Dear Jarod,

Thank you for your interest in submitting a research proposal for funding by Duchenne UK. We look forward to receiving your application and hope that this document will provide all the guidance you need to start developing your proposal, which, as discussed, we would love to co-develop with you.

Our aim is to standardise research project submissions to enable fair, accurate and effective review by our Scientific and Patient Advisory Boards. Hence, we ask you to submit a full project proposal, using the template provided in Appendix 1 and including the following:

- Project summary (including a lay summary)
- Background to project/proposal and rationale
- An explanation of how the proposed project translates to finding an effective treatment for Duchenne and the expected impact
- Complete experimental/project plan
- A simple Gantt chart showing timeline and milestones
- Resources you have available
- Detailed description of activities, resources and costs which will be covered by the funding sought from Duchenne UK
- A list of references

The project summary should be concise. Its purpose is to provide a general overview of the application for our Advisory Boards and other interested parties before considering the full proposal in detail.

Please note that Duchenne UK is committed to the 3Rs relating to the use of animals in research – ‘Refine, Reduce and Replace the use of animals in research’. If you intend to use animals in your project, you should refer to how you have considered the 3Rs principles.

[Only include if relevant: Please also note that research funded outside of the UK must be carried out in the spirit of UK legislation as well as being compliant with all local legislation and ethical review processes.]

Finally, should your application be successful, we expect that you review and complete the Duchenne UK standard contract ready for signing within 12 weeks from our initial offer.

Please do contact us if you wish to discuss anything or have any questions.

Best wishes,

Alessandra Gaeta

Director of Research

t: 020 3198 6381
e: alessandra@duchenneuk.org
a: Unit G20, Workspace, Shepherd’s Building, Charlecroft Way, London, W14 0EE
## Appendix 1

| **Project title:** DUK-PID13  
Developing nutritional guidance, resources and a structured nutritional programme for boys with Duchenne Muscular Dystrophy to inform standards of care in the UK: A mixed-model study |
|---|
| **Lead applicant names:**  
Dr. Jarod Wong (Consultant Paediatric Endocrinologist, Royal Hospital for Children Glasgow)  
Prof Konstantinos Gerasimidis (Professor in Human Nutrition, University of Glasgow) |
| **Contact details**  
**Phone:** 07780732130  
**Email:** jarod.wong@glasgow.ac.uk; Konstantinos.gerasimidis@glasgow.ac.uk |
| **Lead applicant organisation, including address:** |
| **Co-applicants:** provide details (name, organisation) if relevant  
**Prof. Lucy Bray,** Professor in Child Health Literacy, Nursing & Midwifery education, Edgehill University, Liverpool, UK (brayl@edgehill.ac.uk)  
**Dr. Nicola Crabtree,** Consultant Clinical Scientist, Birmingham Children’s Hospital, Birmingham, UK (Nicola.crabtree@nhs.net)  
**Dr. Zoe Davidson,** Senior lecturer in Human Nutrition, Monash University, Melbourne, Australia (zoe.davidson@monash.edu)  
**Dr. Dalia Malkova,** Senior lecturer in Human Nutrition, University of Glasgow, Glasgow, UK (dalia.malkova@glasgow.ac.uk)  
**Dr Natassja Billich,** Research fellow in Human Nutrition, University of Queensland, Australia (t.billich@uq.edu.au) |
| **Expected clinical collaborators (Neuromuscular clinicians):**  
Dr. Anne Marie-Childs, Leeds  
Prof Tracey Willis, Oswestry  
Dr Shuko Joseph, Glasgow  
Dr Deepak Parasuraman, Birmingham |
| **Project summary:**  
Provide a brief overview of the project, highlighting focus, objectives and expected outputs and impact in the field of Duchenne muscular dystrophy. |
The main aim of this project is to develop the evidence base for the development of nutritional resources tailored specifically for boys with DMD and to inform standards of care in the UK. This project is anticipated to form the cornerstone of the set-up of the nutrition working group of DMD Care UK.

There are five parts to this project proposal:

- Three parts are projects/research aiming to inform care in the area of nutrition.
- Two parts are projects/initiatives that will impact on care in the area of nutrition.

All five parts will run in parallel from the initiation of the project.

**Part one** is a retrospective study that aims to identify the timing of weight gain (in particular fat mass from DXA) in boys with DMD following initiation of steroids and also following cessation of ambulation in steroid treated boys.

- We will do this by conducting two retrospective studies. We will access body composition data (fat mass and lean mass) from DXA scans performed as part of clinical monitoring of bone density in boys with DMD for this study. We will also utilise DXA body composition data (fat mass and lean mass) from a completed research study in UK healthy children, which aimed to develop normative data for bone density and has been published. Using body composition data (fat mass and lean mass) in the healthy boys from that study we will develop normative data of DXA derived fat mass and lean mass in children and adolescents without DMD. The availability of this UK data set of normative data of body composition allows for the robust interpretation of DXA fat mass and lean mass in boys with DMD in our retrospective studies; and also future studies.

**Part two** is a prospective case control study that aims to identify the caloric needs of ambulant and non-ambulant boys with DMD on steroid therapy.

- We will do this by conducting two separate case control studies (one for ambulant boys vs controls and another for non-ambulant boys vs controls).

**Part three** aims to identify the opinion of young people with DMD, their carers and health care providers in the UK via surveys, interviews and focus groups on the following issues:

- Current dietary patterns and impact of weight gain/obesity on day to day living.
- Experiences of nutrition input through their clinics.
- Opinion on the design of a structured nutritional programme for boys with DMD with the aim to adapt a recently developed face to face programme (developed in Australia) to ensure that it can be implemented as part of clinical care and nutritional education specific for DMD in the UK.

**Part four** is an initiative to develop nutritional resources tailored specifically for boys with DMD based on current understanding and research; and subsequently adapted based on findings of our research.
These resources include leaflets and videos covering nutritional guidance for DMD based on current understanding. We anticipate that these will be developed within the first year of project initiation. Following completion of the research as described above in particular outputs from part two, we will modify the nutritional resources and guidance.

The plans included in this part of the project ensures that there is early impact on patient care by delivery of DMD specific nutritional guidance based on expert opinion and currently available evidence (within the first year of the project); but that the guidance at the completion of the project will be fully informed by evidence based generate by our research output.

Part five is an initiative where a pathway for national referral for dietetic review with a paediatric dietician with interest in neuromuscular conditions will be developed and for patients to access specialist dietetic advice currently lacking in the NHS.

- Similar to the working model of the psychosocial working group of DMD Care UK, dedicated dietetic time has been allocated and requested to allow for a national referral pathway for dietetic review.
- It is anticipated that cross working with members of the psychosocial working group of DMD Care UK who are accepting national referrals will take place.
- This addresses a significant gap in care identified through patients’ and clinicians feedback.

Summary of project output

- We will develop DMD specific nutritional resources for all boys with DMD based on current knowledge (eg leaflets, recipes, educational videos/modules) as part of DMD Care UK within the first year of the project. The information in these resources will be adapted incorporating findings of our research studies (Part two).
- We will also develop the structure of a DMD specific nutritional programme by refining an existing programme developed in Australia. We anticipate that this would be an online programme but with some direct person to person interaction (Part three). Our retrospective study will also inform the critical time for nutritional intervention following initiation of steroids and following cessation of ambulation (Part one).

Further plans

- Once we have developed the structure and content of the nutritional programme, we will seek further funding to develop the online programme, assess the feasibility of implementing the programme and also potential impact (Not part of the output of this proposal).
- The content of the proposed nutritional programme we develop will be circulated to clinical dieticians in all NorthStar sites for it to be considered to be used as a model of direct clinical care in sites where there are dedicated neuromuscular clinicians prior to the development of the online programme—thus with anticipated impact on clinical care directly.
**Background to project/proposal & project rationale**

Provide detail on the science leading up to the proposal referencing all key papers. Describe any preliminary results which support your submission.

**Background**

Obesity is a very common and serious health complication in Duchenne muscular dystrophy (DMD) [1]. Numerous factors contribute to significant weight gain in DMD which include limited physical activity even in ambulant boys, and the use of long-term steroids which may alter metabolic rate, energy expenditure and increase intake. Whilst there is recognition of the need for dietetic and nutritional input in the management of boys with DMD, this aspect of care is often not addressed in the clinics in the NHS. There are numerous reasons for this which may include limited resources. However, the lack of specific guidance based on evidence in boys with DMD is also a major reason, and this is due to the fact that there is extremely limited information on nutritional needs in boys with DMD. Published recent research including by co-applicants (Dr. Davidson and Dr. Billich) demonstrate that young boys with DMD on steroid treatment with “healthy” weight are already consuming more calories than required [2,3]. This speaks clearly to the need for clear, specific nutritional advice even in a young boy with DMD.

**Extent of clinical problem**

Published literature and lived experience demonstrates that excessive weight gain and obesity are extremely common in boys with DMD.

As part of preparation for this submission, we performed a preliminary analysis of body mass index (BMI) boys managed in the Glasgow neuromuscular clinic. Based on BMI from the last clinic visit for each boy whilst each boy was still ambulant,

- 33% were classified as severely obese (BMI Z scores > +2.68 SD)
- 33% were classified as obese (BMI Z scores > +2.01 SD but < +2.68) and
- 23% were classified as overweight (BMI Z scores > +1.34 SD but < +2.01 ).

This does mean that only 11% of ambulant boys are within a healthy weight range.

In comparison, available data suggests that about 10-15% of boys in Scotland are obese (vs 33% in our boys with DMD) and approximately 5% of children are severely obese (vs 33% of our boys with DMD).

**Consequences of clinical problem of obesity**

Building evidence also points to the negative impact of obesity in DMD on health outcomes like respiratory function [4], cardiovascular outcomes [5, 6], metabolic status [7], and obstructive sleep apnoea and bone outcomes [8]. Most importantly, obesity impacts significantly on the quality of life and mental health of these young people and their family.

**Current clinical situation and experience**
There is currently no structured nutritional and weight management programme for boys with DMD implemented nationally or internationally to the best of our knowledge. In fact, in a UK wide survey of families of boys with DMD (via DMD Care UK), 46% of responders stated that nutritional issues are not monitored or addressed in the clinic. Feedback from the families via the family survey identified that specific nutritional and lifestyle advice catered for these boys would be considered essential, as many self-manage this area of care without clinical advice. The 2018 international standards of care recommend that a registered dietician should assess nutritional status and create a specific nutritional plan [9]. The results of the family survey therefore highlights a major gap in clinical care of boys with DMD.

Need for research in this population
Given the unique issues in young people living with DMD eg the physical limitations (and that more intensive exercise is contraindicated even in young ambulant boys), the neurocognitive issues at least in some (eg autism, specific educational needs), which are common, and the differences in body composition, developing evidence-based nutritional strategies and recommendations that are patient-centric is critical. The patients’ voice as expressed in the DMD Care UK family survey also speaks loudly to the need for research in this area.

### Aims and objectives
Please state the aims and objectives of the project.

The **main aim** of the proposed research is to work with people living with DMD to generate evidence, through research, to inform and guide nutritional advice and management in boys with DMD to allow maintenance of healthy weight.

We anticipate that this project will form the corner stone of the nutrition working group of DMD Care UK. It is anticipated that researchers in this research project (in particular Dr Wong, Dr Davidson, Dr Billich and the nutritionist and clinical dietician funded as part of this project) will play key roles in the working group.

To achieve the main aim of the whole project, we have designed five parallel projects/studies with specific objectives. Please refer to time lines for details of progression of the projects.

The specific objectives of the five parts are:

**PART ONE** aims to identify the timing of abnormal/excessive weight gain and adiposity (fat mass) onset following initiation of steroids and following loss of ambulation.

We will conduct two retrospective studies.

- We first plan to do this by studying changes in fat mass data from dual energy absorptiometry (DXA) following initiation of steroid therapy to pinpoint the critical period of excessive weight gain in a retrospective multi-centre study. We will compare body composition (ie fat mass and lean mass) in boys with DMD in comparison with a group of healthy controls from the UK.
- We will also aim to evaluate the trajectory of weight gain (or loss) and adiposity (fat mass) in a preliminary study to gain insight on nutritional status following loss of ambulation in steroid treated boys with DMD.

- A critical phase of **PART ONE** is also the creation of UK wide body composition centile charts in UK children and adolescents without DMD to allow comparison of body composition (fat mass, lean mass) of boys with DMD in our retrospective study and of use in future studies. We will utilize data from a completed DXA bone density study led by Dr Nicola Crabtree for creation of UK wide DXA bone density centile charts [10]. The original study was funded to develop DXA bone density centile charts and was published in 2017 [10]. We expect approximately 600-800 boys without DMD for development of these centile charts of fat mass and lean mass from DXA.

This study will inform the right timing to implement appropriate nutritional intervention to prevent obesity onset. To date, there is no published data on changes in body composition in boys with DMD following initiation of steroids and with appropriate comparison with body composition in boys without DMD. Body composition data from DXA has not been collected routinely from recently large scale clinical trials of steroid therapy or other therapies in DMD to the best of our knowledge.

**PART TWO** aims to characterize total daily energy needs, and dietary intake in boys with DMD in comparison with control boys (without DMD). We will perform two case control studies.

- We will conduct a case control study in 20 ambulant boys (5-12 years) with DMD; and in another study including 20 non-ambulant (12-21 years) boys with DMD.

- The output in **PART TWO** will guide the development of evidence based nutritional recommendations and tailored to the specific needs of boys with DMD in the UK. There is very limited research in this area in boys with DMD with the majority of studies in less than 20 participants. In addition, there has not been any studies in this area from boys with DMD in the UK.

**PART THREE** aims to understand the young person and carers’ perspective on the impact of weight gain/obesity and their experience of current dietary support they receive for weight management; and their opinion on the development of a nutritional programme tailored to the needs of boys with DMD.

- This will give deeper information on the impact of weight gain/obesity on day to day living; and seek the opinion of all stake holders to co-design a nutritional educational platform that can be developed following completion of our research.

- The opinion of managing clinicians on the development of a nutritional programme for DMD will also be sought. We will seek the opinion of young people with DMD, their carers and UK clinicians on a DMD specific nutritional programme developed in Australia and the feasibility of implementing such a programme in the UK clinics. This will ensure that the opinion of all key stakeholders especially young people with DMD, and their carers are taken into account on the development of nutritional programme and resources that can be developed for use in the UK.
PART FOUR aims to develop nutritional resources for boys with DMD that can be delivered via DMD Care UK.
- Following an initial survey as part of PART THREE, nutritional resources including guidance specific to DMD, and healthy versions of popular food choices identified from the survey will be developed (leaflets, information videos). These guidance will be developed by the team involved in this project and based on current understanding of nutritional needs.
- Following completion of PART TWO, we will modify the information in these resources based on the results of our research output.

PART FIVE aims to address a significant gap in nutritional care of boys with DMD in the clinic. A pathway for national referral for nutritional advice will be developed. Funding of clinical dietetic time as part of this project will allow patients to access specialist advice. This work stream models the working of the psychosocial working group.

Impact
Please, provide an explanation of how the proposed project may translate into finding an effective treatment (or assistive technology, select as relevant) for Duchenne muscular dystrophy or advancing the field.

This research proposal will address a significant gap in the management of boys with DMD. The research will lay the foundation for the development of the nutrition working group of DMD Care UK.

We anticipate the following outputs from this project, leading to long-term impact in the form of improved quality of life and management of DMD:

1- Development of freely available nutritional resources for healthy weight maintenance catered for all boys with DMD in the UK which incorporates the voice of young people with DMD and their carers (eg educational videos, healthy eating recipes or videos) appropriate for different stages of development and information preferences.
   These resources will be developed from the start of the project (anticipate completion within year 1 of project) but information included in the resources will be modified based on results of our research studies. This will mean that the nutritional advice is based on research of energy needs of boys with DMD in the UK, instead of information from children without DMD, which is currently the case.

2- Development of the model (structure and content) of a nutritional programme for boys with DMD starting steroids which can be developed as an online educational module with further funding beyond this research.
   We anticipate applying for future funding to conduct a feasibility study of this structured programme following our research, and also ultimately leveraging NHS clinical services to implement this as standard of care.
The content and structure of the nutritional programme will be shared with all NorthStar clinical sites, and clinical dieticians with dedicated sessions with young people with DMD may utilize our programme during clinical contacts.

This project is anticipated to align with the work stream of other DMD Care UK working groups eg the endocrine/bone working group and the psychosocial working group. The research team will also liaise closely with Dr Anne-Marie Childs from Leeds, a clinical collaborator on this research project. Dr Anne-Marie Childs is developing research into screening for metabolic abnormalities in boys with DMD in particular the complication of non-alcoholic fatty liver disease; and is working closely with Dr Wong. This metabolic complication (ie non-alcoholic fatty liver disease) maybe fairly common in boys with DMD [11]; and there is currently no screening recommendation as part of the 2018 international standards of care. Dr. Childs’ work stream is not included in this current project submission, but this point is raised to highlight how collectively these projects can lead to development of care of boys with DMD as part of the nutrition working group of DMD Care UK.

In summary, this current project has specific deliverables with direct impact on care of young people with DMD in the UK (DMD specific nutritional guidance and resources). The project also creates opportunities for further collaborative research that will inform standards of care for young people with DMD; and supports the workstream of DMD Care UK.

**Project plan**

Provide complete details of your experimental plan, including timelines, work packages, deliverables, milestones, including Go/No-Go decisions, and outputs. If the project is using animals, please indicate how the 3Rs will be integrated into the study design.

**PART ONE (a): Longitudinal study of fat mass in DMD following initiation of steroids**

A retrospective study will be performed to evaluate fat and lean mass prior to initiation of steroids and up to at least 3 years of follow-up. DXA body composition data is not available via recently completed clinical trials in DMD in particular those that investigate steroid regimen.

Fat and lean mass from DXA performed as part of clinical monitoring of bone health (prior to initiation of steroids, at 1, 2, 3 year and maximum follow-up whilst the boy is still ambulant) will be used to calculate fat mass index (fat mass/height$^2$) and lean mass index (lean mass/height$^2$), and will be converted to Z scores in comparison to DXA data from approximately 600-800 healthy boys in the UK (led by co-applicant Dr. Crabtree and research already completed). Body composition can vary significantly between countries. Therefore, we believe that our research design involving boys with DMD in the UK and a group of healthy boys from the UK will allow robust and meaningful interpretation of changes in body composition. Relevant clinical data obtained as part of routine clinical care will also be collected.
We plan to include 40 boys on daily steroids and 40 boys on 10 days on/10 days off steroids in this retrospective study. To date, there is no published study of changes in fat mass following initiation of steroids in DMD with appropriate comparison with control boys. In this retrospective study, we will involve clinical sites in Glasgow, Leeds, Birmingham and Oswestry. We have identified 20 boys with DMD that fulfill the study criteria (started steroids between 2013 and 2019) from the clinic in Glasgow. There are approximately 40 boys with DMD in the neuromuscular clinic in Glasgow at anytime; approximately 80 in Leeds at any time; and approximately 70 in Birmingham and Oswestry. We are also in close contact with other sites with the same DXA scanner which we will consider collaborating with.

The main purpose of conducting this retrospective study is to identify the timing of increase in fat mass following initiation of steroids so that we know the time to introduce nutritional involvement (or other therapies if medical therapies that can be assessed in a research study in the future) upon initiation of steroids.

PART ONE (b) Preliminary longitudinal study of fat mass in DMD following loss of ambulation.

A preliminary retrospective study will be performed to evaluate fat and lean mass before and after loss of ambulation from a cohort of 20 patients managed in Glasgow. All boys will be on steroid therapy before and after cessation of ambulation.

Fat and lean mass from DXA performed as part of clinical monitoring of bone health (1-2 years prior to loss of ambulation, 1-2 years after loss of ambulation and at latest follow-up) will be used to calculate fat mass index and lean mass index as described above. Measurement of height in the non-ambulant population is problematic, with estimation of height based on segmental body measurements like ulnar length and arm-span consistently over-estimating total height. As height is required for accurate analysis and interpretation of body composition ie lean mass index and fat mass index, this needs to be considered. We plan to obtain height for this study based on measurement of bone lengths on DXA image as we previously described ([12,13]).

There are approximately 70 boys with DMD in the neuromuscular clinic database in Glasgow (managed since 2012). Over half the cohort are non-ambulant boys. We will also consider collaborating with Birmingham on this arm of the retrospective study. We have identified approximately 60 boys with DMD in Birmingham who have had annual DXA monitoring for more than 6 years.

The main purpose of conducting this study is to evaluate the trajectory of changes in fat mass in steroid treated boys with DMD following cessation of ambulation. On one hand, loss of ambulation is a time when increase fat mass is expected given the reduction in physical activity. However, given that this generally happens in adolescence, weight loss is also possible with deterioration in the underlying muscle pathology. We will be focusing on the period right after loss of ambulation (within
the first 2 years), to guide development of nutritional advice within the first few years after cessation of ambulation.

PART TWO (a): Case control study of nutritional outcomes in steroid treated ambulant boys with DMD (aged 5-12 years)

We will conduct a case-control study in 20 ambulant boys with DMD (aged 5-12 years) treated with steroids (Prednisolone or Deflazacort) and 20 aged matched control boys to measure nutritional outcomes, specifically to estimate total daily energy (caloric) needs. This will be one of the largest studies to estimate energy needs in young, ambulatory boys with DMD treated with steroids.

There are three key components of total daily energy (caloric) needs:
1) Resting energy expenditure - the amount of energy the body uses at rest.
2) Thermic effect of food - the amount of energy the body uses to absorb food.
3) Energy utilized with physical activity - the amount of energy the body uses to move around and be active.

By measuring the above three components, we can estimate total daily energy (caloric) needs of boys with DMD. This is an essential element of tailoring a nutritional programme/advice for boys with DMD. To date, total daily energy needs in boys with DMD have not been well described. In general, clinical dieticians usually make the assumption that they are the same as children without DMD or make a small reduction based on reduction in physical activity.

We will evaluate the following in all study participants:

1- Dietary intake
   Energy and nutrient intake will be estimated using a four-day food diary filled by carers of boys with DMD and controls. Total energy, the amount of carbohydrate, protein, vitamins and minerals consumed, will be calculated using a specialized dietary analysis software.

2- Resting energy expenditure and thermic effect of food
   At rest and following overnight fasting, the resting energy expenditure of boys with DMD and controls will be determined using the reference method of indirect calorimetry (Quark, COSMED, Italy) which measures the amount of oxygen and carbon dioxide the body consumes and produces. These measurements will allow estimation of energy needs at rest. Participants will then be provided with a standardized breakfast to measure how much energy is used to absorb food.

3- Energy utilized with physical activity
   Boys with DMD and controls will wear accelerometers to record counts and frequency of physical activity. In control participants, we will develop equations to measure energy expended in different types of physical activity (eg walking, jogging, kneeling, crouching, climbing stairs). Subsequently, we will use these equations to estimate energy expended
in children with DMD from their accelerometer readings. Using the estimates of energy at rest, energy to absorb food and energy of physical activity, we will estimate the level of physical activity of each individual participant (Physical Activity Level-PAL).

4- Body composition and auxology

Body composition will be assessed using the reference method of stable isotope technique for this particular cross sectional study. Participants will consume a small volume of special labelled water (looks and tastes like tap water). Saliva samples would be collected after 3 hours and analysed to calculate the amount of muscle and fat. Height, weight and ulnar length will be measured.

PART TWO (b): Case control study of nutritional outcomes in non-ambulant steroid treated boys and men with DMD (aged 12-21 years)

We will conduct a case-control study in 20 non-ambulant boys with DMD (aged 12-21 years) treated with steroids (Prednisolone or Deflazacort) and 20 aged matched control boys to measure nutritional outcomes, specifically to estimate total daily energy (caloric) needs. This will be one of the largest studies to estimate energy needs in non-ambulatory boys with DMD treated with steroids.

All investigations as described above will be performed in this population of non-ambulant boys and men. Standing height will not be obtained.

For both cross sectional studies, participants with DMD will be recruited from the Glasgow neuromuscular clinic, the UK NorthStar network and with support from the DMD Hub, through its central recruitment database. We will also collaborate with the Scottish Muscle Network to distribute information of our research to families who have consented to receiving information including research studies from all over Scotland. We anticipate recruiting 20 boys with DMD from outside the West of Scotland area (10 ambulant and 10 non-ambulant). We will review recruitment every month, and will liaise with the DMD Hub and Duchenne UK regularly for support with achieving our targets.

Study participants will receive feedback breakdown information on their nutritional intake after their study visit (anticipate within 2-3 month), although no specific clinical advice will be provided. Participants will be asked to discuss the results with their clinical teams. Dr Davidson has conducted nutritional research in neuromuscular conditions in Australia where nutritional evaluation conducted as part of research has been fed back to study participants.

The main purpose of conducting this study is to obtain information on caloric needs of ambulatory and non-ambulatory boys with DMD to ensure that nutritional advice is DMD specific.
PART THREE: Co-developing nutritional resources and a nutritional programme for boys with DMD

PART THREE (A): An online carers’ survey
An online survey targeting carers of a young person with DMD will be performed to understand the impact of weight gain/obesity in a young person with DMD, and their opinion on current nutritional input in the NHS. Carers will also be asked to provide examples of the young person’s favourite meals to allow the development of healthy versions of those meals in conjunction with nutritionists involved in the research (PART FOUR). The survey will also aim to gain insight into caregivers’ preferences for the design and delivery of a nutrition/weight management program for boys with DMD. The survey will be circulated online via Duchenne UK, and we will also engage with other UK based patient organisations.

PART THREE (B): Qualitative interviews with young people with DMD and carers
Twenty boys and men with DMD (age 7-25 years) and their carers will be purposefully recruited to understand in more detailed the issues explored in the above survey. Young people and carers will be interviewed separately, and a young person with DMD and a carer do not have to take part as a dyad. Specifically, their opinion on components of the Supporting Nutrition and Optimising Wellbeing Programme for DMD (SNOW-P), a face to face nutritional education programme developed by Dr. Davidson and Dr. Billich will be explored in these interviews [Submitted for publication]. The development of SNOW-P received input from carers and health professionals in Australia. Given the differences in models of health care between the United Kingdom and Australia, input from key stakeholders in the UK is crucial. Each interview with a young people will last about 30-45 minutes and with parents/carers about 60-90 minutes. Interviews will be conducted online with some option for interviews to be conducted at home (for participants from the North West of England).

PART THREE (C): Clinicians focus groups
Up to three facilitated online focus groups will be held with health care professionals including dieticians, neuromuscular clinicians, nurse specialists, physiotherapists, care advisers and other clinicians involved in the care of boys with DMD (eg endocrinology, respiratory and cardiology). Each focus group will last about 60-90 minutes and involve approximately professionals in each group. These focus groups will explore the priorities and perspectives of professionals on the management of weight gain/obesity, and their opinion on SNOW-P.

PART THREE (D): Focus group feedback on revised nutritional programme
Based on the results of the survey and qualitative work, the research team will refine the structured programme of nutritional intervention. Two focus groups, one with carers of a young person with DMD and young people with DMD (approximately 5-6) and one with clinicians (approximately 5-6), will be held to gain their opinion on the revised programme based on SNOW-P.

PART FOUR: Developing nutritional resources for boys with DMD
The need for specific nutritional guidance for boys with DMD is critically important; and an unmet need in the current clinical setting.

To address the gap in the short term, we will set up the nutrition working group of DMD Care UK in the first 6-9 months of the commencement of the project with key input from Dr Davidson, Dr. Wong and staffing involved in this project (research nutritionist, clinical dietician), and other professionals from the rest of the UK.

- We will develop leaflets for nutritional guidance based on current understanding.
- We will also develop healthy versions of popular meals following feedback from the survey in PART THREE (A), as leaflets or instructional videos.
- We anticipate producing these resources within the first 12 months of the project.
- Content of these resources will be developed by members of this present project team together with other members of the nutrition working group of DMD Care UK. Development of these resources will be delivered by the Duchenne UK team as part of an output of DMD Care UK similar to current work model.

Following completion of the research project (PART TWO), we will modify the information on nutritional requirements (caloric requirements)

PART FIVE: A national referral pathway for nutritional advice for boys with DMD
Funding of 0.4 WTE of the clinical dietician with the project will allow the development of a national pathway for referral for dietetic advice, similar to the approach being adopted by the the psychosocial working group of DMD Care UK. A total of 0.2 WTE of the clinical dietician post will be dedicated for direct patient contact online. Following consultation with the steering committee members of DMD Care UK, members of the nutrition working group of DMD Care UK and with input from the patient advisory board of Duchenne UK, a national pathway will be developed.

Project Gantt chart
See attached table
See separate attachment

Resources you have available
This should cover research personnel, technician support, laboratory space, access to scientific/diagnostic equipment, collaborations etc.

The research team:
Given the mixed method research employed in this study, it is critical that researchers of different background are in the research team. We believe we have assembled such a team. Dr Wong and Dr Davidson were also delegates in a recent international workshop on nutrition in DMD in 2018 [14].
The project is led by Dr Wong with critical support from Prof Gerasimidis. Dr. Wong has extensive clinical and research experience on endocrine aspects of boys with DMD. Whilst his focus has been in the areas of bone health, puberty, and adrenal insufficiency, obesity and metabolic consequences falls under the remit of endocrine care and nutritional aspects of health care of boys with DMD overlaps with endocrine care. His leadership in this project will also fit in with the workstream of DMD Care UK as Dr Wong is the clinical lead of the bone and endocrine working group of DMD Care UK, a member of the steering committee of DMD Care UK and also a member of the orthopaedic working group of DMD Care UK. Finally, Dr Wong will move to the academic department of Human Nutrition in the University of Glasgow in January 2023.

**Expertise in nutrition & body composition:**
Prof. Gerasimidis and Dr Malkova (Department of Human Nutrition, University of Glasgow) are experts in clinical research of nutritional status in children and adults with various chronic conditions. Prof. Gerasidimis is an international expert in nutritional aspects of childhood chronic conditions and has collaborated widely with clinicians in gastroenterology, endocrinology metabolic disorders and paediatric intensive care. The department of Human Nutrition in Glasgow is equipped with state of the art facilities in the study of energy balance studies. Together with Dr. Davidson and Dr. Billich (Monash University, Melbourne and University of Queensland, Brisbane), who are experts in nutritional aspects of neuromuscular conditions especially DMD, the core nutritional research team of this project are well positioned to address the research.

Dr. Crabtree is a clinical scientist and densitometrist who is internationally known for her work in assessment of bone density and body composition in adults and young people. Dr.Crabtree also led on a completed UK wide study on normative data of DXA in healthy children in the UK and has access to DXA body composition (i.e. lean mass and fat mass) as the comparative group in the retrospective study. Dr. Crabtree has also published widely on bone health and growth in boys with DMD and is collaborating with Dr Wong on a separate project on vertebral fractures in boys with DMD.

**Expertise in qualitative research:**
Prof. Bray’s (Edge Hill University, Liverpool) specific expertise is in qualitative research approaches including innovative methods which aim to facilitate the involvement of children and young people. Her area of expertise is in qualitative research involving young people with long-term conditions and complex needs with the aim to improve clinical care. Prof. Bray incorporates qualitative research approach in the development of care pathways for young people. It is critical that the voice of the DMD patient community is appropriately captured in the development of the plans in the proposed research which involves clinical care pathways; and this includes the young people with DMD themselves. Prof. Bray is also collaborating with Dr Wong and Dr Crabtree on a project on bone health and vertebral fractures in boys with DMD.
**Budget**

Detailed description of project costs, which will be covered by the funding sought from Duchenne UK, in relation to specific activities and resources required. Please, indicate if an early career researcher will be working on the project and how much of their salary will be covered.

**Total budget requested £408,146**

(£393,146 requested for applicants with £15,000 allocated to Duchenne UK)

**COSTING ASSOCIATED WITH OVERALL RUNNING OF PROJECT**

Post-doctoral research assistant 1.0 WTE, grade 7 for 3 years: £170,690 (University of Glasgow)
- Responsible for overall coordination and management of the entire project alongside Dr. Wong; they will also act as the programme single point of contact for the funder for project reporting and budget management purposes.
- Study set-up including submitting for ethical approval of **PART ONE** (retrospective studies), conducting data analysis of retrospective study.
- Liaise with Dr Nicola Crabtree on development of normative centiles of DXA body composition (**PART ONE**)
- Study set up including submitting for ethical approval of **PART TWO** (case control studies), arranging and performing study visits and data analysis.
- Support clinical dietician to develop nutritional resources (**PART FOUR**).
- Project reporting to the funder.

Paediatric dietician with expertise in neuromuscular conditions 0.4 WTE, band 7 for 3 years: £79,354 (University of Glasgow)
- Assist post-doctoral research assistant in case control study visits (**PART TWO**) and liaise with post-doctoral research assistant to develop feedback of dietary intake from study visits to participants in a simple and easy to understand manner (**PART TWO**)
- Develop nutritional resources (**PART FOUR**)
- Develop national dietetic referral pathway and accept referrals from UK clinical sites (**PART FIVE**)
- Provide clinical consultation to matters arising from the project which pertain to potential clinical management (**OVERALL**)

Conference travel and accommodation costs: £4200 (Total cost)

Researchers involved in **PART ONE** and **PART TWO** (£2100-University of Glasgow)
- Two UK conferences: £600 accommodation for 4 nights (£150 per night), £300 travel (£150 per trip), £400 registration (£200 per conference)
- One European conference: £300 accommodation for 2 nights (£150 per night), £200 travel, £300 conference registration.
Researchers involved in PART THREE (£2100-Edgehill University)
- Two UK conferences: £600 accommodation for 4 nights (£150 per night), £300 travel (£150 per trip), £400 registration (£200 per conference)
- One European conference: £300 accommodation for 2 nights (£150 per night), £200 travel, £300 conference registration.

Open access and publication fees £9000 (University of Glasgow and Edgehill University)
- Three peer review publications from the whole project (one from retrospective studies, one from case control studies, and one from qualitative interviews/focus groups).
- Estimated budget of £3000 per submission (Two submission from Glasgow: £6000 and one submission from EdgeHill: £3000)

PART ONE- Retrospective studies
Research nurse or research assistant time (band 6) total of 624 hours: £21,517 (University of Glasgow)
- Allocated 7 hour per participant for patient identification, patient consent, data extraction, upload and answering data queries (Total of 80 participants)
- For each site, a total of 16 hours will be allocated for regulatory approval and study set up (Projected 4 other sites).
- Funding will be allocated per patient contributed from each site.

Dr Nicola Crabtree senior clinical scientist, grade 8 at 125 hours in total: £6165 (Birmingham Children’s Hospital)
- Responsible for developing reference centiles of body composition in healthy boys with post-doctoral research assistant based in Glasgow and support of analysis of data of retrospective study of body composition

PART TWO- Case control studies
Indirect calorimetry for case control study: £12,000 (University of Glasgow)
- Total of 80 participants ie 40 DMD and 40 controls at £150 per measurement
- Costs include gas calibration, sample line, face masks, alcohol burning tests for control testing.

Deuterium radiolabelled water £10,000 (University of Glasgow)

Actical (accelerometers) £1500 (University of Glasgow)
- Cost of £150 per accelerometer total of 10 accelerometers

Wheel chair weighing mat for use in the Department of Human Nutrition £2500 (University of Glasgow)
- Please note that the Department of Human Nutrition at the University of Glasgow is not based at
the Royal Hospital for Children- approximately 30-40 min away.

Breakfast for participants in case control study £800 (University of Glasgow)
- Total of 80 participants ie 40 DMD and 40 controls at £10 per participant

Vouchers for participants in case control study £6000 (University of Glasgow)
- Total of 80 participants ie 40 DMD and 40 controls at £75 per participant

Travel for participants in case control study £6000 (University of Glasgow)
- Total of 80 participants ie 40 DMD (20 from Glasgow, 20 from outside Glasgow including out of Scotland) and 40 controls
- Travel reimbursement of £50 from Glasgow (60 participants-20 DMD and 40 controls) ie £3000 (University of Glasgow)
- Travel reimbursement of £200 from outside Glasgow (20 participants, budget for train fare of £100 for participant and £100 for a parent) ie £4000

Accommodation for participants in case control study (out of Glasgow): £3000 (University of Glasgow)
- Overnight hotel accommodation for 20 participants from out of Glasgow especially England at £150.

PART THREE- Qualitative research
Post-doctoral research assistant (grade 7) 0.6 WTE for 2 years: £57,200 (Edge Hill University)
- Responsible for development of survey in conjunction with Dr Wong, post-doctoral research assistant in Glasgow, performing interviews, transcribing and interpreting interviews and conducting focus groups.

Transcription of interviews £720 (Edge Hill University)

Travel cost for home visit interviews £500 (Edge Hill University)

Vouchers for participants in interviews £2000 (Edgehill University)
- Total of 40 participants (20 young people with DMD; and 20 carers) at £50 per participant.

PART FOUR- Development of nutritional resources
Development of nutritional resouces eg leaflets, videos- projected 2 short leaflets, 1 recipe booklet and 2 videos: £15,000
(Duchenne UK)
List of references


Lay summary
Please, describe your project in a way that will be accessible to a Parent Advisory Board. These are non-scientists but have a reasonable grasp of key elements of the condition and the science associated with it.
Weight gain leading to obesity is very common following steroid treatment in boys with DMD. This can also be a common problem after the young person loses ambulation and uses a wheelchair full time. Obesity can lead to a range of health problems but also significantly affects the mental health of these young people. There is currently very limited nutritional input in the NHS for boys with DMD.

The main aim of this project is to develop the evidence and resources for nutritional management in DMD to inform standards of care in the UK. We will co-develop nutritional resources with the patient community for all boys with DMD and a structured nutritional programme for boys with DMD when steroids are prescribed. There are five parts to our proposal. These five parts will be initiated concurrently.

The **main objective of the first part** is to find out when weight gain starts once steroids are started, and also after losing ambulation.

- This will help us determine when a structured nutritional programme is likely to be most effective.
- We plan to compare the amount of fat and muscle mass from bone density scans already performed as part of clinical bone monitoring in the clinic in 80 boys with DMD before starting steroids and up to 3 years. We will analyse data of these boys based on the scans which have already been done as part of clinical care and compare those data to the data of fat and muscle mass in about 600-800 boys without DMD.
- This study will also aim to study weight gain (or weight loss) following loss of ambulation in a smaller group of 20 boys following loss of ambulation.

The **objective of the second part** is to find out more detailed information on the food that boys with DMD are currently eating, and the amount of calories they should be eating.

- We will study the nutritional status of ambulant boys with DMD and non-ambulant boys with DMD. This will guide us to develop nutritional resources that a specific to boys with DMD.
- We will perform investigations to find out the number of calories the young person needs to consume daily to maintain bodily function at rest, the amount burnt through activities, and the calories consumed, compared to boys without DMD.

The **objective of the third part** is to gather the opinion of young people with DMD, their carers and clinicians on the impact of weight gain on day-to-day living, their experiences of existing nutritional input in their clinics and on the development of a structured nutritional programme.

- We will also specifically ask all their opinion on a nutritional intervention that has been developed in Australia for boys with DMD to adapt for implementation in the NHS.
- We will also wish to find out the meals that boys with DMD regularly eat to allow us to develop healthy versions of those meals in the resources we plan to develop. We will do all this by performing an online survey, interviews and focus groups.
The **objective of the fourth part** is to develop nutritional resources for boys with DMD in the form of leaflets and videos, as part of the work stream of DMD Care UK.

- We will aim to produce these leaflets within the first year of the project.
- Following completion of the research in part two, we will adapt the information on nutritional requirements in these leaflets so it is based on research evidence rather than expert opinion.

The **objective of the fifth part** is to develop a national referral pathway for dietetic advice for boys with DMD from across the UK.

- As part of the funding, a specialist clinical dietician with experience in paediatric neuromuscular condition will review patients from other centres via online consultations.