

# PROJECT HERCULES: A MODIFIED DELPHI STUDY TO INFORM A BURDEN-OF-ILLNESS STUDY IN DUCHENNE MUSCULAR DYSTROPHY

Evans J<sup>1</sup>, Rose A<sup>1</sup>, Martin A<sup>1</sup>, O'Hara J<sup>1</sup>, Chandler F<sup>2</sup>, Godfrey J<sup>3</sup>

<sup>1</sup>HCD Economics, Daresbury, UK, <sup>2</sup>Alcmena Consulting Ltd, London, <sup>3</sup>JG Zebra Consulting, London, UK

## Introduction

- Duchenne muscular dystrophy (DMD) is a rare disease affecting 15.9-19.5 in 100,000 births in the United Kingdom (UK) (1).
- DMD causes progressive damage and degeneration to muscle tissue and creates a variety of problems including muscular weakness, respiratory impairment and a loss of ambulation (2).
- By mid-teens people with DMD will normally have lost ambulation and are wheelchair bound. Severe respiratory and cardiac problems develop in their twenties and are usually the cause of death (2).
- There is no cure for DMD and treatment options focus on alleviation of symptoms and management of complications. There is an urgent need for therapies which can alter the fundamental course of DMD (2).
- Corticosteroids are the standard of care but are associated with a number of side effects (3,4).
- There is a need for a comprehensive burden of illness (BOI) capturing the impact, epidemiology, costs and treatment associated with DMD across all stages.
- Given the extensive impact of DMD, a review of all aspects, from definitions to prioritisation of questions needs to be undertaken. Findings inform our BOI study design to effectively capture the experience by people with DMD and caregivers.

## Project Hercules

- Project HERCULES is an international multi-stakeholder collaboration led by Duchenne UK that is developing disease-level tools and evidence to support HTA and access decisions for new treatments for Duchenne Muscular Dystrophy. This includes:
  - A bespoke, validated, Quality of Life metric being developed by the University of Sheffield.
  - A natural history model developed for bringing together the largest collection of clinical data in DMD for multiple registries and trials by the University of Leicester.
  - A burden of illness study developed by HCD Economics.
  - A disease level economic model that will be produced by SourceHEOR.

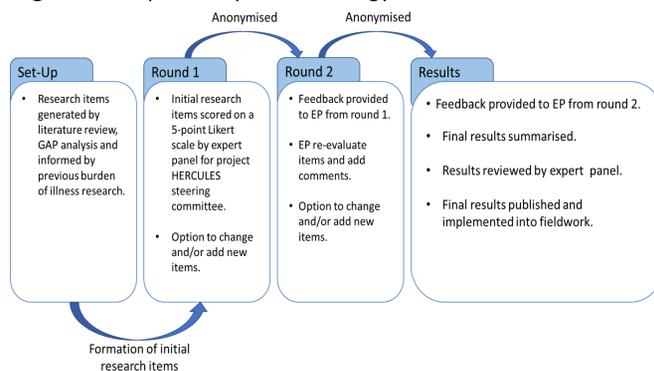
## Aims

- The aim of this study was to establish consensus for a study protocol and material development for a burden of illness (BOI) study.
- Our objective was to define a core set of research items to assess the burden of DMD using a modified Delphi-based survey technique.
- The findings will inform the structure of a BOI study of DMD in the UK, adding rigour and increasing the validity of any outcomes produced.

## Methods

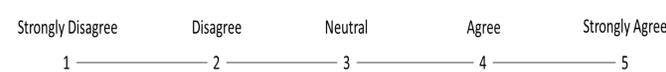
- A modified Delphi process was implemented to inform the generation of research items and questions.
- Invitations to participate in the expert panel (EP) were sent to members of Project HERCULES to include perspectives from multiple stakeholders including:
  - Physicians
  - Parents / Caregivers / Patient advocates
  - Health regulators
  - Industry representatives and health economists.
- The Delphi panel consisted of two rounds, with participants reviewing anonymised responses in the second round from the previous, as shown in Figure 1.

Figure 1. Delphi study methodology



- Members of the steering committee completed the questionnaire by rating the importance of each research item in capturing the BOI of DMD in the UK study in regard to an HTA submission.
- A 5-point Likert scale was used with answers representing level of agreement of capturing the item in the DMD BOI study, with 1 representing strongly disagree, 2 representing disagree, 3 representing a neutral view, 4 representing agree and 5 representing strongly agree (Figure 2).
- After the second round, median ratings in all categories were captured alongside the range of responses and any comments which had been made by participants.

Figure 2. The 5-point Likert scale used to rate each research item.



## Results

- 11 members of the project HERCULES steering committee responded to the first round of the Delphi study with respondents (n = 8) rating all items and completing the questionnaire.
- Participants had a range of expertise and perspectives with participation from industry representatives (n = 4), clinicians (n = 2), patient advocates (n = 1), parent/informal carer (n = 3), payers (health regulator) (n = 2) and health economist perspectives (n = 1).
- 8 members of the project HERCULES steering committee responded to the second round of the Delphi study with all 8 respondents fully completing the questionnaire.

## Results (cont'd)

- Industry representatives (n = 5), clinicians (n = 2), patient advocates (n = 1), a parent/informal carer (n = 1), a payer (health regulator) (n = 1) and health economists (n = 2) participated in the second round.
- In Figure 2, examples of resource utilisation items identified for inclusion in the BOI study are described.

Figure 2. Direct medical, non-medical and indirect costs

Direct Medical	Direct Non-Medical	Indirect	
Hospitalizations Day Case Inpatient and Outpatient Length of stay and ICU	Surgical Procedures Number/Type of surgery Elective or emergency Invasive or laparoscopic	Travel Costs Distance to treatment center Car and public transport	Work Productivity Impact Short term sick leave Medium to long term sick leave (in early retirement)
Consultations specialists Primary Care physician Other HCPs	Tests/Examinations Blood Tests Biopsies Other tests/examinations	Home adaptations/Devices Ventilation requirements Wheelchair Communication devices	Education Adaptions Home education School costs
Current and previous treatment Current treatment and posology Prior 12 month treatment and posology.	Complications Type of complication Diagnosis and treatment Hospitalization	Informal Care Hours per week Loss of earnings	
Professional Caregiver Hourly Wage Hours per week	Palliative care Hospital based setting		

- The highest and lowest median ratings within each category are presented below alongside the overall median for the category.
- Many items reached the highest possible median rating of five after the second round including: fractures, adverse effects of corticosteroids, wheelchair use, mechanical cough assist and consultations such as orthopaedics, pulmonology and physiotherapy.
- Items with a median score of four included: Port-O-Cath, Voice synthesiser, forced expiratory volume (FEV), age of loss of motor skills and consultations such as Nutritionist, Internal medicine and Psychology.
- The lowest rated areas included laundry costs (3), exercise assessments (3) and the KIDSCREEN patient-reported outcome measurements (2.5). The supplements of coenzyme Q-10 and creatine also scored low scores of 2 and 2.5 respectively.

## Conclusions

- This study has collated the views of a variety of perspectives to inform the development of a relevant set of core research items.
- The implementation of these items into the subsequent DMD BOI study will help to effectively describe and quantify the impact of DMD on people with DMD and caregivers.

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## Acknowledgements

The presenting author, Antony Martin (AM), declares the following real or perceived conflicts of interest during the last 3 years in relation to this presentation: AM is employed by HCD Economics who were funded to undertake this research.  
 This project is funded by Duchenne UK, Catabasis Pharmaceuticals Inc, Pfizer Inc, PTC Therapeutics, Roche, Sarepta Therapeutics Inc, Solid Biosciences, Santhera Pharmaceuticals Holding AG, Wave Lifesciences USA Inc,  
 Editorial support (in the form of writing assistance, collating author comments, assembling tables/figures, grammatical editing and referencing) was provided by Jonathan Evans from HCD Economics.

Presented at ISPOR Europe 2019, Copenhagen, 2<sup>nd</sup>-6<sup>th</sup> November 2019