

# Project HERCULES - Burden of steroid use in the treatment of Duchenne Muscular Dystrophy: findings from patient and carer dyads and a focus group

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Project HERCULES is an international multi-stakeholder collaboration led by patient organisation Duchenne UK that is developing disease-level tools and evidence to support HTA and access decisions for new treatments for Duchenne Muscular Dystrophy.


**Background**

- Duchenne Muscular Dystrophy (DMD) is an X-linked, recessive, genetic disorder caused by a mutation in the dystrophin gene, resulting in a deficiency of dystrophin protein.<sup>1,2</sup> This deficiency causes progressive muscle-weakness, first affecting the proximal muscles in the hips and shoulders, before eventually affecting all muscles associated with movement, as well as those involved in cardiac and respiratory function.<sup>1,2</sup>
- There are currently no curative treatments for DMD, and treatment is limited to progression management. Corticosteroids are often used as part of a multi-disciplinary approach, and have been shown to slow the loss of muscle strength, reduce the development of scoliosis, and delay the onset of cardiac and respiratory problems.<sup>2,3,4</sup> However, despite the benefits, there are significant adverse effects associated with the long-term use of steroids including mood changes, weight gain, cushingoid appearance, delayed puberty, and loss of bone strength/ mass.<sup>4,5</sup>
- Previously a targeted literature review and an online patient/parent survey explored the impact of using long-term, high-dose steroids for the management of DMD on patient and parent health-related quality of life (HRQoL), carer burden, and resource use.<sup>6</sup> Here we present qualitative research representing a continuation of this work.

**Objectives**

To perform interviews followed by a focus group, to gather qualitative evidence from patients and their parents on the impact of long-term, high-dose steroid use side effects in DMD, including patient and parent HRQoL impact, personal carer burden, and health service utilisation.

This study was conducted as part of Project HERCULES.



**Methods**

- Six families (parent and son) took part in the research, two patients in the ambulatory DMD health state, two patients in the transfer health state (non-ambulatory but able to support own weight), and two patients in the non-ambulatory health state. Purposive sampling was utilised to ensure representation across all health states, a broad age range, and a blend of mothers and fathers. The demographics of each patient are summarised in **Table 1**.
- The research was split into two phases, the interviews in phase one and the focus group in phase two. An overview of which participants attended the interviews, and the focus group is included in **Figure 1**.
- The topics for discussion in the two dyads and the small group interview were determined based on questionnaires issued to the participants ahead of the interviews. Transcripts were produced for each interview in phase one and explorative thematic analysis of these transcripts determined the topics for discussion at the focus group in phase two (**Table 2**). In all sessions there was opportunity for patients, parents, and health-care professionals to add additional topics they felt should be discussed.
- The opinions on each discussion topic were attained from attendees at the focus group, and further analysed using the explorative thematic analysis approach, resulting in a narrative on the burden that each theme has on the daily lives of people with DMD and their family, with illustrative quotes derived from patient, parent, and health-care professional perspectives.

**Table 1 Patient demographics**

DMD health state	Ambulatory		Transfer		Non-ambulatory	
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age	13 years	8 years	14 years	14 years	24 years	16 years
Time on steroids	8 years	3 years	9 years	10 years	17 years	10 years
Current steroid regimen <sup>a</sup>	Daily deflazacort	Daily deflazacort	10 days on 10 days off	Daily	Daily	Deflazacort
Parent in study	Mother	Father	Mother	Mother	Mother	Father

*Abbreviations: DMD, Duchenne Muscular Dystrophy.*  
*a Current steroid regimen was provided as free text in the questionnaires and therefore it varied how much detail was provided by participants.*

**Table 2 Focus group discussion topics**

Emotional outbursts and behaviour
Anxiety and mood
Broken bones
Sleep and daytime tiredness
Physical appearance
Delayed puberty
Gastrointestinal issues
Caregiver burden and adrenal crisis
Additional resource use (monitoring, psychological support, medication)

**Figure 1 Overview of the two phases of interviews**

**Phase one**

- Small group interview** n=4  
Two patients in the ambulatory HS and their parents (one mother and one father)
- Dyad 1** n=2  
Two patients in the transfer HS
- Dyad 2** n=2  
Two mothers of patients in the transfer HS

**Phase two**

- Focus group**  
Two healthcare professionals  
Two patients in the non-ambulatory HS  
Two parents of patients in the non-ambulatory HS  
One Duchenne UK representative

*Abbreviations: HS, health state.*

**Results**

Five of the most prominent themes from the focus group are summarised in **Figure 2**, with illustrative quotes from attendees across the interviews and focus group.

**Figure 2 Overview of the most prominent themes arising from the focus group**

**Physical appearance**  
“...I was bullied about my weight...people called me fat and were not very nice in general...[patient]”

- Physical appearance was a topic of high concern to both patients and parents and impacted on other areas including mental health, usual activities, and ability to “fit-in” socially.
- Main concerns were weight gain, short stature, and cushingoid appearance, all contributing to patients looking younger than their peers, which often resulted in them being treated differently.

**Delayed puberty**  
“...it’s very slow...he wants to be 5 foot 5 and look like a normal teenager and he’s never going to be because of steroids...[parent]”

- Corticosteroids taken long-term can delay puberty, leading to a multitude of physical and mental complications.
- Testosterone is prescribed by some clinicians to induce puberty but parents reported that this is highly variable however existing neurodevelopmental conditions may be a factor in how a child responds emotionally and behaviourally when starting corticosteroid treatment.
- Patients reported that delayed puberty made them feel self-conscious and socially-isolated.

**Adrenal crisis**  
“...(A&E) are unlikely to know so that is very stressful as a caregiver, children in our community have died because of adrenal failure...[parent]”

- Patients taking long-term, high-dose corticosteroids are unable to produce heightened levels of cortisol required during times of physiological stress risking adrenal crisis, a life-threatening situation.
- Parents found this a huge burden as often emergency services are not trained to recognise the symptoms. Furthermore, schools may not be able to administer the injection and, instead, have to wait for a paramedic to arrive, meaning parents felt a need to always be near-by in case their child was injured/ ill so that they could explain the risks and make sure that the appropriate care was provided.

**Mood and behaviour**  
“...I get a lot of anxiety and a lot of the time you just feel really low about everything...[patient]”

- Some of the parents felt that after starting steroids their child’s behaviour changed drastically, with one parent describing it as the biggest burden they had experienced as a caregiver. HCPs reported that this is highly variable however existing neurodevelopmental conditions may be a factor in how a child responds emotionally and behaviourally when starting corticosteroid treatment.
- Several patients reported suffering with anxiety and low mood, however it is very difficult to ascertain how much is attributable to their condition, and whether taking a steroid exacerbates this or not. Both families and HCPs said there is not enough specialist psychological support available.

**Bone density**  
“...the osteoporosis that’s caused by steroids is really quite devastating...[parent]”

- Long-term corticosteroid use can reduce bone density leading to an increased risk of bone fractures. Both patients and parents reported this as being of high concern as it was linked to increased risk of adrenal crisis and worries over not being able to walk again and becoming non-ambulatory sooner.

*Abbreviations: A&E, accident and emergency (hospital department); HCP, health care professional.*

**Conclusions**

- This qualitative research describes the burden of side-effects associated with long-term steroid treatment in DMD in relation to patient HRQoL, personal carer burden, and health care resource use.
- The data presented here emphasises the importance of understanding the priorities of patients and their families when making clinical decisions on treatment pathways, and highlights a requirement for increased dissemination of patient experiences to assist families in making decisions about their child’s future.
- These data provide valuable insights into the patient, carer, and health service burden associated with steroid use in DMD, as well as a basis for further research and data collection to quantify the impact of steroid side-effects on patient and parent HRQoL (e.g. through supporting the construction of vignettes for utility elicitation), and health service resource use. Ultimately, both the qualitative evidence generated, and further quantitative data, can be utilised in HTA submissions and economic modelling, to support the value proposition for new alternative therapies for DMD.

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