1)
Reducing ‘sometimes’ foods (also known as ‘unhealthy’ or ‘junk’ foods)	0	0	2 (7.4)	2 (7.4)

[1] # 1, 2 and 3 indicating first, second and third topic selected respectively

Supplementary Table 29

Other topics selected by caregivers to be delivered in a healthy lifestyle program [1]

	#1	#2	#3	Any
Mindfulness	6 (22.2)	3 (11.1)	7 (25.9)	16 (59.3)
Improving self-esteem	2 (7.4)	7 (25.9)	6 (22.2)	15 (55.6)
Nutrition supplements	4 (14.8)	7 (25.9)	3 (11.1)	14 (51.9)
Improving body image	4 (14.8)	3 (11.1)	4 (14.8)	11 (40.7)
Reducing screen time	6 (22.2)	1 (3.7)	2 (7.4)	9 (33.3)
Making mealtimes enjoyable	4 (14.8)	4 (14.8)	0	8 (29.6)
Improving sleep	1 (3.7)	1 (3.7)	3 (11.1)	5 (18.5)

[1] # 1, 2 and 3 indicating first, second and third consideration selected respectively

Supplementary Table 30

Preferences for Resources to be Provided in a Healthy Lifestyle Program

	#1	#2	#3	Any
Written information (e.g. booklet or information on a website)	6 (22.2)	4 (14.8)	12 (44.4)	22 (81.5)
Meal plans for your family	5 (18.5)	10 (37.0)	7 (25.9)	22 (81.5)
Recipe and snack ideas	10 (37.0)	8 (29.6)	3 (11.1)	21 (77.8)
Interactive activities to help your family learn about healthy eating and lifestyles	6 (22.2)	2 (7.4)	2 (7.4)	10 (37.0)
Supermarket tours to learn where to find healthy foods	0	1 (3.7)	0	1 (3.7)

Supplementary Table 31

Preferences for Mode of Deliver for the Healthy Lifestyle Program

	#1	#2	#3	Any
In person (e.g. in neuromuscular clinic)	17 (63.0)	7 (25.9)	1 (3.7)	25 (92.6)
Social media (eg. Facebook group/chats/live videos)	2 (7.4)	9 (33.3)	4 (14.8)	15 (55.6)
Over a video call (e.g. using Skype or Zoom)	6 (22.2)	4 (14.8)	4 (14.8)	14 (51.9)
Over the phone	2 (7.4)	3 (11.1)	7 (25.9)	12 (44.4)

Supplementary Table 32

Preferences for Outcome Measures for the Healthy Lifestyle Program

	#1	#2	#3	Any
Quality of life	7 (25.9)	3 (11.1)	5 (18.5)	15 (55.6)
Weight	8 (29.6)	2 (7.4)	4 (14.8)	14 (51.9)
The amount of healthy foods eaten	5 (18.5)	4 (14.8)	2 (7.4)	11 (40.7)
Self esteem	2 (7.4)	3 (11.1)	4 (14.8)	9 (33.3)
Body image	1 (3.7)	4 (14.8)	4 (14.8)	9 (33.3)
Strength	1 (3.7)	3 (11.1)	5 (18.5)	9 (33.3)
Physical function (ability to move)	3 (11.1)	4 (14.8)	0	7 (25.9)
The amount of ‘sometimes’ foods eaten	0	1 (3.7)	2 (7.4)	3 (11.1)
Sleep	0	2 (7.4)	0	2 (7.4)
Lung function	0	0	1 (3.7)	1 (3.7)

Appendix F.

Supplementary Data for Chapter 6

HREC Project Number:	2019.285		
Short Name of Project:	SNOW-P VIRTUAL		
Full Name of Project:	Supporting Nutrition and Optimising Wellbeing Program (SNOW-P) for weight management in Duchenne muscular dystrophy: Feasibility and pilot study		
Principal Researcher:	Dr Zoe Davidson, Post-Doctoral Researcher and Dietitian		
Version Number:	1	**Version Date:**	5/8/2020

Thank you for taking the time to read this **Parent / Guardian Information Statement and Consent Form**. We would like to invite your child to take part in a research project that is explained in this form.

This form is seven pages long. Please make sure you have all the pages.

What is an Information Statement and Consent Form?

An Information and Consent Form tells you about the research project. It explains exactly what the research project will involve. This information is to help you decide whether or not you would like your child to take part in the research. Please read it carefully.

Before you decide if you want your child to take part or not, you can ask us any questions you have about the project. You may want to talk about the project with your family, friends or health care worker.

Taking part in the research project is up to you

It is your choice whether or not your child takes part in the research project. You do not have to agree if you do not want to. If you decide you do not want your child to take part, it will not affect the treatment and care your child gets at The Royal Children's Hospital (RCH).

If you decide that you would not like your child to take part, you can access a dietitian through the neuromuscular clinic at RCH. The dietitian can give you advice on how to manage your son's weight or on any other nutritional issues. Alternatively your son can access a dietitian through your GP, local community health centre or through the Dietitians Association website.

Signing the form

If you want your child to take part in the research, please sign the consent form at the end of this document. By signing the form you are telling us that you:

- understand what you have read
- had a chance to ask questions and received satisfactory answers
- consent to your child taking part in the project
- consent for your child's re-identifiable health information to be stored and used to inform future research

We will give you a copy of this form to keep.

1. What is the research project about?

We are inviting your son to take part in a weight management program for young people with Duchenne muscular dystrophy (DMD). As you may know, many young people with DMD can find managing their weight difficult. Young people with DMD may find that being above a healthy weight can affect the symptoms of their DMD, such as lung function. It can also increase their risk of developing obstructive sleep apnoea, which is a serious sleep disorder. It may also be more difficult for these young people to process the sugar levels in their blood – this is known as insulin resistance.

The aim of our program is to help young people with DMD who are above a healthy weight. It is called the Supporting Nutrition and Optimising Wellbeing Program (SNOW-P). It helps young people with their nutrition, wellbeing and weight management. This type of program has never been done before for people with DMD.

SNOW-P is a six week program that focusses on strategies to help your son manage his weight. All sessions with the dietitian will be done over telehealth (video call) or the phone.

The sessions with the dietitian will include topics on nutrition for a healthy weight, managing appetite, and advice based on your son's current food and drink intake. Our dietitian will provide you with a tailored report based on your son's food diary and written resources. The dietitian will work with you and your son to set goals that are suitable and achievable for your family. You and your son will also have access to online or email support with the dietitian.

We want to find out whether our program:

- works well for young people with DMD and their families
- could be implemented again at RCH and other hospitals in Australia
- improves the health of young people with DMD by improving their weight, physical function, fatigue, quality of life, and quality of their diet.

SNOW-P has been designed by families who have a son with DMD, as well as neuromuscular and nutrition researchers and clinicians. You might have seen or completed the EAT-DMD survey in mid-2019. In this survey we asked parents/guardians of a young person with DMD to help us design a nutrition weight management program. The results of the survey have helped us to design SNOW-P.

2. Who is running the project?

This project will be run through the Neuromuscular Clinic at the RCH. This research has not received specific funding.

Dr Zoe Davidson from Monash University and the Murdoch Children's Research Institute (MCRI) and RCH is leading the research. This research is part of a PhD project for Natassja Billich from Monash University and RCH. Natassja will also be the dietitian running the program.

Researchers from Monash University, MCRI/RCH and Children's Hospital at Westmead are involved in this project and wrote the research protocol.

3. Why is my child being asked to take part?

Your son is being asked to take part in this research as they are a young male with DMD. To be eligible to participate in this research, your son needs to be:

- above a healthy weight range – we have defined as at or above the 97th BMI percentile
- able to understand English so that he can participate in the program
- free from any illness that may make it inappropriate for him to participate.

4. What does my child need to do in this project?

You and your son will have a session with our dietitian **once per week for six weeks**. You and your son will do all of these sessions over telehealth (video call) or the phone. Each session will take

about one hour and each review about 15 minutes. However, the first visit will take around one and a half hours.

See Table one for further information about what you and your son will need to do for this program. During the program we will also ask your son to wear an activity monitor on his wrist, if he or a family member have access to one.

If you decide that your son will take part, the program will be delivered to your son and at least one parent or guardian. Your son may also be able to have some sessions by himself.

Table 1. Program structure			
Time:	**Location, time taken:**	**Measurements taken:**	**What is the session about?**
Pre-program	Home over telehealth or phone 20 minutes	• Weight* - if able to stand • Height* - if able to stand *These will only be done only if they are not available in your son's medical record	Measurements only
Session 1	Home over telehealth or phone, 1.5 hours	• Weight- if able to stand • Height- if able to stand • Waist circumference • Physical function: timed lying-to-stand *or* can stacking exercise, depending on ability • Activity level • How your son feels about his health • Dietary intake using a food diary	• Nutrition for a healthy weight • Managing appetite • Advice based on food diaries • Introduction to online and email dietitian support
Review 1 in week 1	Phone, 15 minutes	None	• Checking progress • Question/answers
Session 2 in week 2	Home over telehealth or phone , 1 hour	None	Choose **one** of these topics: • Healthy lunch boxes • Meal preparation and cooking • Mindfulness • Activities and interests • Nutrition supplements **and;** • Continue Session 1 topics
Review 2 in week 3	Phone, 15 minutes	None	• Checking progress • Question/answers
Session 3 in week 4	Home over telehealth or phone , 1 hour	None	Choose **one** of these topics: • Healthy lunch boxes • Meal preparation and cooking • Mindfulness • Activities and interests • Nutrition supplements **and;** Continue Session 1 topics
Review 3 in week 5	Phone, 15 minutes	None	• Checking progress • Question/answers
Session 4 in week 6	Home over telehealth	• Weight- if able to stand • Height- if able to stand • Waist circumference	Review all topics

	or phone , 1 hour	• Physical function – as in Session 1 • Activity level • How your son feels about his health • Fatigue level • Dietary intake using a food diary	
Session 5 in week 12	Home over telehealth or phone , 30 minutes	• Weight- if able to stand • Height- if able to stand • Waist circumference • Physical function – as in Session 1 • Activity level • How your son feels about his health • Fatigue level • Dietary intake using a food diary	For measurements only

If you decide that you and your son will take part, we will also collect some health information about your son. This health information will help the dietitian understand each families' situation so she can give you appropriate advice. We will collect this health information either from your son's medical record or by asking you and your son questions. The health information we will collect will include:

- social information
- any diagnosis of other conditions such as Autism Spectrum Disorder
- level of physical function
- the mobility equipment your son uses.

We will also use some health information to help describe study participants in scientific journal articles or presentations. We will not use your son's individual information for this purpose. Instead, we will describe the participants as a group. Your son will not be identified in any way in journal articles or presentations.

5. Can my child stop taking part in the program?

Your son can stop taking part in the program at any time. You just need to tell us so. You do not need to tell us the reason why. If your son leaves the program we will use any information already collected unless you tell us not to.

6. What are the possible benefits for my child and other people in the future?

This is a feasibility and pilot study. This type of study looks at whether the way the program is run is acceptable for young people with DMD and their family. This study will give us initial information about the benefits of the program. We will need to test this program further before we can be certain it is beneficial for young people with DMD.

The benefits of this research will include helping clinicians and researchers better understand how to successfully manage weight in young people with DMD.

As this program has never been done before we do not know whether it will improve your son's weight or health. However, some potential benefits for your son include improved weight and diet quality. We would not expect to see large weight losses after participating in this program. Your son may have a small weight loss or stay the same weight.

At the end of the program you will receive a report on topics covered and your son's measurements, if you would like one. You will also be able to access the overall results from the study.

7. What are the possible risks, side-effects, discomforts and/or inconveniences?

There is a risk that discussing the topic of your son's weight or diagnosis of DMD may cause him psychological discomfort. To try and avoid this, the dietitian will not focus on his DMD. Instead, the dietitian will focus on positive nutrition options for the whole family. Also, the dietitian will not focus on weight loss but on optimising overall wellbeing. If your son experiences any psychological discomfort, the dietitian and/or another member of the study team such as the nurse will work together to make sure he is supported.

We do not expect your son to lose a large amount of weight after taking part in this program. However, there is a small risk that this could happen. Losing a large amount of weight can affect a person's growth. To prevent large weight losses, the dietitian will not focus on weight loss. Instead, she will focus on improving your son's dietary quality and overall wellbeing. The dietitian will not ask your son to focus on restricting his calorie intake.

You should also consider that speaking with the dietitian weekly may also cause inconvenience for you and your son.

8. What will be done to make sure my child's information is confidential?

We will collect identifiable information about your son for this research. This identifiable information will include name, address, contact details, UR number and date of birth. We will also collect health information from your son's medical record. Only members of our research team who work in Neurology at RCH will be able to access your son's identifiable information and his medical record. We can only disclose the information with your permission, except as required by law.

We will store your son's identifiable information separately to his health information. Your son's health information will be coded with a participant ID. As your son's health information will be coded with a participant ID, this is called 're-identifiable' information. Only members of the study team who work in Neurology at the RCH will be able to 're-identify' your son's health information.

By agreeing for your son to participate in this research, you will be agreeing for his re-identifiable health information to be stored on a secure drives at both RCH and Monash University.

This is a feasibility and pilot study, the same program may be tested further in future research that includes a larger number of participants across multiple clinics. Your son's re-identifiable information

collected in this feasibility and pilot study may be used to inform this future research. By agreeing for your son to participate in this study you are agreeing that his information may be used in this future research about weight management for young people with DMD.

We will keep the project data for 15 years. After 15 years, the data will be securely destroyed.

RCH and Murdoch Children's Research Institute are research partners. This means that the two organisations will always share research information with each other.

9. Will we be informed of the results when the research project is finished?

We will publish the study results of this research in scientific papers. The papers will also be included as part of a PhD thesis for Natassja Billich. We may also present the results from this research at a scientific/healthcare conference. No identifiable information will be disclosed in any paper or presentation.

We can also give you and your son a report of topics covered during the program and your son's individual measurements at the start and the end. If you would like this, please let us know.

We will also send you a letter at the end of the program telling you where you can access the overall results of the research.

10. Who should I contact for more information?

If you would like more information about the project, please contact:

Name:	Natassja Billich
Contact telephone:	0460 790 775
Email:	Natassja.billich@rch.org.au

In the case of an emergency, please contact:

Name:	Daniella Villano
Contact telephone:	(03) 9345 4633
Email:	Daniella.villano@rch.org.au

You can contact the Director of Research Ethics & Governance at The Royal Children's Hospital Melbourne if you:

- have any concerns or complaints about the project
- are worried about your child's rights as a research participant
- would like to speak to someone independent of the project.

The Director can be contacted by telephone on (03) 9345 5044.

CONSENT FORM

HREC Project Number: 2019.285

Short Name of Project: SNOW-P

Version Number: 3 **Version Date:** 25/11/2019

- I have read this information statement and I understand its contents.
- I understand what my child and I have to do to be involved in this project.
- I understand the risks my child could face because of their involvement in this project.
- I voluntarily consent for my child to take part in this research project.
- I have had an opportunity to ask questions about the project and I am satisfied with the answers I have received.
- I understand that this project has been approved by The Royal Children's Hospital Melbourne Human Research Ethics Committee. I understand that the project and any updates will be carried out in line with the National Statement on Ethical Conduct in Human Research (2007).
- I understand I will receive a copy of this Information Statement and Consent Form.

_____
Child's Name

Parent/Guardian Name	Parent/Guardian Signature	Date
Name of Witness to Parent/Guardian's Signature	Witness Signature	Date

Declaration by researcher: I have explained the project to the parent/guardian who has signed above. I believe that they understand the purpose, extent and possible risks of their child's involvement in this project.

Research Team Member Name	Research Team Member Signature	Date

Note: All parties signing the consent form must date their own signature.

SNOW-P Food and hunger diary

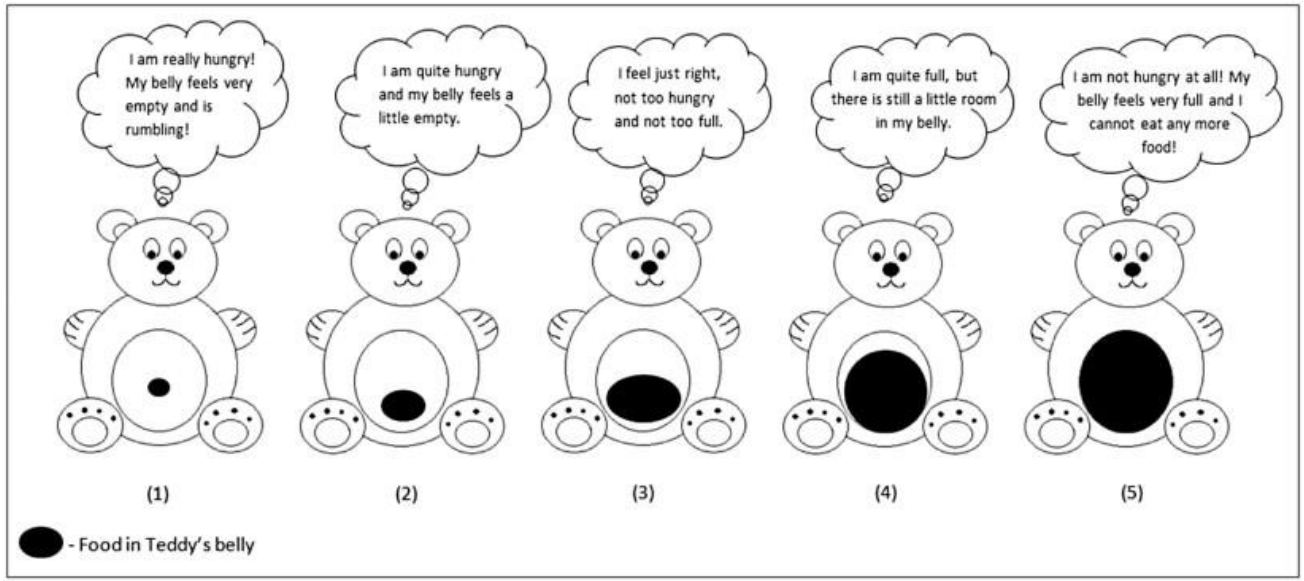
Food diary number: Study phase: Participant ID:

Instructions: Fill in the food diary below for **2 weekdays** and **1 weekend day** (**3 days in total**) for the young person participating in the program. Please record all meals, snacks and drinks consumed and the amount. A parent or guardian may complete the food diary for the young person or they may complete it themselves, if they are able to. Use the hunger rating scale below to help rate the young persons hunger before and after each meal or snack.

Hunger rating scale:

Source:

Bennet *et al*.Appetite. 2014;78:40-8.



Please record who will be completing this food diary:

Day (weekday 1):				**Date:**			
Meal (include time)	**Where are you eating?**	**Who are you eating with?**	**Thoughts and feelings before you ate?**	**Hunger Before Eating (Hunger Scale 1-5)**	**Food eaten and drinks (include brand names where possible)**	**Amount eaten/drunk**	**Hunger/fullness after eating (Hunger scale 1-5)**

Day (weekday 2):				Date:			
Meal (include time)	**Where are you eating?**	**Who are you eating with?**	**Thoughts and feelings before you ate?**	**Hunger Before Eating (Hunger Scale 1-5)**	**Food eaten and drinks (include brand names where possible)**	**Amount eaten/drunk**	**Hunger/fullness after eating (Hunger scale 1-5)**

Day (weekend day 1):				Date:			
Meal (include time)	**Where are you eating?**	**Who are you eating with?**	**Thoughts and feelings before you ate?**	**Hunger Before Eating (Hunger Scale 1-5)**	**Food eaten and drinks (include brand names where possible)**	**Amount eaten/drunk**	**Hunger/fullness after eating (Hunger scale 1-5)**

Food diary report

SNOW-P

Supporting **N**utrition and **O**ptimising **W**ellbeing **P**rogram for weight management **DMD**

Dear <inert participant name>,

Thank you for participating in *SNOW-P* and for completing the pre-program food diary. The food diary will help us understand what you are eating, where, who with and how hungry you are feeling.

Please see below feedback from your food diary. Note that this is an average taken from the <insert days> you recorded in the food diary.

Nutrient or food group	**What you are having…**	**What you are recommended to have…**	**Healthy tips and tricks:**
Energy			
Protein			
Grains			
Vegetables			
Fruit			
Dairy & alternatives			
Meat/fish/chicken & alternatives			
Water			
'Sometimes foods'			
Sugary drinks			
Advice based on hunger levels, where you are eating and who with:			

Goals:

If you have any questions about these recommendations, please chat to <insert name> in your next study session or call <insert number> or email <insert email>.

Thank you,

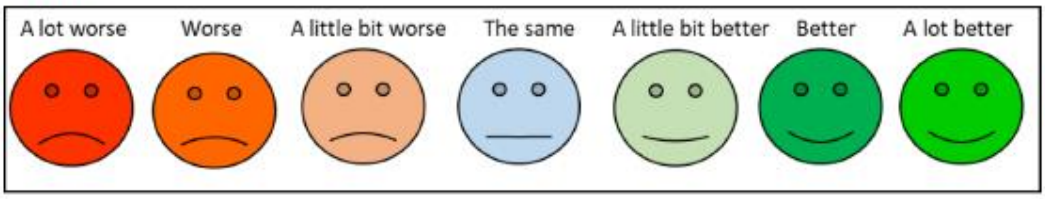
<insert name>

Fatigue Global Rating of Change Sesson 4

Please complete the survey below.

Thank you!

If you think about how tired you feel across the day, how do you feel now compared to the start of the program 6 weeks ago?



	A lot worse	Worse	A little bit worse	The same	A little bit better	Better	A lot better
Select your answer:	○	○	○	○	○	○	○

Post-program questionnaire (parent/guardian)

Dear Parent/Guardian,

Thank you for participating in SNOW-P. We would like to know how you think the program went. Please help us by filling in this short 5-10 minute questionnaire.

On a scale of 0 to 5, how satisfied you are with the program:

- ◯ 0 Not satisfied at all with the program
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5 Very satisfied with the program

Would you recommend this program to another family who has a son with Duchenne muscular dystrophy?

- ◯ Yes
- ◯ No
- ◯ I do not know

If no, please write why not:

Overall, do you think the program was beneficial to your son?

- ◯ Yes
- ◯ No
- ◯ I do not know

If yes, please write why it was beneficial:

Overall, do you think the program was beneficial to you?

- ◯ Yes
- ◯ No
- ◯ I do not know

If yes, please write why it was beneficial:

Do you think it was easy for your son to wear an activity monitor during the program?

- ◯ Yes
- ◯ No
- ◯ My son did not wear an activity monitor

On a scale of 0 to 5, how easy was it to participate in the program?

- ◯ 0 Not very easy to participate
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5 Very easy to participate

Please write any barriers that you experienced when trying to participate in the program:

Do you think this type of program should be offered through the Neuromuscular Clinic at RCH to families?

- ◯ Yes
- ◯ No
- ◯ I do not know

Please write why/why not:

Which parts of the program do you think were most beneficial?

Which parts of the program do you think should change?

Did the COVID-19 (corona virus) lock down make it difficult your son to take part in the program?

- ◯ Yes
- ◯ No

If yes, why was it difficult?

Did you like that your son could do the program all from home?

- ◯ Yes
- ◯ No

Do you think the program was a good thing for your son to do during COVID-19 (corona virus) lock down?

◯ Yes
◯ No

Please write any other comments you have:

Post-program questionnaire (young person)

Dear Participant,

Thank you for completing SNOW-P! We would like to know how you think the program went. Please help us by filling in this short 5 minute questionnaire.

On a scale of 0 to 5, please tell us how happy you are with the program:

- ◯ 0 Not happy at all with the program
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5 Very happy with the program

Would you recommend this program to someone else who has Duchenne muscular dystrophy?

- ◯ Yes
- ◯ No
- ◯ I do not know

If no, please write why not:

Do you think the program made a difference to the way you feel?

- ◯ Yes
- ◯ No
- ◯ I do not know

If yes, please write how it made a difference:

On a scale of 0 to 5, was it easy to do the program?

- ◯ 0 Not very easy to do the program
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5 Very easy to do the program

If you think about the goals you set and the topics you learnt in the program, do you think it would be good to keep going with these in clinic at RCH?

- ◯ No
- ◯ Yes
- ◯ I do not know

Do you think it was easy wearing an activity monitor during the program?

- ◯ Yes
- ◯ No
- ◯ I did not wear an activity monitor

What do you think the best parts of the program were?

Which parts of the program do you think should change?

Did the COVID-19 (corona virus) lock down make it difficult for you to take part in the program?

- ◯ Yes
- ◯ No

If yes, why was it difficult?

Did you like that you could do the program all from home?

- ◯ Yes
- ◯ No

Do you think the program was a good thing to do during COVID-19 (corona virus) lock down?

- ◯ Yes
- ◯ No

Please write any other comments you have:

Withdrawal survey

Dear Parent/Guardian,

Thank you for your interest in participating in SNOW-P.

We have recorded that your son withdrew from the program.

We would like to know whether if there are any ways we can facilitate participation or make improvements to this program in the future. Please help us by filling in this short 5 minute questionnaire.

1) Please write the reason your family withdrew from the program, if you would prefer not to say please write "prefer not to say":

2) Please write any barriers (things that made it difficult) to participating in the program:

3) Please write any recommendations you have for changing the program in the future to ensure it is acceptable and feasible for families:

4) Did COVID-19 make it difficult for you or your son's ability to participate in the program?

- ◯ Yes it made it difficult for me to participate in the program
- ◯ Yes it made it difficult for my son to participate in the program
- ◯ Yes it made it difficult for both of us to participate in the program
- ◯ No, our ability to participate in the program had nothing to do with COVID-19

5) Please make any other comments about COVID-19 during this program:

_____

Supplementary Table 33

Dietary Intake of SNOW-P Participants at Baseline (n=6)

Energy and Nutrients	
Energy (kJ)	7137 (6797, 8383)
Protein (g)	86.3 (84.9, 87.4)
Carbohydrate (g)	207 (179, 224)
Fat (g)	60.3 (58.1, 62.2)
Saturated fat (g)	26.6 (22.1, 27.9)
Fibre (g)	19.6 (18.7, 24.3)
Calcium (mg)	893 (710, 1037)
Iron (mg)	9.3 (7.8, 10.3)
Folate (mg)	556 (547, 701)
Zinc (mg)	10.8 (8.4, 14)
Vitamin C (mg)	79.2 (33, 138)
Vitamin B12 (ug)	4.3 (3.0, 6.3)
Vitamin A (ug)	565 (493, 818)
Food groups	
MFP serves	1.6 (1.0, 2.0)
Grain serves	4.6 (4.2, 5)
Veg serves	1.2 (0.8, 1.8)
Fruit serves	0.9 (0.4, 2.7)
Dairy serves	1.9 (1.6, 2.1)
Discretionary serves	2.2 (2, 4.5)
Discretionary (kJ)	1312 (1226, 2698)
Discretionary %kJ	18.5 (16.1, 36.7)

Supplementary Table 34

PedsQL DMD Scores

Participant (age)	**Baseline**	**Week 6**	**Week 12**
1 (11.0)	49	81	Not completed
2 (15.8)	Withdrew	Not completed	Not completed
3 (12.3)	53	46	36
4 (8.9)	Not completed	Not completed	Not completed
5 (4.9)	56	Not completed	63
6 (11.7)	44	Not completed	Ongoing
7 (7.9)	74	Not completed	Ongoing
All	51 (46, 68)	-	