HEALTH-RELATED QUALITY OF LIFE (HRQoL) AND ECONOMIC BURDEN OF DUCHENNE MUSCULAR DYSTROPHY (DMD): A SYSTEMATIC LITERATURE REVIEW

#188

Iff J[1], McCloskey C[2], Fidler C[2], Goemans N[3]

[1] Sarepta Therapeutics, Inc., Cambridge, MA; [2] Decision Resources Group, Bicester, UK; [3] University Hospitals Leuven, KU Leuven, Belgium.

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INTRODUCTION

Duchenne muscular dystrophy (DMD) is a rare, fatal genetic disorder caused by a lack of dystrophin protein which leads to progressive and irreversible muscle damage from birth.[1] Loss of ambulation occurs at approximately 12 years.[2, 3] The median age of death with standard of care is 26–28 years,[4, 5] with the major causes of death being respiratory insufficiency and cardiomyopathy.[1, 4] Due to the size and age of the population, determining the humanistic and economic impact of the disease on patients and their families can be challenging.

The objective of this systematic literature review (SLR) was to review the available evidence on health-related quality of life (HRQoL), economic impact, and healthcare resource utilisation associated with DMD.

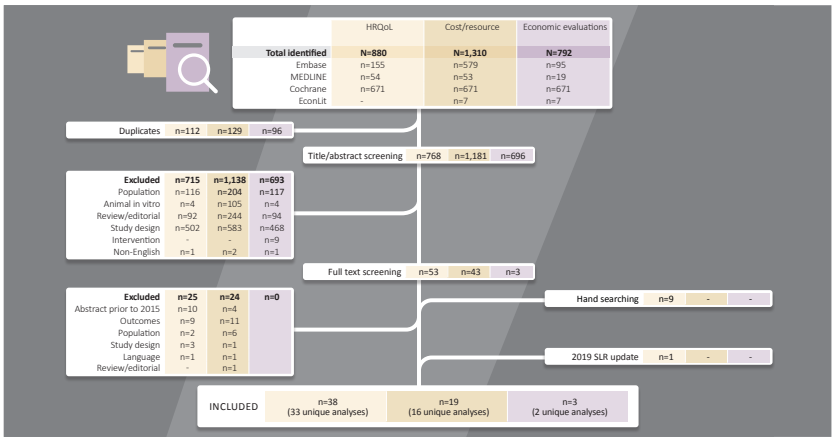
METHODS

The SLR was conducted on 29th November 2018, and updated on 24th June 2019

Embase, MEDLINE, the Cochrane Library, and EconLit were searched, and identified citations were screened for inclusion using predefined eligibility criteria

Additional relevant studies were identified by hand searching of international conference proceedings

Figure 3: PRISMA flow diagram of included and excluded HRQoL, cost/resource and economic evaluation publications



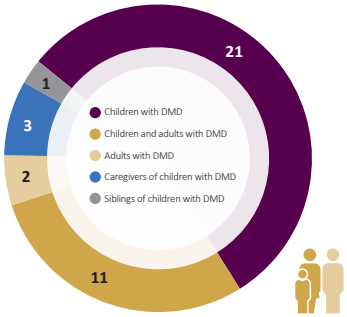
RESULTS

HRQoL

- Most commonly used instrument to assess HRQoL is PedsQL (n=17), followed by SF-36 (n=9), WHOQOL (n=4) and EQ5D (n=4). However PedsQL has a number of limitations
- DMD has a significant impact on HRQoL of children and adults, and also caregivers
- DMD appears to have greater impact on physical aspects of HRQoL than mental aspects
- There is disagreement between parent proxy and self-reported HRQoL, which could be explained by coping

The SLR identified 38 HRQoL publications on 33 unique analyses (Figures 1 and 3)

Figure 1: Included publications by population



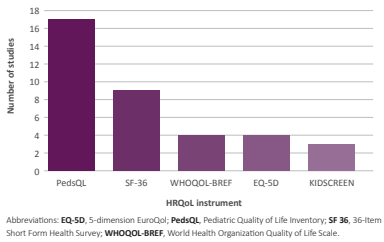
The most common instrument for the assessment of HRQoL in patients with DMD was the Pediatric Quality of Life Inventory (PedsQL), which was used in 17 studies (Figure 2)

Several studies listed limitations with the use of PedsQL for DMD:

- Certain questions on the PedsQL regarding mobility and running may be difficult to answer[6]
- The PedsQL ordinal scale may not account for heterogeneity[7]
- Although PedsQL may be appropriate to assess HRQoL at baseline, it may not accurately detect changes over 12 months[8]

The Pediatric Outcomes Data Collection Instrument (PODCI) was reported to better correlate with 6MWT scores than PedsQL, although it was only used in two of the studies identified[9]

Figure 2: Most commonly used HRQoL instruments (≥3 studies)



Abbreviations: **EQ-5D**, 5-dimension EuroQol; **PedsQL**, Pediatric Quality of Life Inventory; **SF 36**, 36-Item Short Form Health Survey; **WHOQOL-BREF**, World Health Organization Quality of Life Scale.

The literature consistently showed that DMD is associated with a reduction in HRQoL in both children and adults with DMD.

Disability progression was associated with a decline in HRQoL (n=6 studies)

- Statistically significant associations between ambulatory status and HRQoL and health utility were reported (Landfeldt et al, 2016)[7]
  - PedsQL scores were significantly associated with ambulatory status (p<0.001)
  - Mean health utility was significantly reduced from 0.75 for early ambulatory to 0.10 for those requiring ventilatory support (p<0.001)

In general, the impact of DMD appears to be greater on physical aspects of HRQoL than mental aspects

- Six studies compared HRQoL self-reported by children with DMD with that calculated from parent proxy-reporting – overall, agreement between patients and caregivers was only moderate and in general HRQoL reported by children with DMD was higher than that reported by their parents; it is possible that this relates to adaptation in patients with DMD who have had to cope with a progressive limitation since early childhood[10]

DMD has a substantial impact on the HRQoL of caregivers

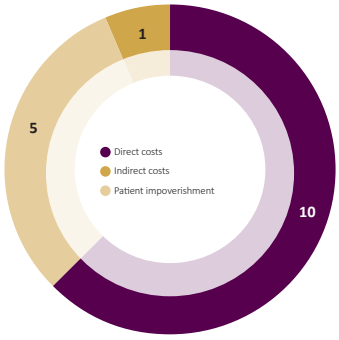
- In the survey of 770 pairs of patients and caregivers, half of all caregivers (383 of 770) reported being moderately or extremely anxious or depressed, significantly higher than general population reference data (p<0.001)[11]

Cost and resource use

- Healthcare costs for DMD are high, with considerable variation across countries
- Direct costs include rehabilitation services; medical aids; drugs; consultations
- Indirect costs include home modifications; informal care; losses due to reduced employment and productivity
- Costs related to ventilation, hospitalisation and home modification are high

Nineteen publications (16 unique studies) on cost and resource use were identified (Figure 3 and 4)

Figure 4: Included studies by cost type



DMD is associated with substantial direct and indirect costs; there is considerable variation among countries, with a gap between Eastern and Western Europe[12-14]

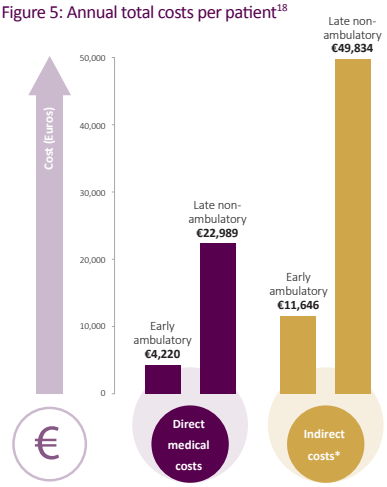
- Direct healthcare costs ranged from €505 (Hungary) to €27,185 (Germany) for adults, and from €850 (Hungary) to €38,022 (France) for children (ref year 2012)[12]
- The presence of cardiac disease significantly increases the length of hospital stays and cost,[15] and healthcare costs for patients requiring ventilatory support can be very high (one study found costs for users of non-invasive ventilatory support and continuous tracheostomy mechanical ventilation as high as $239,805 and $269,370 per year, respectively; ref year 2014[16])
- Mean total cost per hospitalisation for DMD is $42,751 (ref year 2009), and mean length of stay 9 days[17]

Indirect costs of DMD include the expense of home modifications, time spent providing informal care, and losses due to reduced employment and productivity

- The main driver of indirect costs is time spent providing informal care
- Reported indirect costs across Europe ranged from €9,671 in Bulgaria to €34,603 in the UK (ref year 2012)[12]

Healthcare costs increase as DMD progresses from the early ambulatory to the late non-ambulatory stage[18] (Figure 5)

Figure 5: Annual total costs per patient[18]



*excluding losses due to reduced employment and productivity; Ref year 2013

Economic evaluations

- Few published economic evaluations were identified in the SLR
- The only study relevant to a general DMD population was highly theoretical

Two economic evaluations (reported by three publications) were identified (Figure 3)

One study modelled the cost-effectiveness of destination therapy ventricular assist device (DT VAD) therapy in patients with DMD and advanced heart failure using a Markov state transition model[19]

The second study presented three possible modelling strategies for assessing the cost-effectiveness of hypothetical DMD interventions that might slow disease progression[13]

Evidence gaps

While there is considerable literature on HRQoL in DMD, most of the identified studies were small (n=5 studies with >100 patients)

Health utility data in the literature are limited (n=4 studies) and the instruments used have limitations and do not capture the full domains of the disease

Among cost studies, there is some variability in what costs are measured, with indirect costs associated with DMD inconsistently captured

In particular, the costs associated with lost working time for patients and caregivers varied considerably across studies

CONCLUSION

DMD is associated with a significant HRQoL and economic burden, driven primarily by the physical aspects of the disease, which increase with disease progression.

The management of DMD is costly, both from healthcare system and societal perspectives, particularly in the later non-ambulatory disease stages when patients may require ventilatory support.

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