Targeted Literature Review of Economic Burden and Modelling Techniques for Duchenne Muscular Dystrophy

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INTRODUCTION

- Duchenne muscular dystrophy (DMD) and Becker muscular dystrophy (BMD) are rare X-linked recessive ailments impacting 1 in 7,250 people in the United States (U.S.). The global prevalence of DMD ranges between 1/3,500 - 1/9,300 male births.[1,2]
- Due to dystrophin protein modifications, DMD results in swift and severe neuromuscular degeneration and muscle wasting, leading to elevated disability.[3,4]
- Currently, DMD has no known cure. Disease management is aimed at preserving the quality of life and extending survival.[4]
- Economic evaluation plays a crucial role in informing healthcare resource allocation decisions for DMD interventions, given the high cost of the interventions and limited healthcare budgets.[4]

OBJECTIVE

- To assess economic burden, current economic evaluation techniques, and data sources for DMD economic evaluation.
- To identify evidence gaps in DMD burden and provide details on the value of existing DMD treatments.

METHODS

- A targeted literature review (TLR) of the economic evaluation of DMD treatments was conducted by searching electronic databases (PubMed and Google Scholar) and Tufts Cost-Effectiveness Analysis (CEA) Registry, from 2015 to 2022.
- The following key terms "cost-benefit analysis," "cost-effective," "economic model," "decision-analytic models," "cost-utility," and "economic evaluation" were used during the search. Final studies were selected based on inclusion/exclusion criteria as outlined in below PICOS scheme **(Table 1)**.
- Where applicable, costs were inflated to 2023 USD using the medical component of Consumer Price Index (CPI).

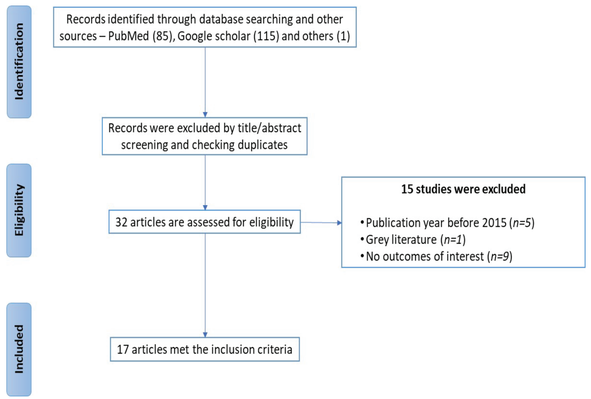
Table 1: PICOS Criteria for Selection

PICOS	COMPONENT OF INTEREST
POPULATION	Patients with Duchenne Muscular Dystrophy (DMD)
INTERVENTION	Any Intervention
COMPARATOR	Any Comparator
OUTCOMES	Direct Costs Reflecting Economic Burden of DMD and Modelling Techniques
STUDY DESIGN	Modelling studies, Economic evaluation studies
OTHERS	English language; only journal articles (grey literature excluded)

RESULTS

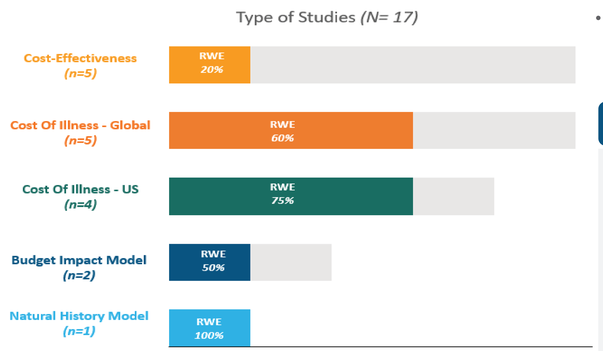
- Out of the 32 studies assessed for eligibility, 17 were included for analysis that met the PICOS criteria represented in the PRISMA flow **(Figure 1)**.

Figure 1: PRISMA Diagram



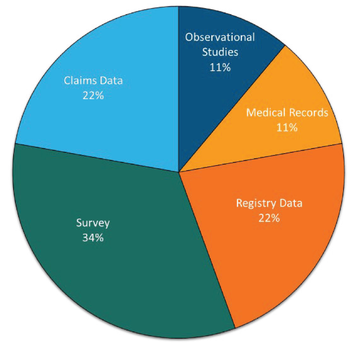
- Studies on the burden of disease were most frequently identified in the literature, either focusing on global (*n=5*) or the US (*n=4*). Following these, more Cost-Effectiveness analyses were identified (*n=5*) compared to Budget Impact analysis (*n=2*) **(Figure 2)**.
- The degree to which the selected studies utilized RWE varied considerably, with 67% of cost of illness analyses but only 20% of cost effectiveness studies doing so **(Figure 2)**.

Figure 2: The Proportion of Economic Evaluation Studies using RWE



- The most utilized RWE sources were surveys (34%), followed by claims (22%) and registry data (22%) **(Figure 3)**.

Figure 3: Distribution of RWD Sources for Economic Evaluation



- The most frequently used method for assessing the cost-effectiveness of an intervention for DMD was the Markov state-transition model, followed by the partitioned survival model and the decision-tree structure **(Table 2)**.
- Deflazacort is the most assessed intervention in economic modeling studies against available comparators (standard of care, Prednisone, and no treatment). When compared with Prednisone, Deflazacort is more expensive but improves the quality of life (QOL) for DMD patients. ICUR (Deflazacort vs. Prednisone) is higher than standard thresholds (in existing literature), hence it is not cost-effective **(Table 2)**.[7,8,9]
- Evaluating the cost-effectiveness of treatments for DMD remains challenging due to a lack of evidence. Thus, some of the studies used simulated scenarios based on assumptions to complete the models.

Table 2: Modelling Approach & Overview of the Included Studies

AUTHOR (YEAR)	MODELLING TECHNIQUE	MODEL STRUCTURE	INTERVENTION	COMPARATOR	TIME HORIZON	OUTCOMES	KEY FINDINGS
Atehortu (2018)	Cost-Effectiveness	Decision Tree Model	Diagnostic Strategies: IHC, MLPA, PCR, WB	All diagnostic strategies are compared with each other	<1 year	Total Cost, Total Effectiveness, ICERs	WB was cost-effective diagnosing strategy followed by IHC
Broomfield (2021)	Natural History Model	Markov Multi-state Model	Not Specified	Not Specified	NR	NR	22 years of survival (median)
Carlton (2018)	Budget Impact	NA	Deflazacort (new scenario)	No Treatment (base scenario)	3 years	Total costs (PMPM)	Deflazacort is a less costly alternative to no treatment
Landfeldt (2017)	Cost-Effectiveness	Markov-state Transition Model	Hypothetical Intervention	Standard of Care	Lifetime	Total Costs, LYs, QALYs, and ICER	An ICER of $2,223,758 (in 2023 USD)
Lin (2019)	Cost-Effectiveness	Partition Survival Model	Deflazacort Eteplirsen + Prednisone	Prednisone	Lifetime	Total Costs, LY's, QALYs, and ICER	The ICUR of Deflazacort is above accepted thresholds, thus it is not cost-effective
Lin (2019)	Budget Impact	NA	Deflazacort (new scenario)	Prednisone (base scenario)	5 years	Total costs (per patient), Budget Impact	The BI of Deflazacort resulted in an increase in budget of $66,489 (in 2023 USD)
Magnetta (2018)	Cost-Effectiveness	Markov-state Transition Model	Ventricular Assist Device Destination Therapy (VAD)	Medical Management	5 years	Total Costs, QALYs, and ICER	An ICER of $203,052 (in 2023 USD)
Quach (2019)	Cost-Effectiveness	Partition Survival Model	Deflazacort	Prednisone	Lifetime	Total Cost, Total QALY, ICERs	An ICER of $871,087/QALY gained (in 2023 USD)

Key: BI, Budget Impact; ICER, Incremental cost-effectiveness ratios; ICUR, Incremental cost-utility ratio; IHC, Immunohistochemistry; LYs, Life years; MLPA, Multiplex ligation-dependent probe amplification; NA, Not applicable; NR, Not reported; PCR, Polymerase chain reaction; PMPM, Per member per month QALYs, Quality adjusted life year; WB, Western blot; WTP, Willingness to pay

CONCLUSIONS

- DMD is a costly condition with an annual burden of over $40,000 per patient (2023 USD) in the US, which increases with age and disease progression.[4,5,6]
- Survey, claims, and registry data are the most utilized RWE sources for economic evaluations, while the Markov state-transition model is the most frequently used method for cost-effectiveness analyses for DMD.
- There is a scarcity of RWD-based evidence of DMD treatments, thus creating challenges for decision-makers to make informed decisions on the value of treatments.
- To provide the latest cost of illness estimates and evaluate budget impacts and cost-effectiveness more accurately, future economic assessments of DMD and other rare disease treatments based on real-world data are needed.

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