# The burden of illness in Duchenne Muscular Dystrophy – how much evidence is available?

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## Introduction

'Burden of illness' (BoI) or 'Burden of Disease' (BoD) studies attempt to capture the impact of a disease on a patient, their family, and the healthcare system (cost of illness studies being a subset of BoI studies) (Greenberg, Ibrahim, & Boncz, 2014).

The areas covered by a BoI study will vary by disease, but it is important to capture all areas which are notably impaired. In diseases of advanced age such as Alzheimer's, these impacts are likely to mainly relate to the impact on the patient and on carers. In a working age population – for example those suffering from knee injury (typically aged around 35) the most relevant data would be on quality of life and impact on work/productivity. It is therefore important to consider which areas data is needed on, given the disease profile (both who is affected, and how they are affected). From there the relevant evidence can be assessed. In this instance as the disease primarily affects children, the effects on the children directly, but also on their parents and carers should be the focus.

The aim of this project is to understand the available BoI data in Duchenne Muscular Dystrophy (DMD) with a view to informing what further data will be needed to inform health economic modelling and health technology appraisal (HTA) for newly launched products. This involves identifying the areas where data is likely to be needed, and then performing a review of existing BoI studies, as well as searches for data available in each specific area. We do not present a systematic or definitive critique of the evidence, but instead a subjective view of both the quantity and quality of published data. In each section of the report, what appear to be the key studies are also highlighted in tabular form. Other relevant studies are discussed in text. The table includes the information on the publication, and also whether stage specific information is reported in a format suitable for modelling is reported, or whether reanalysis (if possible) would be required. Recommendations are also reported on what data would be required from any data collection exercise

It should be stressed that the views given are of the adequacy of the data for use in economic modelling, and not a comment on the intrinsic value of the research that has been conducted.

## Methods

In order to determine the areas for inclusion, multiple steps were taken. Firstly commonly researched areas from published burden of illness studies were included, then areas from past experience with HTA were included. Finally consideration was given to the specific issues surrounding Duchenne, a disease of children and young adults. This was then shared the patient group Duchenne UK and companies developing medicines in the field (as relevant topic experts). The final areas considered in the review (and justifications for each) are given below.

- Incidence & prevalence of the condition – all HTA processes have some element of budget impact consideration. Thus whilst not used in models per se, good evidence on the number of patients likely to be affected is important to the process
- Inpatient healthcare costs and disease management healthcare resource use – the cost of treating acute symptoms of the disease is likely to include hospitalisation costs, and ultimately palliative care costs. Wider healthcare costs are likely to include appointments with different specialists within the healthcare system, as well as appointments with General Practitioners (GPs) and other healthcare professionals (such as physiotherapists) that constitute the mainly outpatient management of the condition. Whilst the proportion that is publicly funded will vary between healthcare systems, the resource use should be captured regardless
- Other medical costs – beyond the direct healthcare costs, patients with DMD are likely to have substantial other healthcare needs. Most notably these will include medical devices such as wheelchairs, respiratory devices, and technology for enabling independent living, some of which will be publicly funded, and some of which may be provided by the private or third sector
- Other governmental costs – The trajectory of DMD is such that patients will likely interact with a number of other governmental departments where further costs will be incurred, most notably the education (either in specialist schooling, or enabling patients to access mainstream schooling), and care sectors
- Cost of living – the cost of living with a long term disability is likely to be higher, with adaptations or limitations to housing, and modes of transport needing to be accounted for in modelling
- Impact on quality of life & the quality of life of family/carers – this has not been reviewed as it is the topic of a separate workstream
- Productivity losses –patient productivity losses are often captured in BoI studies, but here it is important to capture the impact on parents or carers - likely to be heavily involved in care given patient age
- Impact on families – the wider impact of families DMD should also be investigated as there are likely to be other costs or factors when one (or more) children are diagnosed with a serious progressive illness

The materials used for this review include
- Prior HTA submissions to NICE and the SMC i.e. Ataluren HST submission
- Prior HTA scope (HST) for lists of outcomes of interest
- Identification of existing burden of illness studies in PubMed
- Brief searches in MedLine (via PubMed) for each area of interest to find relevant material if this was not included

When searching for additional materials, the relevant terms for each search were combined

## Results

The evidence on each area was searched, and key studies extracted, with quality assessed. The results of this are presented below including assessment of whether there was a sufficient quality of evidence to estimate effects, and whether the quality of the evidence was sufficient to have confidence in the results presented.

| | Hits | Adequate quality? | Adequate quantity? |
|---|---|---|---|
| Burden of illness studies | 61 | - | - |
| Incidence & prevalence | - | Yes | Yes |
| Healthcare resource use | 308 | No | Yes |
| Other medical costs | 496 | No | No |
| Broader governmental costs | 23 | No | No |
| Cost of living impact | 128 | No | No |
| Productivity losses | 437 | No | No |
| Impact on families | 62 | No | No |
| Quality of life of family and carers | - | - | - |

Whilst many studies were identified, in general the quality was poor for use in economic modelling. Even where good studies were available, these did not report results in a useful format for modelling or estimating the impact of treatments. The main issues were twofold

- Either results were given as costs for a given year without disaggregated results being presented to allow data to be adjusted for inflation, or different costs in other countries, or
- Results were not given by disease stage – preventing an understanding of how resource use changed as the disease progressed

Results presented below show the key studies available in each of the areas, and whether data is available for each of these areas

### Incidence & Prevalence

The evidence on incidence and prevalence of the disease appears well established and of high certainty.

| Author | Year | Country/countries included | Stage specific data available? | Data on units and cost reported? |
|---|---|---|---|---|
| Landfelt et al | 2014 | Germany, Italy, UK, US | N/A | N/A |

### Inpatient healthcare costs and disease management healthcare resource use

The evidence in this area is lacking in quality.
Further evidence collection (which preferably would include reanalysis of existing studies) should focus on capturing healthcare resource use (not just total cost) by disease stage – in general this is not reported. Whilst the totality of data with assumptions could be used for modelling, at present no single study presents appropriate data on the resource use by disease stage.

| Author | Year | Country/countries included | Stage specific data available? | Data on units and cost reported? |
|---|---|---|---|---|
| Larkindale et al | 2014 | US | No | No |
| Landfelt et al | 2014 | Germany, Italy, UK, US | Partial | No |
| Schreiber-Katz et al | 2014 | Germany | Yes | No |
| BURQOL-RD | 2016 | Bulgaria, France, Germany, Hungary, Italy, Spain, Sweden, UK | No | No |
| Teoh et al. | 2016 | Australia | No | Yes |
| TREAT-MND DMD | 2017 | 'Global' | No | No |

### Other medical costs

The evidence in this area is lacking in quantity and quality.
Further evidence collection (which preferably would include reanalysis of existing studies) should focus on capturing healthcare resource use (not just total cost) by disease stage, which is seldom reported – no singe study would alone provide robust model inputs at present.

| Author | Year | Country/countries included | Stage specific data available? | Data on units and cost reported? |
|---|---|---|---|---|
| Larkindale et al | 2014 | US | No | No |
| Landfelt et al | 2014 | Germany, Italy, UK, US | No | No |
| Schreiber-Katz et al | 2014 | Germany | Yes | No |
| BURQOL-RD | 2016 | Bulgaria, France, Germany, Hungary, Italy, Spain, Sweden, UK | No | No |
| Teoh et al. | 2016 | Australia | No | Yes |
| TREAT-MND DMD | 2017 | 'Global' | No | No |
| Rodger et al. | 2015 | UK, Germany, Denmark, Bulgaria, Hungary, Poland, Czech Republic | No | No |

### Other governmental costs

The evidence in this area is lacking in quantity and quality.
Further evidence collection (which preferably would include reanalysis of existing studies) should focus on understanding where Duchenne patients require governmental support, and how this varies by disease stage.

| Author | Year | Country/countries included | Stage specific data available? | Data on units and cost reported? |
|---|---|---|---|---|
| Schreiber-Katz et al | 2014 | Germany | Yes | No |
| BURQOL-RD | 2016 | Bulgaria, France, Germany, Hungary, Italy, Spain, Sweden, UK | No | No |
| TREAT-MND DMD | 2017 | 'Global' | No | No |
| Read et al. | 2010 | UK | No | Yes |
| Rodger et al | 2015 | UK, Germany, Denmark, Bulgaria, Hungary, Poland, Czech Republic | No | Yes |

### Cost of living

The evidence in this area is lacking in quantity and quality.
Further evidence collection (which preferably would include reanalysis of existing studies) should focus on understanding where Duchenne patients incur higher cost of living in both static costs (moving house or adapting houses), as well as ongoing costs (for example transport), as well as how this varies by disease stage.

| Author | Year | Country/countries included | Stage specific data available? | Data on units and cost reported? |
|---|---|---|---|---|
| Larkindale et al | 2014 | US | No | No |
| Schreiber-Katz et al | 2014 | Germany | Yes | No |

### Productivity losses

The evidence in this area is lacking in quantity and quality.
Further evidence collection would ideally include reanalysis of existing studies and give the number of hours of care required, as well as hours worked by carers (compared to matched controls).

| Author | Year | Country/countries included | Stage specific data available? | Data on units and cost reported? |
|---|---|---|---|---|
| Larkindale et al | 2014 | US | Partial | No |
| Schreiber-Katz et al | 2014 | Germany | Yes | Yes |
| BURQOL-RD | 2016 | Bulgaria, France, Germany, Hungary, Italy, Spain, Sweden, UK | No | Yes |

### Impact on families

The evidence in this area is lacking in quantity and quality.
Further evidence collection would ideally include reanalysis of existing studies, as well as quantitative assessments of the impact on families as a whole – from the impact of sibling activities and wellbeing, through to adaptations needed to lifestyle, split by disease stage.
What does exist is a lot of qualitative data that may be useful for context in submission dossiers, even if not in modelling directly.

| Author | Year | Country/countries included | Stage specific data available? | Data on units and cost reported? |
|---|---|---|---|---|
| Read et al. | 2010 | UK | No | Yes |
| Landfelt et al | 2014 | Germany, Italy, UK, US | No | No |
| Nozoe et al. | 2016 | Brazil | No | Yes |

## Discussion

Whilst there is a large volume of data on the burden of illness with Duchenne, the quality and reporting is poorly suited to use in economic models. Even where suitable studies are available, these are unlikely to be able to be used in other time periods or jurisdictions without reanalysis.

Whilst there are several studies looking at direct medical costs, particularly inpatient costs these do not reflect the full burden of DMD, particularly non health care costs and costs associated with the impact on families and education.

Duchenne UK is seeking access to the data in studies discussed above and will commission additional work to address the gaps identified in this project. There are plans to develop patient and family surveys that will

Work will also be carried out to scrutinise the available healthcare resource use data an establish if this a true reflection of all healthcare resource use associated with DMD. Work will focus on clinical and patient and family perspectives on how closely patient experience matches the resource use that has been captured in these studies.

Where possible this further work will be published and presented in accordance with ISPOR best practice guidelines.

Beyond the immediate impact of data collection in Duchenne, those reporting burden of illness studies should consider ISPOR best practice guidelines in reporting resource use and costs separately, to allow data to be more easily used in a different context. Further developments in the field may allow access to more granular data for re-analysis (with care taken to suitably anonymise).

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