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REAL WORLD EVIDENCE ON THE BURDEN OF DISEASE FOR PATIENTS AND THEIR NEAREST RELATIVES – THE CASE OF DUCHENNE MUSCULAR DYSTROPHY

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BACKGROUND

- Duchenne Muscular Dystrophy (DMD) is a progressive genetic disease with a prevalence of 1 per 3,600–6,000 male births.[1,2] Incidence in Denmark is around 6 male births per year.
- Early symptoms manifest as muscle weakness, difficulties to raise from floor, run and climb stairs. Cognition and language development are often affected as well.[3]
- Patients are typically diagnosed at age 4-7 years, will become permanent wheelchair users in their early teens, and often need respiratory aids by their mid to late teens, as well as many will have behavioral and learning difficulties.[4]
- DMD patients have a median survival age of about 30 years and impaired quality of life.[5-9]
- There is no curative treatment of DMD, but standard treatment, incl. corticosteroid, have improved life expectancy.[4]
- Previous studies on the burden of disease of DMD have had survey-based approaches, while a recent review concluded that register studies are necessary to improve evidence of disease development over time as well as information on impact on close relatives.[10,11]

OBJECTIVE

- The aim of the study was **to assess the burden of disease of DMD in Denmark**, i.e. incidence and prevalence, healthcare utilization, labour market participation, educational outcomes, and overall attributable costs due to DMD.
- Impact on the DMD disease on the closest relatives (siblings and parents) was also investigated.

METHODS

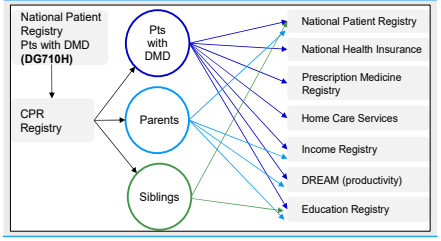
STUDY DESIGN AND DATA SOURCES

- Using comprehensive Danish national registers DMD patients (ICD10: G71.0H) were identified in the National Patient Register (1994-2021).
- Parents and siblings were afterwards identified in the Central Person Register.
- Data from a number of national registries were combined for the study analyses (Figure 1).
- Outcomes of patients, parents and siblings were each compared to matched control groups (1:10) drawn from the general Danish population. Matching criteria were age, sex, region of residence at diagnosis, parents' education and employment status.
- Outcomes included incidence, prevalence, healthcare utilization, comorbidities, surgeries, labour market participation, educational outcomes, and attributable costs due to DMD.

STATISTICAL ANALYSIS

- Participants were followed up to five years before occurrence of the DMD diagnosis (Jan 1994) and potentially 20 years after diagnosis, unless death, emigration or end of follow-up occurred first (latest December 31 2021).

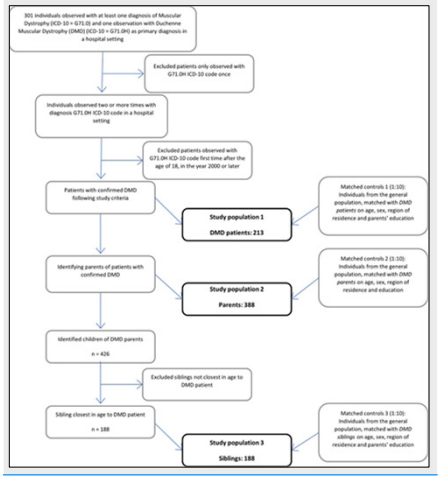
Figure 1. National Danish registers included



RESULTS

- Data on 213 unique DMD patients (2,106 matched controls), 388 parents (3,800 matched controls), and 188 siblings (1,879 matched controls) were included (Figure 2).
- Median age at diagnosis was 6 years (IQR:4-10).
- The prevalence of DMD is increasing with incidence having a stationary trend (6.5 new cases per year (median)).

Figure 2. Flowchart of study populations



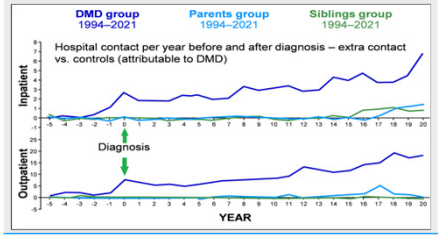
CLINICAL OUTCOMES

- Mortality: DMD patients had 23.3 times higher mortality hazard compared to matching controls.
- Mean age at dead was 26.8 years (IQR: 19-34).
- Ventilation and assistive devices: 73% of the patients were found to have respiratory failure and 67% were dependent on assistive devices such as respirator or wheelchair.
- Mean age at first respiratory therapy was 15.3 years (141/213 pts), and 23.2 years for in-home mechanical ventilation (127/213 pts).
- Surgery: Most frequent surgery for DMD patients were scoliosis (38%) or Achilles tendon surgery (29%).

COSTS OF DMD

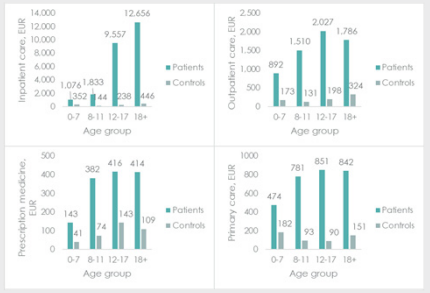
- Hospital contacts were significantly higher for DMD patients two years before/after diagnosis versus controls leading to 60 extra hospital admissions and 200 extra outpatient visits 20 years post-diagnosis (Figure 3).

Figure 3. Hospital contacts per year due to DMD



- Healthcare costs of DMD patients compared to controls increased with age (Figure 4).

Figure 4. Age-related costs per year (Euros (€))



- 20 years following DMD diagnosis the total direct extra healthcare costs due to DMD were € 1,524,000 per average DMD patient.
- Labour market: Productivity loss was € 20,200 annually for DMD patients, whereas no difference were found for parents and siblings.
- Education: Both DMD patients and siblings had lower school grades and required more special education than controls. For patients, the costs of this was € 180,900 (11 years school period).
- Total attributable costs due to DMD: For a DMD patient reaching the age of 30 this total extra cost due to DMD becomes €2,365,800.

CONCLUSIONS

- DMD patients use of healthcare services and attributable costs due to DMD significantly increased over time and with progression.
- A conservative estimate - personal assistants and production loss from short term sick-leave and premature death not included.
- Signs of a burden for parents and siblings – particularly for siblings having lower school grades, more sick-leave and unemployment.

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DISCLOSURE OF INTEREST

JV has acted as advisory board consultant or speaker for Amicus Therapeutics, argenx BVBA, Arvinas, Atamyo Therapeutics, Biogen, Dyne Therapeutics, Fulcrum Therapeutics, Horizon Therapeutics, Lupin, ML Biopharma, Novartis Pharma AG, Regeneron, Roche, Sanofi Genzyme, Sarepta Therapeutics, UCB Biopharma SPRL and Pfizer, and received research grants, travel support and/or speaker fees from Alexion, AstraZeneca Rare Disease; Edgewise Therapeutics; Fulcrum Therapeutics; Sanofi Genzyme; and UCB Biopharma SPRL. *APB* has acted as advisory board member or speaker for Biogen, Novartis, Novartis Gene Therapies, Roche and Pfizer, and has received speaker honoraria from Roche. *JHR* and *JO* are employees of EY Denmark and acted as paid vendor on behalf of Pfizer Denmark Aps. *MS* and *PBP* are employees of Pfizer Denmark Aps., and both own shares in Pfizer Inc. *UW, CO,* and *NI* have no conflict of interest to report.

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