Original research

Observational study of changes to glucocorticosteroid prescribing patterns in duchenne muscular dystrophy in the UK over the last decade

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ABSTRACT

Background Glucocorticosteroids (GC) are standard-of-care treatment for most boys with duchenne muscular dystrophy (DMD). GC use has changed over time with evolving evidence, and we describe GC patterns, dosing and side-effects in the UK over 11 years.

Method NorthStar data from 2012 to 2022 were analysed to understand GC type, regime and starting age. GC dose with age, patterns of GC switching and side-effect profiles by type and regime were also analysed. Participants attributed to 'other' regimes were queried and details were included.

Results Data on GC usage were available for 1117 boys, across 6905 observations, with 74% of boys GC treated. Prednisolone was the most common regime in the period (65% of assessments) but deflazacort prescription has increased (17% in 2012 and 43% in 2022). Daily regimes were more common (66% of assessments), and the incidence of intermittent (10 days on/10 days off) regimes has declined (46% in 2012 and 26% in 2022). Older participants were more commonly on less than recommended doses, and this was more common in those on deflazacort or daily regimes. Gastrointestinal symptoms and cushingoid features were more common in those on deflazacort than prednisolone, while increased appetite, cushingoid features, gastrointestinal symptoms and insomnia were more common in those on daily than intermittent regimes.

Conclusions The use of deflazacort and daily regimes has steadily increased across the UK North Star Network in the last decade. This study provides one of the largest up-to-date real-world set of data of evolution in prescription patterns and the occurrence of side-effects in different groups of GC-treated DMD.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ While the majority of boys with duchenne muscular dystrophy in the UK are treated with glucocorticosteroids (GC), there is variability in the type, regime and dose prescribed, particularly since the last audit in the UK 11 years ago. Differential GC side-effects have also been observed by GC type and regime.

WHAT THIS STUDY ADDS

⇒ In the UK, deflazacorts and daily prescriptions are increasing with time, although prednisolone still remains the most commonly prescribed GC type, while dose per kilo tends to fall below recommended levels as boys get older.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This work provides useful insights for clinicians on GC prescriptions, side-effects and dosing, which can help inform clinical decision-making given changing GC availability.

INTRODUCTION

Duchenne muscular dystrophy (DMD) is a progressive X-linked recessive neuromuscular disorder caused by *dystrophin* gene mutations.[1 2] This results in decreased dystrophin protein, which helps maintain the structure and function of myofibres.[3 4] Typically, boys with DMD are diagnosed by age 5 years with delayed motor development and proximal muscle weakness, achieve a peak motor ability by age 7 years[5–7] and, if untreated, lose ambulation at age 9.5 years.[8] In the second decade of life, young men with DMD develop orthopaedic, respiratory and cardiac complications, which lead to premature death.[9 10]

Despite continuous therapeutic developments, including the approval of Ataluren,[11] exon skipping therapies[12–14] and gene therapies[15] in some countries, glucocorticosteroids (GC) represent the standard-of-care (SoC) treatment for the majority of boys with DMD.[3] Predominantly, deflazacort or prednisone (or its active metabolite prednisolone) are prescribed, and there are several typical treatment regimes, such as daily, intermittent (such as 10 days on, 10 days off or 10 days on and 20 days off), alternate day and weekend only, which are popular in different regions and countries,[10 16 17] with the participants in the UK prescribed with daily or intermittent (10 days on and 10 days off) regimes.

In boys with DMD, GC use improves muscle strength and function, including delaying loss of ambulation.[8 10 18 19] However, differential efficacy by GC type and regime has been reported in observational studies,[20 21] and the recent 3-year FOR-DMD randomised control trial of GC in DMD found that daily regimes, whether prednisolone or deflazacort, increased motor function outcomes significantly more than intermittent prednisolone.[22]

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There is limited efficacy data available for other GC regimes: a small, short-term trial showed weekend-only high-dose prednisolone was as effective as daily prednisolone (over 12 months),[23] while alternate day prednisone was shown to induce short-term, non-sustained muscle function gains, with a similar volume of side-effects as in the daily regime.[24] Earlier GC initiation is associated with slower functional decline,[10] later loss of ambulation[25] and an increased risk of growth-related side-effects.[26] Consequently, the SoC recommend starting treatment 'before significant physical decline', when the motor function benefits outweigh their side-effects.[3]

Chronic GC use is associated with several side-effects, including stunted growth, excess weight gain, behavioural difficulties, osteoporosis and endocrine complications such as delayed puberty, increased blood pressure and glucose intolerance. Natural history studies have shown differential side-effects by GC type. Compared with prednisolone, deflazacort-treated participants experienced higher frequencies of growth delay, cushingoid appearance and cataracts.[20 27] Prednisolone is associated with greater weight gain than deflazacort,[18 22] and daily prednisolone regime has been shown to have the greatest effect on increasing BMI.[28]

The side-effects of traditional GC have driven research into the new generation steroids and has led to the development of the steroid analogue vamorolone for use in DMD. Vamorolone has been shown to have similar motor function efficacy over 3 years to prednisolone and deflazacort.[29 30] Vamorolone-treated patients display a differential side-effect profile, with observed linear growth and lack of decline in bone turnover markers compared with those on daily prednisolone.[31]

Aims

This paper aims to describe how the prescribing patterns of GC for DMD have changed in the UK's NorthStar cohort over the last decade with regards to type, regime, dose prescribed and age of initiation. This will provide an update on the last large-scale description of prescribing trends in the NorthStar network which was published 11 years ago.[10] We also describe patterns of participants who switch GC type or regime, and the prevalence of selected GC side-effects in the NorthStar cohort.

METHODS

This retrospective study examined GC prescribing trends and side-effects, for boys with DMD in the UK, by analysing data routinely and prospectively collected as part of their clinical care and entered in the NorthStar database between 2012 and 2022.

The Northstar database

The NorthStar database was established in October 2006 to collect longitudinal data from children with confirmed diagnosis of DMD across all 24 paediatric neuromuscular centres in the UK.[28] Neuromuscular clinicians complete standardised medical and physiotherapy forms at 6-monthly standards of care clinical appointments, in line with the international care recommendations for DMD.[3] Conditional on obtained informed consent, clinical data are recorded on an electronic database managed by Certus Ltd[32] and the NorthStar project has been given the approval of the local Caldicott Guardian.

Within the NorthStar database, participants are classified as on-GC or off-GC, with options to record GC regime (daily, intermittent (10 days on and 10 days off) or other), type (prednisolone or deflazacort) and dose. The recorded GC-related side-effects include objective clinical evaluations (ie, weight, height, blood pressure, bone density measurements, presence of vertebral fractures, cataracts, cushingoid features, hirsutism and acne pubertal status and glycosuria) and adverse events reported by the families/boys and logged by the doctor as mild, moderate or severe (including behavioural changes, sleep difficulties, gastro-oesophageal reflux disease, increased appetite, immune suppression and gastrointestinal (GI) symptoms) which were discussed and agreed at national consensus meetings at the formation of the network.[10] This paper analysed data for on five side-effects which were more well captured using the ordinal data modality: changes to appetite, behavioural changes, cushingoid features, sleep difficulties and GI symptoms (dyspepsia, in particular a burning pain in the stomach, peptic ulcer disease and oesophagitis).

Patient population

NorthStar database observations between 1 January 2012 and 1 January 2023 were considered for the analysis, yielding 1618 participants across 13 569 observations. Only boys aged <18 years recorded with a confirmed diagnosis of DMD (as opposed to those with becker muscular dystrophy, intermediate muscular dystrophy or manifesting carriers) were included in this study. Duplicate observations were classed as assessments taken on the same day for the same patient, and in these cases the assessment with the higher amount of missing data was removed. All assessments after a participant recorded as on a trial (which were assumed to be interventional) were removed. Details of the data cleaning, which was consistent with previous works,[7 28] and the final patient population are shown in figure 1.

Covariates

The 'first GC prescribed' was the first GC type and regime recorded within 1 year of the reported GC initiation date. For the recorded GC type/regime, if participants were recorded as on the same GC type/regime at two separate time points, and this information was missing at all intermediate time points, the type/regime was imputed under the assumption that there was no change.

The dose in mg/kg was calculated using the dose (mg) field divided by weight, and if either field was missing the dose per kg field was used. Weights recorded as below 2 kg, or above 200 kg were discarded. The recommended dose per kg is 0.75 mg/kg for prednisolone and 0.9 mg/kg for deflazacort,[3] which are equivalent to 3 mg/kg hydrocortisone.[33] Dosing was considered 'correct' if participants were recorded as receiving at least 66% of the recommended dose using the most generous definition in the SoC.[3] For the participants reported to be on an 'other' regime, further information was sought from their local neuromuscular centre about the prescribed regime.

Statistics

For each of the continuous variables, the median and IQR are presented, while for discrete variables the number of participants (N) or the number of assessments (M), and the corresponding proportions are presented. To compare the prescribing patterns in 2012 to those in 2022, the first prescribed versus all-time prescribed GC, those on correct dose by GC type and regime, and the differential rate of side-effects, a χ^2 test with Yates' continuity correction was used. To compare the difference in GC initiation age and time between diagnosis and initiation in 2012 and 2022, a t-test was used.

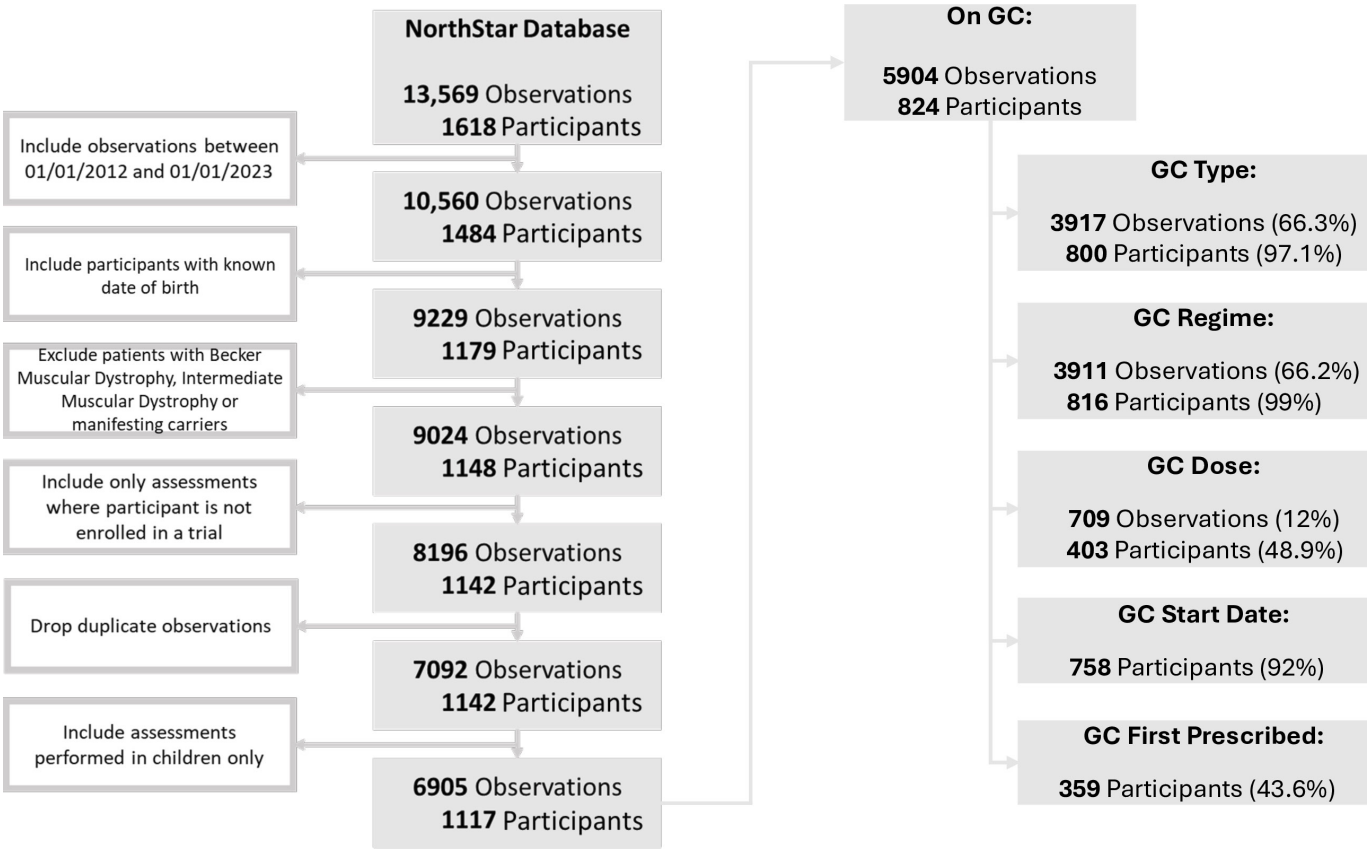

Figure 1 Data cleaning and summary of GC data completeness. GC, glucocorticosteroids.

RESULTS

The inclusion criteria detailed in figure 1 resulted in a cohort of 1117 participants spanning 6905 observations. On average, participants were recorded across 6 (range: 1–21) visits. Within this cohort, 824 (74%) participants were recorded on GC treatment, across 5904 assessments. The remaining 293 participants were GC naïve, or with no recorded GC information across all their observations. The completeness of the data is described in figure 1. For most participants, GC type and regime were recorded in at least one visit.

GC prescription in the NorthStar network

Type and regime across all time points

The cross-tabulation of GC types and regimes at all time points and first visit after GC initiation is presented in table 1. During at least one observation, 318 (40% of the 800 participants who ever had a GC type documented) were recorded as on deflazacort and 557 (70%) as on prednisolone. During at least one observation, 547 (67% of the 816 participants who ever had a GC regime documented) were recorded as on daily GC, 365 (45%) on intermittent GC, and 79 (10%) on 'other' regime. Of the 824 participants ever recorded as on GC treatment, 75 (9%) are recorded as being on different GC types and/or regimes at different times—these participants are described as 'switchers'. We note here that participants who switched GC type or regime are recorded in each category, so some participants are recorded more than once.

GC type and regime at initiation of treatment

The date of initiation of GC treatment was available for 758 participants (92%). Data for GC type and/or regime at their first appointment (or within 1 year of starting GC) was available for 209 participants (25%). For some participants, the GC type but not the regime was recorded, or vice versa. There was no significant difference ($p=0.143$) in the proportion of participants prescribed prednisolone at all times (65%) versus at the first visit (70%). However, there was a significant difference in the GC regime; the daily regime was the first regime prescribed in 39%, and across all time points in 67% of observations where a GC regime was recorded ($p<0.01$).

Table 1 Number of participants recorded in at least one observation on each type and regime, across all time points and at first visit

All visits					
	Daily	Intermittent	Other	Unknown	Total
Deflazacort	250	93	22	35	318
Prednisolone	331	270	52	62	557
Unknown	60	42	11	–	108
Total	547	365	79	95	824
First visit					
	Daily	Intermittent	Other	Unknown	Total
Deflazacort	29	29	2	0	60
Prednisolone	49	88	4	2	143
Unknown	3	2	1	–	6
Total	81	119	7	2	209

Note here switchers are recorded across multiple types/regimes and as such the row totals/ column totals do not add up.

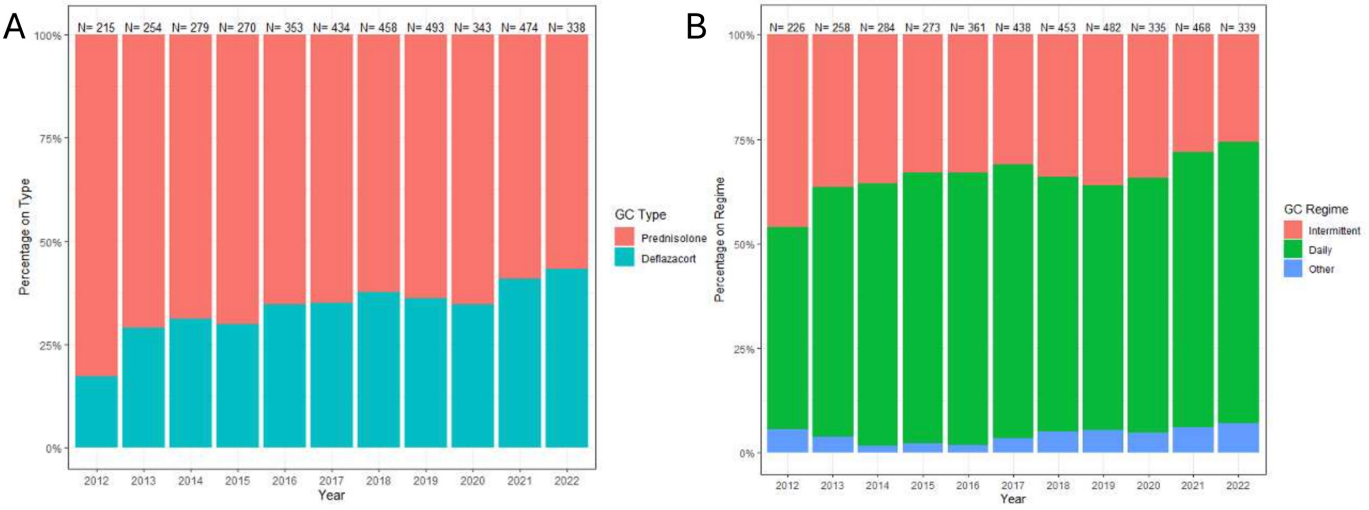

Figure 2 Changes in (A) type and (B) regime of GC prescribed over time. GC, glucocorticosteroids.

Trends in GC prescription in the NorthStar database

While in 2012 deflazacort was reported in 17% versus prednisolone in 83% of the records, in 2022 this number was significantly higher ($p<0.001$) (43% were prescribed deflazacort vs 57% prednisolone). The proportion of visits where patients were on daily regimes has increased significantly over the study period (48% in 2012 vs 67% in 2022, $p<0.001$), while the proportion on intermittent regimes fallen (46% in 2012 vs 26% in 2022). The number of observations recorded as 'other' regimes has remained stable (6% in 2012, 7% in 2022). This is shown in figure 2.

'Other' regimes

Of the 79 (10%) participants recorded as being prescribed 'other' regimes, the largest cohort of these was on the alternate-day regime (43, 5%). Additionally, 3% of participants were recorded as 'other' in error, with the majority of these participants on the daily regime. Other reported patterns included the first 10 days of the month (intermittent 10–20, 0.4%), alternating a high and low dose (2, 0.2%), and weekends only (2, 0.2%). The full breakdown of 'other' regimes is given in online supplemental table S1.

GC dose prescribed

GC dose information was available for 49% of participants, but only 12% of observations. Participants tended to be on a lower-than-recommended dose with increasing age, with a peak of participants on the recommended dose in the 4–7 years group, followed by a progressive decline. Those on deflazacort were more often on a lower than recommended dose for their body weight compared with those on prednisolone ($p<0.001$, figure 3A), while those on daily regimes were more commonly on lower than recommended doses per kg than those on intermittent ($p<0.001$, figure 3B).

Age at initiation of GC treatment

Across the whole cohort, the median GC starting age was 5.71 years (IQR: 4.87–6.83). The spread of GC starting age has increased with time: the median GC starting age was 5.68 years (IQR: 4.95–6.58) in 2012 and 6.86 years (IQR: 6.27–7.074) in 2022, as shown in figure 4A. Notably, there are fewer recorded GC starting ages in recent years, which may be due to increasing data quality with age or recruitment of younger boys into clinical trials. However, the time between diagnosis and GC treatment has decreased from 2.11 years (IQR: 0.95–3.37) in 2012 to 0.47 years (IQR: 0.24–1.94) in 2022, as shown in figure 4B, although these were not significantly different ($p=0.069$).

Side effects

The increased appetite, behavioural changes, cushingoid features, GI symptoms and insomnia GC side-effect fields were completed in 49% of assessments. There was no significant difference in the rate of completing the side-effects fields across the GC types and regimes ($p=1$ for all). There was also no significant difference in the rate of completing side-effects fields between participants recorded as on the optimal dose versus those not on the optimal dose (appetite, $p=0.591$; behavioural changes, $p=0.142$; cushingoid, $p=0.691$; GI symptoms, $p=0.703$; insomnia, $p=0.276$). The frequency of individual side-effects in relation to GC type and regime is reported in table 2.

There is a significantly higher rate of reporting of cushingoid appearance, GI symptoms and insomnia in the prednisolone group compared with the deflazacort group, while there is a significantly higher rate of reporting side-effects of increased appetite, cushingoid appearance, GI symptoms and insomnia in the daily than intermittent regime.

Switchers

The switching patterns in this cohort are described in table 3. In total, 75 participants were recorded as switching GC type, with the majority of participants switching from prednisolone to deflazacort (87%). Additionally, 167 participants are recorded as switching GC regime, with the majority of participants switching from the intermittent to daily regime (54%).

DISCUSSION

Our study provides insights into how GC prescribing patterns in DMD have evolved over the past decade in the UK. In keeping with recent international studies, we showed an increase in deflazacort prescriptions in recent years, accounting for nearly half of all GC prescribed in 2022. This is likely due to the reported side-effect profile of deflazacort, including milder weight gain than prednisolone.[18 20] Additionally, some observational studies report a later loss of ambulation in deflazacort-treated boys compared with prednisolone treated,[20] although this could be caused by the more recent availability of deflazacort.

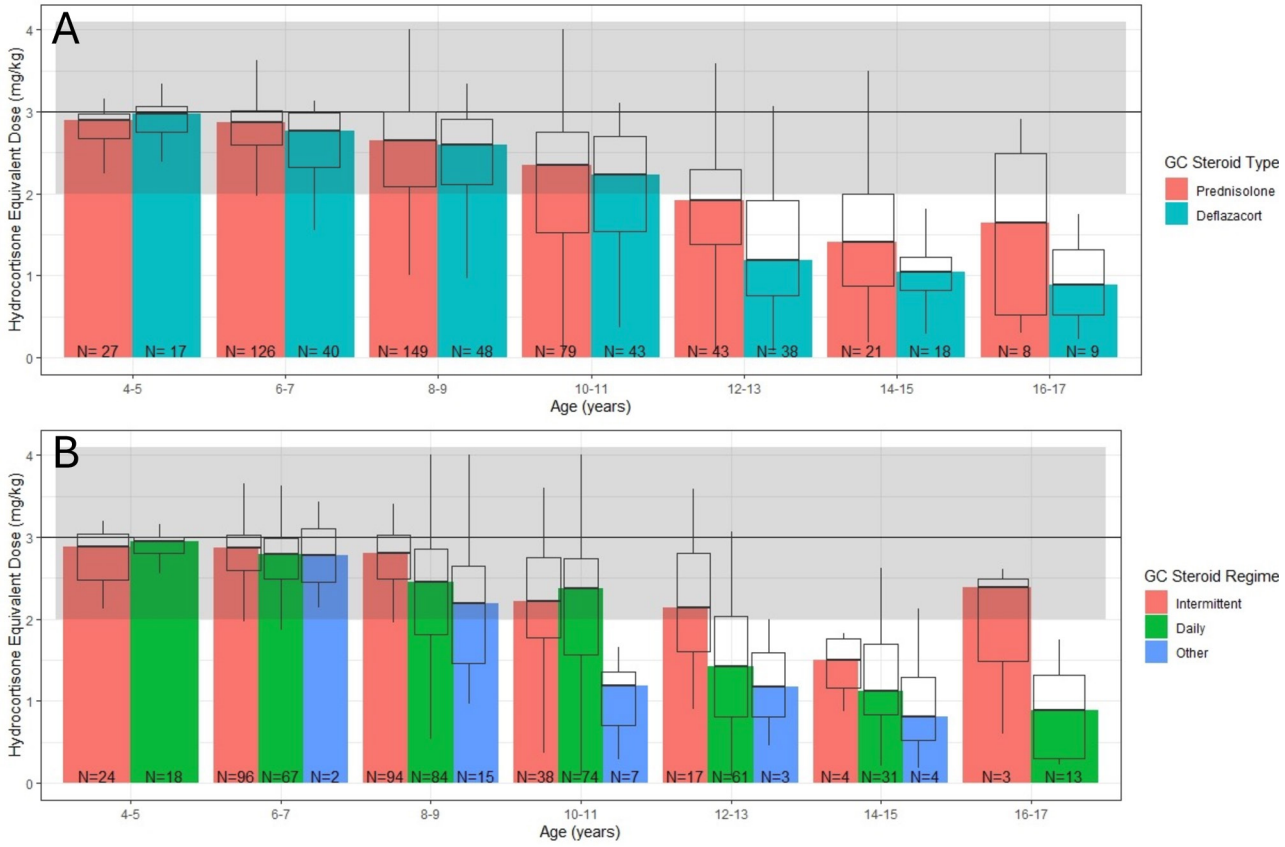

Figure 3 Hydrocortisone equivalent dose of GC prescribed by age and GC regime. GC, glucocorticosteroids.

Over the last decade, intermittent regimes have become less common, likely due to increasing evidence that daily regime being associated with a delay in loss of ambulation compared with intermittent.[10] For example, the results of the FOR-DMD[22] study support earlier observational studies which showed that daily prednisolone and deflazacort regimes have increased efficacy on motor function compared with intermittent prednisolone,[32] which may lead to even lower rates of intermittent regimes in the future. Nevertheless, several studies have shown that intermittent GC may reduce side-effects compared with daily regimes,[10 22 28] and this might be the reason why this regime is still relatively common in clinical practice.

Our study found that the first recorded GC regime was more commonly intermittent, while the daily regime was most common overall, leading to intermittent to daily switching. However, recent findings from the FOR-DMD study support the use of a daily regime over intermittent as initial treatment for boys with DMD. Discussion is regularly held across the North-Star network on how to best counsel families about long-term safety and efficacy data when proposing GC initiation, but also on how to maintain an individualised approach based on individual response, side-effect profile and family's preferences.

Overall, unlike previous international cohort studies[17 20] which were based on data collected prior to or shortly after the introduction of the original SoC,[34] our study reports few patients on regimes other than daily or intermittent (10 days on/10 days off). When we investigated further about the small group of participants recorded to be on 'other' regimes, they were found to be mainly on alternate-day regimes.

When considering the long-term benefits of GC and the comparison between deflazacort and prednisolone, one of the challenges is the impact that underdosing can have on the interpretation of clinical outcomes. It is likely that variability in GC dosing contributes to the heterogeneity of disease progression trajectories in DMD, and some trials now specify a minimum dose and exposure to GC for inclusion. We found that younger participants (<8 years) were mostly prescribed the recommended dose (0.75 mg/kg prednisolone, 0.9 mg/kg deflazacort and 3 mg/kg hydrocortisone equivalent), while older participants were often on lower than recommended doses (<2 mg/kg hydrocortisone) of both deflazacort and prednisolone. This is likely related to a lack of dose increasing in line with weight or increasing side-effects with age leading to a clinically indicated reduction in dose, while changes in dosing after loss of ambulation may also occur. It is still unclear if the decline in function observed in the later stages of DMD is linked to lower than recommended doses, and what the impact of stopping GC at transition to adult services is long term. Further research into this area is needed to understand the benefit of maintaining patients on the target GC dose into adulthood.

Initiating GC soon after diagnosis would be in keeping with the DMD SoC[3 34] which advice early GC initiation before deterioration in function. In our study, we showed that the median age of GC initiation and the spread of ages when GC are initiated has fluctuated over the 11-year study period, with the age of initiation increasing in the last 2 years. However, there were no significant differences between GC starting age and time between diagnosis, and the trend is not significant. The reasons for this are unclear at this stage; however, there are multiple aspects that could be contributing to this fact. It may be that delays in diagnosis, due to COVID-19 or other reasons, or relocation from other countries may have led to later GC initiation

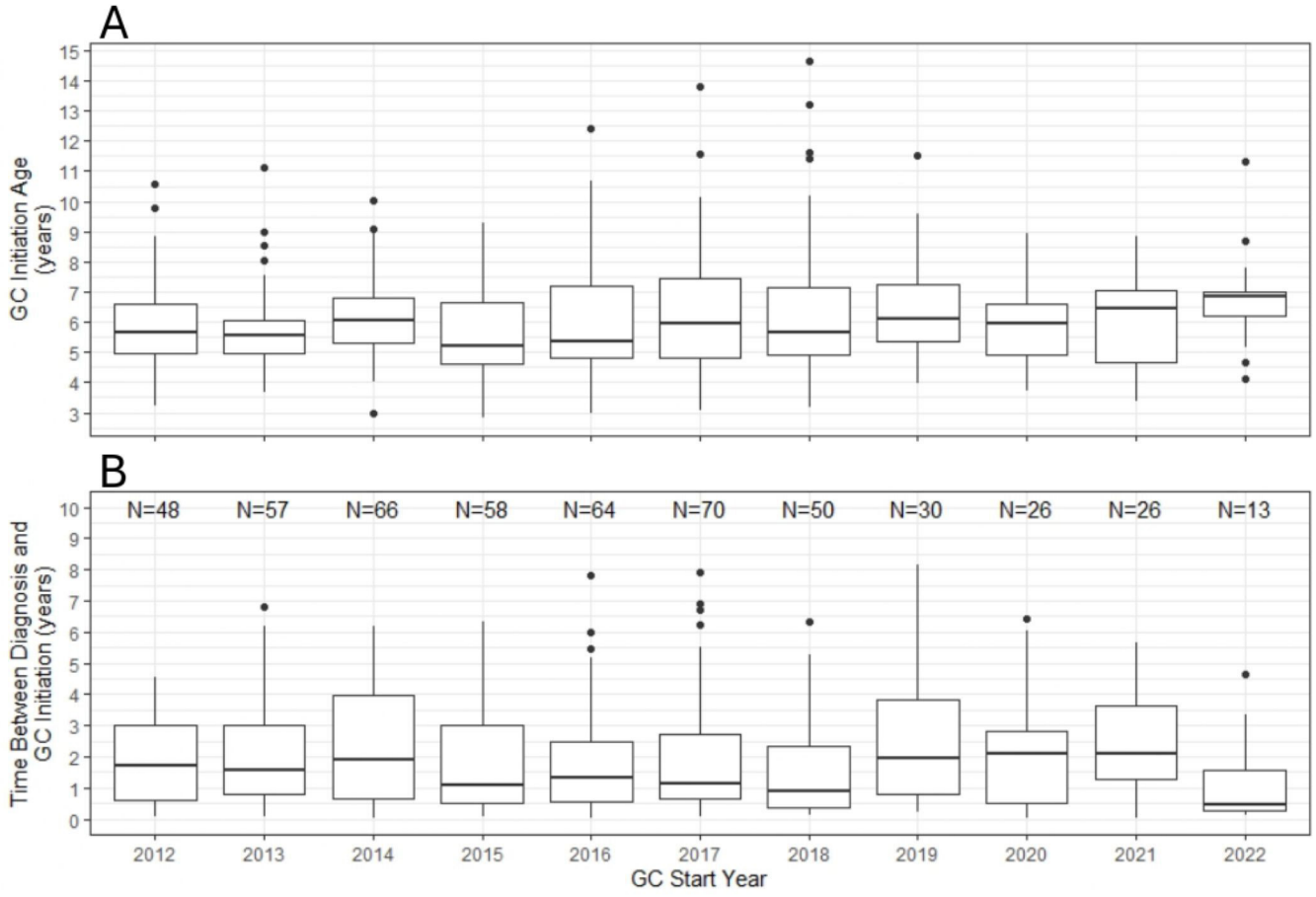

Figure 4 Trends in GC start age and time to treat by year. GC, glucocorticosteroids.

in patients who in other circumstances may have started earlier. Alternatively, increasing initiation at older ages due to increasing evidence of the benefit of GC in older ambulant and non-ambulant boys may have skewed the data. Additionally, this study excluded those participants who were included in trials, and as trials often target younger boys, it may be that the patients who initiated GC younger were more likely to be enrolled and therefore unobserved.

We investigated the occurrence of five GC side-effects: increased appetite, GI symptoms, behaviour changes, cushingoid features and insomnia. Participants on daily regimes had higher rates of increased appetite, GI symptoms, cushingoid features and insomnia compared with those on intermittent regimes. These findings are consistent with previous findings, which identified a higher, non-significant, reporting rate of increased appetite and a significantly higher rate of GI symptoms, cushingoid features and insomnia in those on daily prednisolone compared with intermittent prednisolone.[10] The deflazacort group reported significantly more GI symptoms, cushingoid features and insomnia than those on prednisolone. These findings are partly consistent with previous studies[8 18] and can provide further guidance to clinicians when discussing GC options and associated side-effects with participants and their caregivers.

The differential profile of GC on weight gain, height stunting, delayed puberty, bone density, fractures and hypertension in DMD is also of key interest; however, the complexity of these

Table 2 Rates of side-effect reporting by GC type

	Increased appetite		Behavioural changes		Cushingoid features		GI symptoms		Insomnia	
	Prednisone	Deflazacort	Prednisone	Deflazacort	Prednisone	Deflazacort	Prednisone	Deflazacort	Prednisone	Deflazacort
None	49.1%	52.2%	59.8%	57.8%	44.3%	32.2%	90.5%	85.3%	84.1%	79.6%
Mild	31.9%	28.3%	26.4%	26.2%	36.8%	36.4%	7.9%	13.3%	11.2%	15.7%
Moderate/severe	18.9%	19.4%	13.8%	16.0%	18.9%	31.4%	1.5%	1.4%	4.7%	4.7%
Difference by type (p value)	0.134		p=0.264		p<0.001		<0.001		0.004	
	Intermittent	Daily	Intermittent	Daily	Intermittent	Daily	Intermittent	Daily	Intermittent	Daily
None	53.7%	48.6%	57.3%	59.4%	62.9%	28.2%	92.4%	86.7%	85.5%	81.3%
Mild	29.8%	31.1%	28.9%	25.4%	29.1%	40.2%	6.7%	11.3%	10.5%	13.5%
Moderate/severe	16.5%	20.3%	13.7%	15.2%	8.1%	31.6%	0.8%	1.9%	4%	5.2%
Difference by regime (p value)	0.016		0.118		0.001		0.001		0.022	

GC, glucocorticosteroids; GI, gastrointestinal.

Table 3 Number of participants with a recorded switch in GC type and regime

Type switching							
From	Prednisolone			Deflazacorts			Multiple switches
To	Deflazacorts			Prednisolone			
N	65			4			6
Regime switching							
From	Daily	Daily	Intermittent	Intermittent	Other	Other	Multiple switches
To	Intermittent	Other	Daily	Other	Daily	Intermittent	
N	8	13	90	14	9	2	31

GC, glucocorticosteroids.

outcomes, and in particular how they impact motor function meant they were beyond the scope of this study. The impact of GC on other adverse events such as growth, weight, bone density and fractures in the NorthStar database has previously been reported.[28 35–37]

One limitation of the NorthStar database is the considerable degree of missing data, which is typical for large-scale, multicentre observational studies. Consequently, changes in GC prescribing patterns with time, dose with age and side-effect were presented by GC type and regime separately (ie, daily prednisolone and daily deflazacort were grouped together to analyse against intermittent prednisolone and intermittent deflazacort). However, when GC type and regime were cross tabulated, we observed a higher rate of intermittent regimes in participants on prednisolone compared with deflazacort. Consequently, the GC type or regime groups are not directly comparable, and as such this should be considered in the interpretation of the results. The NorthStar database also contains data from 24 sites, and it is likely there are prescribing differences across the sites, which will have changed with time. As such, care across the UK may be differential based on location, although efforts to prevent this, such as adherence to the DMD standards of care,[3 38 39] have been undertaken.

Additionally, the analysis of the GC side-effects was limited by low numbers, and consequently, it was not possible to analyse the side-effect profile in switching patients. It is crucial to understand to what extent side-effects impact decision-making for GC type and regime switching. For this, a survey of clinicians, parents and participants on reasoning behind switching will be needed.

Conclusion

This study provides one of the largest up-to-date real-world set of data on change in prescription patterns, adherence to the recommended dose and occurrence of side-effects in different groups of GC-treated boys with DMD. We showed that in the last decade, the most common GC regime prescribed in the UK for DMD was the daily regime, thus highlighting a change from the intermittent regime that was predominant 11 years ago.[10] The most common GC type was prednisolone, although deflazacort prescription has increased in recent years. We also captured the dose drift with age, where patients are more likely to be on a lower than recommended dose with age. We described the differential impact of GC type and regime on five side-effects (increased appetite, behavioural changes, cushingoid features, GI symptoms and insomnia). These are increasingly important given the development of new-wave steroids including vamorolone,[30 31] which have alternative side-effect profiles. This information will help clinicians in the discussion with patients and families on the relative benefits of different GC treatment approaches. By the time this paper was under consideration for publication, NICE has announced the draft approval for vamorolone in DMD, with the final approval expected January 2025.[40]

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Competing interests MG has participated in advisory boards for PTC Therapeutics, Capricor, Pfizer and NS Pharma. She has research collaborations with ReveraGen, she is or has been Principal Investigator for clinical trials with Roche, Italfarmaco, Santhera, ReveraGen, Summit, Pfizer, PTC Therapeutics; FM reports participation to Scientific Advisory boards and teaching initiatives for Novartis, Biogen, Roche, he is involved as an investigator in clinical trials from Novartis, Biogen, and Roche, both institutions (UCL and GOSH) receive funding from Biogen and Roche for the SMAREACH SMA registry; GB is PI of clinical trials by Pfizer, NS Pharma, and Reveragen, and has received speaker and/or consulting fees from Sarepta, PTC Therapeutics, Biogen, Novartis Gene Therapies (AveXis), and Roche and has worked as principal investigator of SMA studies sponsored by Novartis Gene Therapies, and Roche; GL, GS, AYM and AS have no conflict of interest to declare.

Patient consent for publication Not applicable.

Ethics approval The NorthStar project is a natural history clinical audit of the National Neuromuscular Database, in which data from DMD boys have been collected since 2006. Caldicott guardian approval has been obtained at every site in the NorthStar network. Ethical approval, in order for the NorthStar network to be established as a research project, is ongoing (IRAS Project ID: 242567). Participants gave informed consent to participate in the study before taking part.

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