

RESEARCH ARTICLE

Prognostic indicators of disease progression in Duchenne muscular dystrophy: A literature review and evidence synthesis

Nermina Ferizovic^{1,2*}, Jessica Summers¹, Igor Beitia Ortiz de Zárate³, Christian Werner⁴, Joel Jiang⁵, Erik Landfeldt⁶, Katharina Buesch⁷

1 MAP BioPharma Ltd, Cambridge, England, United Kingdom, **2** BresMed Health Solutions, Sheffield, England, United Kingdom, **3** PTC Therapeutics France SAS, Paris, France, **4** PTC Therapeutics Germany GmbH, Frankfurt/Main, Germany, **5** PTC Therapeutics, South Plainfield, New Jersey, United States of America, **6** ICON plc, Stockholm, Sweden, **7** PTC Therapeutics Switzerland GmbH, Zug, Switzerland

✉ These authors contributed equally to this work.

* nermina.ferizovic@hotmail.co.uk



OPEN ACCESS

Citation: Ferizovic N, Summers J, de Zárate IBO, Werner C, Jiang J, Landfeldt E, et al. (2022) Prognostic indicators of disease progression in Duchenne muscular dystrophy: A literature review and evidence synthesis. *PLoS ONE* 17(3): e0265879. <https://doi.org/10.1371/journal.pone.0265879>

Editor: Otavio R. Coelho-Filho, Faculty of Medical Science - State University of Campinas, BRAZIL

Received: April 23, 2021

Accepted: March 9, 2022

Published: March 25, 2022

Copyright: © 2022 Ferizovic et al. This is an open access article distributed under the terms of the [Creative Commons Attribution License](https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the paper and its [Supporting Information](#) files.

Funding: This study was funded by PTC Therapeutics (<https://www.ptcbio.com/>). The funder had a role in the design of the study, and review of the draft manuscript for important intellectual content, but did not have a role in the conduct of the study or management and analysis of the data. The publication of study results was

Abstract

Background

Duchenne muscular dystrophy (DMD) is a rare, severely debilitating, and fatal neuromuscular disease characterized by progressive muscle degeneration. Like in many orphan diseases, randomized controlled trials are uncommon in DMD, resulting in the need to indirectly compare treatment effects, for example by pooling individual patient-level data from multiple sources. However, to derive reliable estimates, it is necessary to ensure that the samples considered are comparable with respect to factors significantly affecting the clinical progression of the disease. To help inform such analyses, the objective of this study was to review and synthesise published evidence of prognostic indicators of disease progression in DMD. We searched MEDLINE (via Ovid), Embase (via Ovid) and the Cochrane Library (via Wiley) for records published from inception up until April 23 2021, reporting evidence of prognostic indicators of disease progression in DMD. Risk of bias was established with the grading system of the Centre for Evidence-Based Medicine (CEBM).

Results

Our search included 135 studies involving 25,610 patients from 18 countries across six continents (Africa, Asia, Australia, Europe, North America and South America). We identified a total of 23 prognostic indicators of disease progression in DMD, namely age at diagnosis, age at onset of symptoms, ataluren treatment, ATL1102, BMI, cardiac medication, DMD genetic modifiers, DMD mutation type, drisapersen, edasalonexent, eteplirsen, glucocorticoid exposure, height, idebenone, lower limb surgery, orthoses, oxandrolone, spinal surgery, TAS-205, vamorolone, vitlolarsen, ventilation support, and weight. Of these, cardiac medication, DMD genetic modifiers, DMD mutation type, and glucocorticoid exposure were designated core prognostic indicators, each supported by a high level of evidence and significantly affecting a wide range of clinical outcomes.

not contingent on the funder's approval of the manuscript.

Competing interests: We have read the journal's policy and the authors of this manuscript have the following competing interests: NF has acted as consultant to PTC Therapeutics through her employment at MAP BioPharma Limited and Bresmed Health Solutions and declares that she has no personal, commercial, academic, or financial conflicts of interest. JS has acted as consultant to PTC Therapeutics through her employment at MAP BioPharma Limited and declares that she has no personal, commercial, academic, or financial conflicts of interest. IB, CW, JJ, and KB are employees of PTC Therapeutics and may own stock/options in the company. EL has acted as a consultant to PTC Therapeutics through his employment at ICON plc. and declares that he has no personal, commercial, academic, or financial conflicts of interest. This does not alter our adherence to PLOS ONE policies on sharing data and materials.

Conclusion

This study provides a current summary of prognostic indicators of disease progression in DMD, which will help inform the design of comparative analyses and future data collection initiatives in this patient population.

1. Introduction

Duchenne muscular dystrophy (DMD) is a rare, neuromuscular disease characterised by progressive muscle degeneration caused by mutations in the X-linked *DMD* gene [1, 2]. The *DMD* gene encodes dystrophin, a structural protein which forms part of complexes predominantly found in muscle cells where it plays a significant role in the stabilisation of cell membranes [3]. To date, over 1,100 mutations have been identified, including 891 responsible for DMD phenotypes [4]. The incidence of DMD has been estimated at between 1 in 3,500 and 5,000 live male births [5, 6].

Patients with DMD are diagnosed around the age of four years, but many boys show symptoms earlier due to proximal muscle weakness resulting in delayed physical milestones (e.g., walking, running, and climbing stairs). As the disease progresses, patients become non-ambulatory usually in their early teens, followed by increasing loss of upper limb strength and function [7–11]. Respiratory and cardiac decline ensue, with patients eventually requiring mechanical ventilation support for survival [9, 10]. The median life expectancy at birth is around 30 years [12]. At present, there is no cure for DMD, and standard of care is mainly aimed at managing disease symptoms and promoting patient quality of life [13].

In medical research, it is occasionally necessary to pool patient-level data from different studies to indirectly assess the efficacy of a treatment due to low statistical power because of small patient samples and/or the absence of direct comparators in randomised controlled trials (RCTs). To minimize bias in such analyses, it is important to ensure that the populations to be compared are sufficiently homogeneous with respect to factors that would be expected to directly or indirectly affect outcomes of interest [14]. For example, in the context of DMD, it would be relevant to adjust any indirect comparison for the current age of the patient, among other factors, given the progressive, age-related nature of the disease. However, to date, no study has systematically reviewed the body of evidence for factors affecting disease progression outcomes in DMD. To bridge this evidence gap, the objective of this study was to review and synthesise the published evidence on prognostic indicators of disease progression in DMD.

2. Methods

This literature review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [15]. The study protocol is not publicly available due to intellectual property restrictions.

2.1. Search strategy

We searched MEDLINE (via Ovid), Embase (via Ovid) and the Cochrane Library (via the Wiley online platform) for records of studies published from inception up until April 23 2021, reporting evidence of prognostic indicators of disease progression in DMD. The search string contained “Duchenne muscular dystrophy” as a Medical Subject Heading term or free text term in combination with variations of the free text term “prognostic indicator”. For example,

the MEDLINE population terms were: 1. “exp Muscular Dystrophy, Duchenne/”, 2. “(Duchenne and dystro*).mp.” and 3. “1 or 2”. These were combined with the prognostic indicator terms; 4. “(prognos* or (disease adj3 course) or (disease adj3 impact) or natural history or (disease adj3 predict*) or (disease adj3 outcome) or (disease adj3 progres*)).mp.” and 5. “3 and 4”. Then the searches filtered out irrelevant study designs with the following; 6. “(comment or letter or editorial or notes or review).pt.”, 7. “(exp animals/ or exp invertebrate/ or animal experiment/ or animal model/) and (human/)” and 8. “(exp animals/ or exp invertebrate/ or animal experiment/ or animal model/) not 7”, 9. “6 or 8” and 10. “5 not 9”. Full search strings are provided in [S1 Appendix](#).

2.2. Selection criteria

Eligibility criteria based on the Population, Intervention, Comparison, Outcomes and Study design (PICOS) framework for study inclusion are presented in [Table 1](#). Only English language texts were included. For the purposes of this review, a prognostic indicator was defined as any factor, either endogenous or exogenous, affecting the clinical progression of disease.

2.3. Screening and data extraction

One investigator (NF) initially screened article titles and abstracts for eligibility, and subsequently reviewed full-text versions of selected records. The reason for exclusion was recorded and confirmed by a second investigator (JS). For all articles that met the inclusion criteria upon full-text review, the following information was extracted into a pre-designed data extraction form: Author, year, geographical setting, study design, interventions, patient sample population characteristics, disease progression outcome measures, prognostic indicators, and the impact of the prognostic indicators on disease progression. For the purpose of this review, we only considered statistically significant prognostic indicators (as reported in the included studies).

We synthesised extracted evidence of the impact of identified prognostic indicators of disease progression in DMD into eight outcome categories: cardiac health and function, loss of independent ambulation, lower extremity and motor function, muscle strength, respiratory health and function, scoliosis, survival, and upper extremity function. Although loss of ambulation is a clinical milestone within the lower extremity and motor function domain, we decided to report evidence separately for this factor given its central role in DMD research (e.g., as a primary endpoint in RCTs). Due to the monotonic progression of DMD, we did not

Table 1. PICOS eligibility criteria for study inclusion.

	Inclusion	Exclusion
Population	Patients diagnosed with DMD	Patients without a diagnosis of DMD
Intervention	Any	None
Comparators	Any	None
Outcome	Prognostic indicator of disease progression	None
Study design	Any	Systematic literature reviews and meta-analyses were not formally included, but screened for relevant references

Note: Population, Intervention, Comparison, Outcomes and Study design (PICOS). Duchenne muscular dystrophy (DMD).

<https://doi.org/10.1371/journal.pone.0265879.t001>

consider current age a prognostic factor of interest, nor bisphosphonate therapy because of the negative impact from both glucocorticoids and DMD on bone health [13].

2.4. Level of evidence

The level of evidence of included studies was established using a modified version of the grading system of the Centre for Evidence-Based Medicine (CEBM) [16]. Specifically, five levels of evidence were designated based on study design: (1) systematic review of randomised trials or n-of-1 trials, (2) randomised trial or observational study with dramatic effect, (3) non-randomised controlled cohort/follow-up study, (4) case-series, case-control studies, or historically controlled studies, and (5) mechanism-based reasoning. For reporting purposes, we categorised evidence levels 1 and 2 as “high level of evidence”, level 3 as “moderate level of evidence”, and levels 4 and 5 as “low level of evidence”.

3. Results

The search was performed on April 26 2021, and resulted in the identification of 3,018 publications (including journal articles and congress/conference abstracts) reporting evidence of prognostic indicators of disease progression in DMD (Fig 1). Of these, 740 records were duplicates, 1,966 excluded following title and abstract screening, and 312 selected for full-text review. An additional 54 articles were included from the reference searches of identified systematic literature reviews (SLRs) and meta-analyses (MAs). Finally, 294 publications were considered for data extraction, with 135 studies reporting statistically significant prognostic indicators of disease progression that were subsequently included for evidence synthesis and grading. Summary details of the included studies are presented in Table 2. Identified studies encompassed 25,610 patients with DMD from 18 countries (Argentina, Australia, Belgium, Canada, China, Denmark, Egypt, France, Germany, Holland, India, Italy, Japan, Korea, Sweden, Turkey, the United Kingdom and the United States).

We identified a total of 23 prognostic indicators of disease progression in DMD. Endogenous indicators included age at diagnosis, age at onset of symptoms, DMD genetic modifiers, DMD mutation type, height, weight and body mass index (BMI). Exogenous indicators included ataluren treatment, ATL1102, cardiac medication, drisapersen, edasalonexent, eteplirsen, glucocorticoid exposure (including age at glucocorticoid treatment initiation, dose, duration of exposure, pharmacological agent, and regimen), idebenone, lower limb surgery, orthoses, oxandrolone, spinal surgery, TAS-205, vamorolone, vitlolarsen, and ventilation support. The evidence for these prognostic indicators across the pre-defined outcome categories is summarised below and illustrated in Fig 2.

3.1. Cardiac health and function

We identified 29 studies presenting evidence of prognostic indicators of disease progression in DMD measured in terms of cardiac health and function [17–45, 91, 111, 199]. In total, seven prognostic indicators were identified: BMI, cardiac medication, DMD genetic modifiers, DMD mutation type, glucocorticoid exposure, idebenone and ventilation support (Table 2). Angiotensin-converting enzyme (ACE) inhibitors, including timing of treatment initiation, have been shown to be significantly associated with improved left ventricular ejection fraction (LVEF) [CEBM Evidence Level 2] [29, 32–34, 42–44], and left ventricular end diastolic and systolic dimension (LVEDd/LVESd) [Level 2]; [30, 31, 45] and left ventricular free wall systolic myocardial velocity [Level 2] [30], beta blockers, when administered in combination with ACE inhibitors, with improved LVEF [Level 4] [32–35], left ventricular fractional shortening (LVFS) [Level 2] [31], LVEDd and LVESd [Level 2] [35], left ventricular myocardial

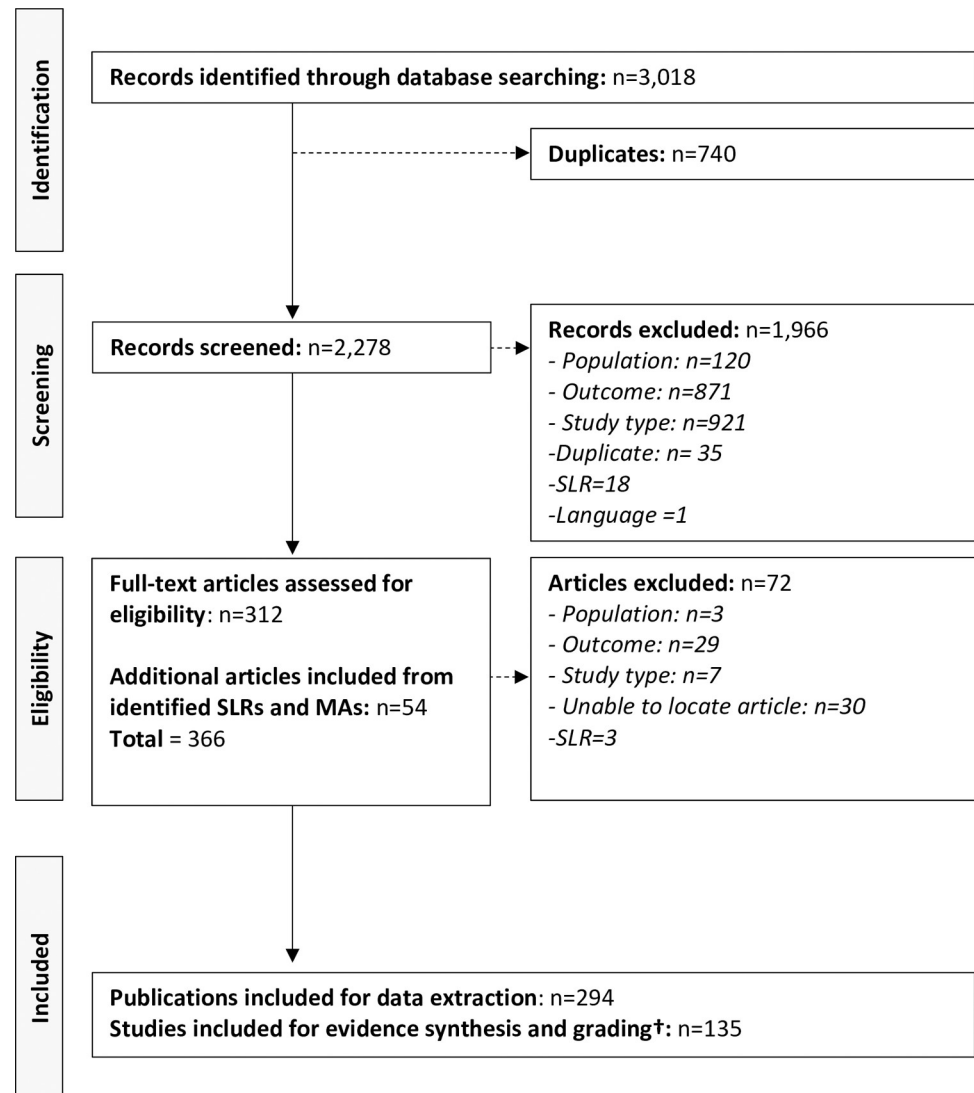


Fig 1. PRISMA diagram of the selection process of the included publications. Note: † Studies reporting evidence of statistically significant prognostic indicator of disease progression in DMD. Systematic literature reviews (SLRs). Meta-analyses (MAs).

<https://doi.org/10.1371/journal.pone.0265879.g001>

performance index (LVMPI) [Level 4] [35], and left ventricular sphericity index [Level 4]; [35] beta blockers with reduced heart failure and arrhythmia [Level 3] [37], and improved LVMPI [Level 2]; [30] timing of unspecified cardiac medication with later onset of cardiomyopathy [Level 4]; [38] eplerenone (EPL) with improved left ventricular systolic strain, LVEF, and end systolic volume (ESV) [Level 2]; [36] and ventilation support in combination with cardiac medication with decreased LVEF and left atrium diameter [Level 4] [39]. Glucocorticoid exposure has been shown to be significantly associated with improved LVEF [Level 4] [17–19, 21, 22, 25], LVFS [Level 3] [17–19, 25–27], LVEDd [Level 4] [19, 25, 26], meridional wall stress (mWS) [Level 4] [26], stabilisation of velocity of circumferential fibre shortening (VCFc) [Level 4] [26], reduction in cardiomyopathy [Level 4] [18, 20, 25, 199], and increases in summed rest score [Level 3] [24], as well as increased risk of cardiomyopathy [Level 4] [28], and decline in LVEF [Level 4] [23] linked to duration of glucocorticoid exposure. Idebenone

Table 2. Characteristics of included studies and identified prognostic indicators in DMD.

Author, year (country)	Study design (level of evidence)†	Interventions, DMD genetic modifiers, and/or DMD mutation types	Patient population	Disease progression outcome category	Disease progression outcome results	Identified prognostic indicator‡
Biggar et al., 2006 (CA) [17]	Non-randomised controlled cohort (Level 3)	DFZ	74 patients with DMD (mean age: NR, range: 10–18 years)	Cardiac Health and Function	Improved fractional shortening and ejection fraction	Glucocorticoid exposure
				Respiratory Health and Function	Improved and sustained FVC	
Houde et al., 2008 (CA) [18]	Case-control study (Level 4)	DFZ	79 patients with DMD treated with DFZ (mean age: 13 years, range: NR) or no treatment (mean age: 18 and 10 years, range: NR)	Cardiac Health and Function	Improved fractional shortening, ejection fraction, and reduced risk of cardiomyopathy	Glucocorticoid exposure
				Scoliosis	Lower mean degrees of scoliosis	
				Loss of Ambulation	Delay in loss of ambulation	
				Respiratory Health and Function	Improved FVC	
				Muscle Strength	Improved muscle strength as given by MRC	
Silversides et al., 2003 (CA) [19]	Case-control study (Level 4)	DFZ	33 patients with DMD treated with DFZ (mean age: 14 years, range: 10–18 years) or no treatment (mean age: 16 years, range: 11–18 years)	Cardiac Health and Function	Improved fractional shortening, ejection fraction, and LVEDd	Glucocorticoid exposure
				Respiratory Health and Function	Preserved pulmonary function	
				Loss of Ambulation	Delay in loss of ambulation	
Barber et al., 2013 (US) [20]	Case-control study (Level 4)	DFZ and PDN/PRED	462 patients with DMD (mean age: NR, range: NR)	Cardiac Health and Function	Reduced risk of cardiomyopathy onset versus untreated and linked to duration of use	Glucocorticoid exposure
				Loss of Ambulation	Delay in loss of ambulation linked to duration of use	
Bello et al., 2019 (IT) [21] Bello et al., 2019 (IT) [22]	Case series (Level 4)	DFZ and PDN/PRED LTBP4, minor alleles at SPP1, and CD40 SNPs Dp140 and Exon 8 skipping	374 patients with DMD (mean age: NR, range: NR)	Cardiac Health and Function	<i>DFZ and PDN/PRED</i> Improved ejection fraction <i>LTBP4</i> Preserved ejection fraction	Glucocorticoid exposure; DMD genetic modifiers; and DMD mutation type
				Respiratory Health and Function	<i>Dp140</i> Reduced FVC <i>DFZ and PDN/PRED</i> Improved FVC <i>SPP1 and CD40 SNPs</i> Reduced FVC <i>Exon 8 skipping</i> Higher PEF	
Tandon et al., 2015 (US) [23]	Case series (Level 4)	DFZ and PDN/PRED	98 patients with DMD (mean age: NR, range: NR)	Cardiac Health and Function	Decline in LVEF linked to duration of use	Glucocorticoid exposure
Zhang et al., 2015 (CN) [24]	Non-randomised controlled cohort study (Level 3)	DFZ and PDN/PRED	77 patients with DMD (mean age: NR, range: 2–13 years)	Cardiac Health and Function	Increased summed rest score	Glucocorticoid exposure

(Continued)

Table 2. (Continued)

Author, year (country)	Study design (level of evidence)†	Interventions, DMD genetic modifiers, and/or DMD mutation types	Patient population	Disease progression outcome category	Disease progression outcome results	Identified prognostic indicator‡
Schram et al., 2013 (CA) [25]	Case series (Level 4)	DFZ and PDN/PRED All patients were receiving cardiac medication (ACE inhibitors/ARBs)	86 patients with DMD (mean age: NR, range: NR)	Cardiac Health and Function	Reduced risk of cardiomyopathy, improved fractional shortening, ejection fraction, and LVEDd	Glucocorticoid exposure
				Survival	Reduction in all-cause mortality	
Markham et al., 2008 (US) [26]	Case-control study (Level 4)	DFZ and PDN/PRED	37 patients with DMD (mean age: NR, range: NR)	Cardiac Health and Function	Improved LVEDd, shortening fraction, mWS, and VCFC	Glucocorticoid exposure
Markham et al., 2005 (US) [27]	Case-control study (Level 4)	DFZ and PDN/PRED	111 patients with DMD treated with DFZ and PDN/PRED (mean age: 11 years, range: 3–21 years) or no treatment (mean age: 12 years, range: 3–21 years)	Cardiac Health and Function	Improved fractional shortening	Glucocorticoid exposure
Kim et al., 2017 (US) [28]	Case series (Level 4)	DFZ and PDN/PRED	255–660 patients with DMD (mean age: NR, range: NR)	Cardiac Health and Function	Increased risk of cardiomyopathy linked to duration of use	Glucocorticoid exposure
				Respiratory Health and Function	Reduced FVC function linked to duration of use	
Aikawa et al., 2019 (JP) [29]	Case series (Level 4)	ACE inhibitor (cilazapril or enalapril)	21 patients with DMD (median age: 12 years, IQR: 6–16 years)	Cardiac Health and Function	Improved LVEF	Cardiac medication
Kwon et al., 2012 (KR) [30]	Randomised trial (Level 2)	ACE inhibitor (enalapril) or BB (carvedilol)	23 patients with DMD (mean age: 13 years, range: NR)	Cardiac Health and Function	BB Improved LVMPI ACE Improved LVESd and left ventricular free wall systolic myocardial velocity	Cardiac medication
Kajimoto et al., 2006 (JP) [31]	Non-randomised controlled cohort (Level 3)	ACE inhibitor (enalapril), or ACE inhibitor (enalapril) and BB (carvedilol)	25 patients with DMD treated with ACE inhibitors/BBs (mean age: 18 years, range: 7–27 years) or ACE inhibitors (mean age: 15 years, range: 8–29 years)	Cardiac Health and Function	ACE Improved LVEDd ACE/BB Improved LVFS	Cardiac medication
Thrush et al., 2012 (US) [32] Thrush et al., 2012 (US) [33]	Case-control study (Level 4)	ACE inhibitor (drug NR), or ACE inhibitor (drug NR) and BB (drug NR)	25 patients with DMD treated with ACE inhibitors/BBs (mean age: 16 years, range: NR) or ACE inhibitors (mean age: 14 years, range: NR)	Cardiac Health and Function	Both ACE inhibitor and ACE inhibitor/BB improved ejection fraction compared to natural history	Cardiac medication
Viollet et al., 2012 (US) [34]	Case-control study (Level 4)	ACE inhibitor (lisinopril), or ACE inhibitor (lisinopril) and BB (metoprolol)	54 patients with DMD treated with ACE inhibitors/BBs (mean age: 16 years, range: 10–24 years) or ACE inhibitors (mean age: 14 years, range: 7–27 years)	Cardiac Health and Function	Improved ejection fraction versus natural history control	Cardiac medication

(Continued)

Table 2. (Continued)

Author, year (country)	Study design (level of evidence)†	Interventions, DMD genetic modifiers, and/or DMD mutation types	Patient population	Disease progression outcome category	Disease progression outcome results	Identified prognostic indicator‡
Jefferies et al., 2005 (US) [35]	Case series (Level 4)	ACE inhibitor (drug NR) and BB (drug NR)	62 patients with DMD (mean age: NR, range: NR)	Cardiac Health and Function	Improved LVEDd, LVEF, LVMPI, and left ventricular sphericity index	Cardiac medication; and DMD mutation type
		Exon 51 and 52			Cardioprotective	
		Exon 12,14, 15, 16, and 17			Onset of cardiomyopathy	
Raman et al., 2015 (US) [36]	Randomised trial (Level 2)	EPL and PLC	42 patients with DMD treated with EPL (mean age: 15 years, range: 12–19 years) or PLC (mean age: 15 years, range: 11–19 years)	Cardiac Health and Function	Improved left ventricular systolic strain, LVEF, and ESV	Cardiac medication
Matsumura et al., 2010 (JP) [37]	Non-randomised controlled cohort study (Level 3)	BB	54 patients with DMD treated with BBs (mean age: 19 years, range: 11–29 years) or BSC (mean age: 23 years, range: 15–35 years)	Cardiac Health and Function	Reduction in heart failure and arrhythmias	Cardiac medication
Van Ruiten et al., 2017 (UK) [38]	Case control (Level 4)	Cardiac medication (drug NR)	108 patients with DMD (mean age: NR, range: NR)	Cardiac Health and Function	Timing of cardiac medication impacts on cardiomyopathy	Cardiac medication
		DFZ and PDN/PRED		Loss of Ambulation	Delay in loss of ambulation	Glucocorticoid exposure
				Respiratory Health and Function	Improved FVC	
Faysoil et al., 2018 (FR) [39]	Case series (Level 4)	Ventilation support in combination with cardiac medication (drug NR)	101 patients with DMD (median age: 21 years, IQR: 18–26 years)	Cardiac Health and Function	Decreased left atrium diameter and LVEF	Ventilation support
Nagai et al., 2020 (JP) [40]	Case-control study (Level 4)	ACTN3 null genotype	77 patients with DMD (median age: NR; IQR: 7.9–11.5 years)	Cardiac Health and Function	Earlier onset of cardiac dysfunction; early onset of LV dilation; lower LV dilation-free rate	DMD genetic modifier
Cheeran et al., 2017 (US) [41]	Case-control study (Level 4)	BMI	43 patients with DMD (median age: 21 years; IQR: 21–24 years)	Cardiac Health and Function	Higher BMI is associated with reduced cardiomyopathy	BMI
Duboc et al., 2005 (FR) [42] Duboc et al., 2007 (FR) [43]	Randomised trial (Level 2)	Perindopril and PLC	57 patients with DMD (mean: NR; range: 9.5–13 years)	Cardiac Health and Function	Maintains LVEF	Cardiac medication
				Survival	Improvement in survival	
Ishikawa et al., 1999 (NR) [44]	Follow-up study (Level 3)	ACE (enalapril and lisinopril) and BB	11 patients with DMD (mean age: 17; range: 12.6–22.8)	Cardiac Health and Function	Increased LVEF	Cardiac medication
Ramaciotti et al., 2006 (USA) [45]	Case-series (Level 4)	ACE (enalapril)	50 patients with DMD (mean age: NR; range: 10–20 years)	Cardiac Health and Function	Improved left ventricular function	Cardiac medication
King et al., 2007 (US) [46]	Case-control study (Level 4)	DFZ and PDN/PRED	143 patients with DMD treated with DFZ and PDN/PRED (mean age: 17 years, range: 6–31 years) or no treatment (mean age: 14 years, range: 2–40 years)	Scoliosis	Lower mean degrees of scoliosis	Glucocorticoid exposure
				Loss of Ambulation	Delay in loss of ambulation	

(Continued)

Table 2. (Continued)

Author, year (country)	Study design (level of evidence)†	Interventions, DMD genetic modifiers, and/or DMD mutation types	Patient population	Disease progression outcome category	Disease progression outcome results	Identified prognostic indicator‡
Balaban et al., 2005 (NR) [47]	Case-control study (Level 4)	DFZ and PDN/PRED	49 patients with DMD treated with DFZ (mean age: 14 years, range: NR) or PDN/PRED (mean age: 15 years, range: NR) or no treatment (mean age: 14 years, range: NR)	Scoliosis	Reduced number of spinal surgeries versus untreated	Glucocorticoid exposure
				Respiratory Health and Function	Improved FVC between 7–15 years old versus untreated	
				Muscle Strength	Grip and pinch strength (maximum hand-held weight which could be lifted overhead) improved in DFZ and PDN/PRED versus untreated	
				Lower Extremity and Motor Function	Improved walk/run 9 metres, STS, and 4SC versus untreated	
Alman et al., 2004 (CA) [48]	Non-randomised controlled cohort study (Level 3)	DFZ	54 patients with DMD treated with DFZ (mean age: 9 years, range: NR) or no treatment (mean age: 9 years, range: NR)	Scoliosis	Decrease in rate of scoliosis > 20 degrees and need for spinal surgery	Glucocorticoid exposure
Lebel et al., 2013 (CA) [49]	Non-randomised controlled cohort study (Level 3)	DFZ	54 patients with DMD treated with DFZ (mean age: 9 years, range: NR) or no treatment (mean age: 9 years, range: NR)	Scoliosis	Decrease in rate of scoliosis > 20 degrees and need for spinal surgery	Glucocorticoid exposure
				Survival	Reduction in mortality	
Kinali et al., 2007 (UK) [50]	Case series (Level 4)	KAFOS; PDN/PRED	123 patients with DMD (mean age: NR, range: NR)	Scoliosis	KAFOS Longer duration of use reduces scoliosis severity PDN/PRED Later age at scoliosis onset linked to duration of use	Orthoses; and Glucocorticoid exposure
McDonald et al., 2018 (*) [51]	Observational study with dramatic effect (Level 2)	DFZ and PDN/PRED	440 patients with DMD (mean age: NR, range: 2–28 years)	Survival	Reduction in mortality (>1 year of exposure)	Glucocorticoid exposure
				Loss of Ambulation	Delay in loss of ambulation (>1 year of exposure) and favouring DFZ	
				Upper extremity function	Retained hand function as given by Brooke score (>1 year of exposure) and favouring DFZ	
				Lower Extremity and Motor Function	Improved STS (>1 year of exposure) and favouring DFZ	
Ogata et al., 2009 (JP) [52]	Case series (Level 4)	ACE inhibitor (enalapril/lisinopril) and BB (bisoprolol/carvedilol/metoprolol)	52 patients with DMD receiving symptomatic treatment (mean age: 18 years, range: NR) or asymptomatic treatment (mean age: 20 years, range: NR)	Survival	Overall survival improved in the early treatment (asymptomatic) group	Cardiac medication
Rall and Grim, 2012 (DE) [53]	Case-control study (Level 4)	Ventilation support	94 patients with DMD (mean age: NR, range: NR)	Survival	Improved overall survival	Ventilation support

(Continued)

Table 2. (Continued)

Author, year (country)	Study design (level of evidence)†	Interventions, DMD genetic modifiers, and/or DMD mutation types	Patient population	Disease progression outcome category	Disease progression outcome results	Identified prognostic indicator‡
Jeppesen et al., 2003 (DK) [54]	Case-control study (Level 4)	Ventilation support	159 patients with DMD (mean age: NR, range: NR)	Survival	Reduction in all-cause mortality	Ventilation support
Eagle et al., 2007 (UK) [55]	Case-control study (Level 4)	Spinal surgery and ventilation; ventilation no spinal surgery; no spinal surgery or ventilation	100 patients with DMD (mean age: NR, range: NR)	Survival	Spinal surgery/ ventilation and ventilation no spinal surgery improved survival with spinal surgery/ventilation having a larger impact	Ventilation support; and spinal surgery
Eagle et al., 2002 (UK) [56]	Case-control study (Level 4)	Nocturnal ventilation support	183 patients with DMD (mean age: NR, range: NR)	Survival	Reduction in mortality	Ventilation support
Gomez-Merino et al., 2002 (NR) [57]	Case-control study (Level 4)	Non-invasive respiratory aids	91 patients with DMD (mean age: NR, range: NR)	Survival	Prolongation of survival	Ventilation support
Kieny et al., 2013 (FR) [58]	Case-control study (Level 4)	Ventilation support	119 patients with DMD (mean age: NR, range: NR)	Survival	Prolongation of survival	Ventilation support
Ishikawa et al., 2011 (JP) [59]	Case-control study (Level 4)	Non-invasive respirator aids (including mechanically assisted coughing)	187 patients with DMD (mean age: NR, range: NR)	Survival	Prolongation of survival compared to invasive treatment	Ventilation support
Adorisio et al., 2019 (NR) [60]	Case-control study (Level 4)	Left ventricular assist device in combination with cardiac medication and OMT	12 patients with DMD (mean age: NR, range: NR)	Survival	Improved survival	Left ventricular assist device
Davidson et al., 2012 (AU) [61]	Case series (Level 4)	DFZ and PDN/PRED	144 patients with DMD (mean age: NR, range: NR)	Loss of Ambulation	Reduction in risk of loss of ambulation	Glucocorticoid exposure; and DMD mutation type
		Dystrophin gene deletions			Increased risk of loss of ambulation	
Bonifati et al., 2006 (IT) [62]	Non-randomised controlled cohort study (Level 3)	DFZ and PDN/PRED	48 patients with DMD (mean age: NR, range: NR)	Loss of Ambulation	Early treatment initiation and increased treatment duration delay loss of ambulation	Glucocorticoid exposure
Bello et al., 2015 (*) [63] Bello et al., 2015 (*) [64] Bello et al., 2015 (*) (IT) [65]	Observational study with dramatic effect (Level 2)	DFZ and PDN/PRED	340 patients with DMD (283 for the genotype sub-population) (mean age: 16 years, range: 5–33 years)	Loss of Ambulation	Delay in loss of ambulation; DFZ more favourable	Glucocorticoid exposure; and DMD genetic modifiers
		TG/GG genotype at SPP1 rs28357094			Earlier loss of ambulation	
		LTBP4 haplotype			Delayed loss of ambulation	
Bello et al., 2014 (*) [66]	Observational study with dramatic effect (Level 2)	DFZ and PDN/PRED	332 patients with DMD (mean age: NR, range: NR)	Loss of Ambulation	Delay in loss of ambulation, DFZ more favourable	Glucocorticoid exposure; and DMD genetic modifiers
		G allele at SPP1rs28357094			Earlier loss of ambulation	
Bello et al., 2016 (*) [11]	Observational study with dramatic effect (Level 2)	DFZ and PDN/PRED	212 patients with DMD (mean age: NR, range: NR)	Loss of Ambulation	Delay in loss of ambulation	Glucocorticoid exposure; and DMD mutation type
Deletion of exon 3–7 and exon 44 skipping		DMD mutation type				
Bello et al., 2016 (*) [67]		Exon 44 skipping				
Goemans et al., 2019 (*) [68] Goemans et al., 2019 (*) [69]	Case series (Level 4)	DFZ and PDN/PRED	85 patients with DMD (mean age: 9 years, range: NR)	Loss of Ambulation	Predictive of loss of ambulation	Glucocorticoid exposure; greater weight; lower height; and lower BMI (in combination)

(Continued)

Table 2. (Continued)

Author, year (country)	Study design (level of evidence)†	Interventions, DMD genetic modifiers, and/or DMD mutation types	Patient population	Disease progression outcome category	Disease progression outcome results	Identified prognostic indicator‡
Kim et al., 2015 (US) [70]	Observational study with dramatic effect (Level 2)	DFZ and PDN/PRED	477 patients with DMD (mean age: NR, range: NR)	Loss of Ambulation	Delay in loss of ambulation with larger effect for those treated longer in the <11 year olds	Glucocorticoid exposure
Schara et al., 2001 (DE) [71]	Case-control study (Level 4)	DFZ	13 patients with DMD (mean: NR, range: 9–18 years)	Loss of Ambulation	Delay in loss of ambulation	Glucocorticoid exposure
				Respiratory Health and Function	Improved FVC	
				Muscle Strength	Improved muscle strength as given by MRC scale	
				Lower Extremity and Motor Function	Improved Vignos functional score, STS, 4SC, and walking ability	
Van den Bergen et al., 2014 (NL) [72]	Retrospective observational study (Level 2)	Glucocorticoids (drug NR)	336 patients with DMD (mean age: NR, range: NR)	Loss of Ambulation	Delay in loss of ambulation	Glucocorticoid exposure
Van den Bergen et al., 2014 (NL) [73]	Case control study (Level 4)	Glucocorticoids (drug NR) Exon 44 (vs. 45, 51, and 53)	114 patients with DMD (mean age: NR, range: NR)	Loss of Ambulation	Delay in loss of ambulation	Glucocorticoid exposure; and DMD mutation type
Wang et al., 2014 (US) [74]	Online survey (Level 5)	DFZ and PDN/PRED	1,057 patients with DMD (mean age: NR, range: NR)	Loss of Ambulation	Delay in loss of ambulation with DFZ favourable over PDN/PRED	Glucocorticoid exposure
		Age at diagnosis			Delay in loss of ambulation	
Ricotti et al., 2012 (UK) [75] Ricotti et al., 2011 (UK) [76] Ricotti et al., 2011 (UK) [77]	Case series (Level 4)	PDN/PRED	334–400 patients with DMD (mean age: NR, range: 3–15 years)	Loss of Ambulation	Delay in loss of ambulation in daily PDN-treated compared to intermittent PDN	Glucocorticoid exposure
DeSilva et al., 1987 (US) [78]	Non-randomised controlled cohort study (Level 3)	PDN/PRED	54 patients with DMD (mean age: NR, range: NR)	Loss of Ambulation	Delay in loss of ambulation	Glucocorticoid exposure
Yilmaz et al., 2004 (TR) [79] Yilmaz et al., 2004 (TR) [80] Tunca et al., 2001 (TR) [81]	Historically controlled cohort study (Level 4)	PDN/PRED	88 patients with DMD treated with PDN/PRED (mean age: 7 years, range: 3–11 years) or no treatment (mean age: 7 years, range: 5–9 years)	Loss of Ambulation	Delay in loss of ambulation	Glucocorticoid exposure
				Lower Extremity and Motor Function	Improved 10WRT at 6 months	
				Muscle Strength	Improved muscle strength as given by Lovett’s tests	
Yilmaz et al., 2004 (TR) [79] Yilmaz et al., 2004 (TR) [80]	Historically controlled cohort study (Level 4)	PDN/PRED	88 patients with DMD treated with PDN/PRED (mean age: 7 years, range: 3–11 years) or no treatment (mean age: 7 years, range: 5–9 years)	Loss of Ambulation	Delay in loss of ambulation	Glucocorticoid exposure
				Lower Extremity and Motor Function	Improved 10WRT at 6 months	
				Muscle Strength	Improved muscle strength as given by Lovett’s tests	
Biggar et al., 2001 (CA) [82]	Case control (Level 4)	DFZ	54 patients with DMD (mean age: NR, range: NR)	Loss of Ambulation	Delay in loss of ambulation	Glucocorticoid exposure
				Respiratory Health and Function	Improved FVC	
				Lower Extremity and Motor Function	Improved 4SC and STS	

(Continued)

Table 2. (Continued)

Author, year (country)	Study design (level of evidence)†	Interventions, DMD genetic modifiers, and/or DMD mutation types	Patient population	Disease progression outcome category	Disease progression outcome results	Identified prognostic indicator‡
Ciafaloni et al., 2013 (US) [83] Ciafaloni et al., 2016 (US) [84]	Observational study with dramatic effect (Level 2)	Age at onset of symptoms	825 patients with DMD (mean age: NR, range: NR)	Loss of Ambulation	Earlier loss of ambulation for earlier symptom development	Age at onset of symptoms
Bello et al., 2016 (*) [85]	Genome-wide association study (Level 4)	Minor allele at rs1883832	109 patients with DMD (mean age: NR; range: NR)	Loss of Ambulation	Delay in loss of ambulation	DMD genetic modifiers
Haber et al., 2021 (US) [86]	Case control study (Level 4)	Exon 8 and Exon 44 skip deletions	358 patients with DMD (mean age: NR; range: NR)	Loss of Ambulation	Delay in loss of ambulation	DMD mutation type
Mercuri et al., 2020 (NR) [87]	Non-randomised controlled study (Level 3)	ATA compared to external controls	181 patients with DMD (mean age: NR, range: NR) or external control (mean age: NR, range: 2–28 years)	Loss of Ambulation	Delay in loss of ambulation	ATA treatment
				Lower Extremity and Motor Function	Improved STS and 4SC	
Wang et al., 2018 (*) [88]	Case series (Level 4)	Glucocorticoids; DMD mutation type	765 patients with DMD (mean age: NR; range: NR)	Loss of Ambulation	Delay in loss of ambulation: Glucocorticoids, exon 44, exon 3–7, exon 45, exon 8 Earlier loss of ambulation: Exon 51, exon 49–50	Glucocorticoid exposure; DMD mutation type
Forst et al., 1995 [89] (GER)	Observational study with dramatic effect (Level 2)	Lower limb surgery	213 patients with DMD (mean age: 6.56 years; range: 4.02–8.26)	Loss of Ambulation	Delay in loss of ambulation	Lower limb surgery
Forst et al., 1995 [90] (GER)	Observational study with dramatic effect (Level 2)	Lower limb surgery	123 patients with DMD (mean age: NR; range: NR)	Loss of Ambulation	Delay in loss of ambulation	Lower limb surgery
Servais et al., 2015 (FR) [91]	Case-control study (Level 4)	Exon 53	53 patients with DMD (DMD 53: mean age: 13.9, range: NR or DMD-all-non-53: mean age: 14 years, range: NR or DMD-del-non-53: mean age: 14.1, range: NR)	Loss of Ambulation	Delay in loss of ambulation compared to DMD-all-non-53 and DMD del-non-53	DMD mutation type
				Cardiac Health and Function	Lower LVEF and higher contracture score compared to DMD-del-non-53	
				Muscle Strength	Lower pinch strength in exon 53 compared to DMD-all-non-53	
Escolar et al., 2011 (US) [92]	Randomised controlled trial (Level 2)	PDN/PRED (daily dose with PLC at weekend; weekend dose with PLC during weekdays)	64 patients with DMD (mean age: 7 years, range: NR)	Respiratory Health and Function	Weekend dosing equivalent to daily dosing as given by MVV; MIP	Glucocorticoid exposure
				Upper Extremity Function	Weekend dosing equivalent to daily dosing as given by Brooke score	
				Muscle Strength	Weekend dosing equivalent to daily dosing as given by QMT and MMT	
				Lower Extremity and Motor Function	Weekend dosing equivalent to daily dosing as given by STS, 4SC and 10WRT	

(Continued)

Table 2. (Continued)

Author, year (country)	Study design (level of evidence)†	Interventions, DMD genetic modifiers, and/or DMD mutation types	Patient population	Disease progression outcome category	Disease progression outcome results	Identified prognostic indicator‡
Tachas et al., 2020 (NR) [93]	Randomised trial (Level 2)	ATL1102 compared to external natural history control	29 patients with DMD (mean age: 14.9 years, range: 12–18 years) or external control (mean age: 15.61, range: NR)	Upper Extremity Function	Improved upper limb function as given by PUL	ATL1102 treatment
Daftary et al., 2007 (US) [94]	Case-control study (Level 4)	DFZ and PDN/PRED	35 patients with DMD (mean age: NR, range: 7–21 years)	Respiratory Health and Function	Long-term glucocorticoid therapy improves PCF and MEP	Glucocorticoid exposure
Abresch et al., 2013 (*) [95]	Case-control study (Level 4)	DFZ and PDN/PRED	341 patients with DMD (mean age: NR, range: 6–28 years)	Respiratory Health and Function	Improved MIP, MEP and PCF	Glucocorticoid exposure
Henricson et al., 2013 (*) [96]	Case series (Level 4)	DFZ and PDN/PRED (current users vs. naïve users)	340 patients with DMD (mean age: NR, range: 2–28 years)	Respiratory Health and Function	Improved FVC; MIP; PEFr; FEV ₁	Glucocorticoid exposure
				Upper Extremity Function	Improved Brooke score	
				Lower Extremity and Motor Function	Improved Vignos, STS, 4SC, and 10WRT	
McDonald et al., 2018 (*) [97]	Case control study (Level 4)	DFZ and PDN/PRED	397 patients with DMD (median: 9 years, IQR: 2–28 years)	Respiratory Health and Function	Improved FVC	Glucocorticoid exposure
Henricson et al., 2017 (US) [98] McDonald et al., 2017 (US) [99]	Case control (Level 4)	DFZ and PDN/PRED	233 patients with DMD (mean age: 13 years, range: 6–28 years)	Respiratory Health and Function	Sustained FVC and PEFr	Glucocorticoid exposure
Ricotti et al., 2011 (UK) [77]	Case series (Level 4)	PDN/PRED	334–400 patients with DMD (mean age: NR, range: 3–15 years)	Respiratory Health and Function	Sustained FVC in daily PDN	Glucocorticoid exposure
Pradhan 2006 (IN) [100]	Non-randomised controlled cohort study (Level 3)	PDN/PRED	34 patients with DMD (mean age: NR, range: NR)	Respiratory Health and Function	Improved short-term PEFr	Glucocorticoid exposure
				Muscle Strength	Improved MRC	
Fenichel et al., 1991 (US) [101]	RCT (Level 2)	PDN/PRED	103 patients with DMD (mean age: NR, range: 5–15 years)	Respiratory Health and Function	Daily and alternate day PDN/PRED improved FVC and MVV at 12 months	Glucocorticoid exposure
				Muscle Strength	Daily and alternate day PDN/PRED improved muscle strength using an unspecified measure at 6 months but more sustained with daily Both doses improved muscle mass as given by creatinine excretion	
				Lower Extremity and Motor Function	Daily and alternate day PDN/PRED improved STS and 4SC	

(Continued)

Table 2. (Continued)

Author, year (country)	Study design (level of evidence)†	Interventions, DMD genetic modifiers, and/or DMD mutation types	Patient population	Disease progression outcome category	Disease progression outcome results	Identified prognostic indicator‡
Dubow et al., 2016 (NR) [102]	RCT (Level 2)	DFZ and PDN/PRED	45 patients with DMD (mean age: NR, range: NR)	Respiratory Health and Function	1.2 mg/kg/day dose of DFZ versus PLC improves MVV	Glucocorticoid exposure
Comi et al., 2017 (*) [103] McDonald et al., 2016 (*) [104]	Historically-controlled study (Level 4)	ATA	167 patients with DMD (mean age: 16 years, range: NR)	Respiratory Health and Function	Improved FVC	ATA treatment
Kelley et al., 2019 (*) [105]	Case series (Level 4)	Gly16 ADRB2 polymorphism	175 patients with DMD (mean age: NR, range: 3–25 years)	Respiratory Health and Function	<i>Gly16 genotype</i> 6.52X likelier of receiving nocturnal ventilation compared to Arg16 <i>Patient weight</i> Predictor of need for nocturnal ventilation	DMD genetic modifier; weight
Angliss et al., 2020 (AU) [106]	Case control (Level 4)	Ventilation	29 patients with DMD (median: 14.66; IQR: NR)	Respiratory Health and Function	FVC improved in steroid naïve but accelerated decline in steroid users	Ventilation support
Bello et al., 2020 (IT) [107]	Case control (Level 4)	DMD mutation type and DMD genetic modifiers; Glucocorticoids	327 patients with DMD (mean age: 11.7, range: NR)	Respiratory Health and Function	<i>Exon 44 3' mutation:</i> Lower FVC, lower FEV1 and lower PEF <i>Glucocorticoid</i> Increased FVC, FEV1 and PEF <i>Skip 51, Skip 53</i> Decreased FVC, decreased FEV1, decreased PEF <i>Splice site, Skip 8, Skip 44</i> Increased FVC Skip 8, splice site Increased FEV1, increased PEF <i>Nonsense mutation</i> Decreased FVC and FEV1 <i>Dominant G genotype at rs28357094 in the SPP1 promoter</i> Reduced FVC and PEF <i>Additive T genotype at rs1883832 in the CD40 5' untranslated region</i> Reduced FVC, FEV1 and PEF	Glucocorticoid exposure; DMD mutation type; DMD genetic modifiers
Iff et al., 2020 (US) [108]	Case control (Level 4)	ETEP versus untreated controls	283 patients with DMD (mean age: 14.1 years, range: NR)	Respiratory Health and Function	Attenuates respiratory function (indirectly measured)	ETEP exposure
McDonald et al., 2020 (*) [109] McDonald et al., 2020 (*) [110]	Randomised trial (Level 2)	ATA versus external natural history control	95 patients with DMD (mean age: NR, range: NR)	Respiratory Health and Function Loss of Ambulation	Delay in respiratory decline as given by FVC Delay in loss of ambulation	ATA treatment
Buyse et al., 2011 (BE) [111]	Randomised trial (Level 2)	IDE and PLC	21 patients with DMD (mean age: NR, range: 8–16 years)	Respiratory Health and Function Cardiac Health and Function	Improved PEF Improved peak systolic radial strain in the LV inferolateral wall	IDE treatment

(Continued)

Table 2. (Continued)

Author, year (country)	Study design (level of evidence)†	Interventions, DMD genetic modifiers, and/or DMD mutation types	Patient population	Disease progression outcome category	Disease progression outcome results	Identified prognostic indicator‡
Karafilidis et al., 2018 (NR) [112]	Randomised trial (Level 2)	IDE and PLC	64 patients with DMD (mean age: NR, range: 10–18 years)	Respiratory Health and Function	Improved PEF and FEV1	IDE treatment
Khan et al., 2019 (NR) [113] Khan et al., 2019 (NR) [114] Khan et al., 2019 (NR) [115]	Randomised trial (Level 2)	ETEP and natural history control	414 patients with DMD (mean age: NR, range: 7–16 years) or natural history control (mean age: NR, range: 2–28 years)	Respiratory Health and Function	Reduced decline in respiratory decline as given by percent predicted FVC	ETEP treatment
Mendell et al., 2014 (NR) [116] Mendell et al., 2014 (NR) [117] Mendell et al., 2014 (NR) [118]	Randomised trial (Level 2)	ETEP and PLC	12 patients with DMD (median age: 9.7 years, IQR: NR; range: 7–13 years)	Respiratory Health and Function	Improved MEP and FVC	ETEP treatment
Mendell et al., 2014 (NR) [119] Mendell et al., 2014 (NR) [120] Mendell et al., 2015 (NR) [121] Kaye et al., 2014 (NR) [122] Kaye et al., 2015 (NR) [123] Kaye et al., 2015 (NR) [124] Kaye et al., 2015 (NR) [125]				Lower Extremity and Motor Function	Improved 6MWT	
Mendell et al., 2021 (NR) [126] Mendell et al., 2016 (NR) [127] Mendell et al., 2017 (NR) [128] Mendell et al., 2016 (NR) [129] Mendell et al., 2016 (NR) [130]	Randomised controlled trial (Level 2)	ETEP compared to external controls	12 patients with DMD (mean age: 9.4 years, range: 7–13 years) or no treatment (mean age: 9.6 years, range: 7–13 years)	Loss of Ambulation Lower Extremity and Motor Function	Delay in loss of ambulation Improved 6MWT	ETEP treatment

(Continued)

Table 2. (Continued)

Author, year (country)	Study design (level of evidence)†	Interventions, DMD genetic modifiers, and/or DMD mutation types	Patient population	Disease progression outcome category	Disease progression outcome results	Identified prognostic indicator‡
McDonald et al., 2020 (*) [131]	Randomised trial (Level 2)	Analysis of PLC arm data; DFZ and PDN/PRED	115 patients with DMD (mean age: NR, range: 7–14 years)	Lower Extremity and Motor Function	Improved 4SC, 6MWT, STS and NSAA	Glucocorticoid exposure
Lawrence et al., 2018 (NR) [132]	Randomised trial (Level 2)	IDE and PLC	23 patients with DMD (mean age: NR, range: 10–18 years)	Respiratory Health and Function	Improvement in respiratory function as given by reduced bronchopulmonary adverse events	IDE treatment
Rummy et al., 2018 (NR) [133]	Follow-up study (Level 3)	IDE and PLC	64 patients with DMD (mean age: 14.3 years, range: 10–18 years)	Respiratory Health and Function	Improved PEF	IDE treatment
Kanazawa et al., 1991 (JP) [134]	Follow-up study (Level 3)	cDMD deficit	24 patients with DMD (mean age: 14.2 years; range: NR) or non-deficit group: mean age: 14.7 years, range: NR)	Respiratory Health and Function	Worse pulmonary function	DMD mutation type
Hussein et al., 2006 (EG) [135]	Case-control (Level 4)	PDN/PRED	18 patients with DMD (mean age: 5 years, range: NR)	Muscle Strength	Improvement in muscle strength as given by MRC scale	Glucocorticoid exposure
Angelini et al., 1994 (IT) [136]	RCT (Level 2)	DFZ	28 patients with DMD treated with DFZ (mean age: 8 years, range: NR) or PLC (mean age: 8 years, range: NR)	Muscle Strength Lower Extremity and Motor Function	Improvement in muscle strength as given by MRC scale (>1 year of treatment) Improved STS	Glucocorticoid exposure
Fenichel et al., 1991 (US) [137]	Historically-controlled study (Level 4)	PDN/PRED	92 patients with DMD (mean age: NR, range: 5–15 years)	Muscle Strength	Improved muscle strength using an unspecified measure versus controls Improved more for >0.65mg/kg dose compared to <0.65mg/kg	Glucocorticoid exposure
Hu et al., 2015 (CN) [138]	RCT (Level 2)	PDN/PRED	66 patients with DMD (mean age: NR, range: 4–12 years)	Muscle Strength Lower Extremity and Motor Function	Stabilised MRC Improved 10WRT, 4SC, and STS	Glucocorticoid exposure
Rifai et al., 1995 (US) [139]	Case-control (Level 4)	PDN/PRED	6 patients with DMD (mean age: NR, range: 5–8 years)	Muscle Strength	Improved muscle strength and mass as given by MMT, QMT, and creatinine excretion)	Glucocorticoid exposure
Backman and Henriksson, 1995 (SE) [140]	RCT (Level 2)	PDN/PRED	37 ambulatory (mean age: 8 years, range: 4–11 years) or non-ambulatory (mean age: 13 years, range: 8.0–19 years) patients with DMD	Muscle Strength Lower Extremity and Motor Function Upper Extremity Function	Improved muscle strength as given by grip strength (strain gauge) and myometric evaluation Scott functional testing improved during first 3 months of treatment Brooke score improved during first 3 months of treatment	Glucocorticoid exposure

(Continued)

Table 2. (Continued)

Author, year (country)	Study design (level of evidence)†	Interventions, DMD genetic modifiers, and/or DMD mutation types	Patient population	Disease progression outcome category	Disease progression outcome results	Identified prognostic indicator‡
Connolly et al., 2002 (US) [141]	Historically controlled cohort study (Level 4)	PDN/PRED	42 patients with DMD (mean age: NR, range: NR)	Muscle Strength	Improvement in grip (Jamar grip meter) and upper extremity strength using a myometry	Glucocorticoid exposure
				Lower Extremity and Motor Function	STS, walk/run 9m, and 4SC improved in younger boys versus older boys	
Griggs et al., 1993 (CA/US) [142]	RCT (Level 2)	PDN/PRED	107 patients with DMD (mean age: NR, range: 5–15 years)	Muscle Strength	Improved muscle strength as given by muscle mass increases (creatinine excretion), myometric evaluation and MMT Larger improvement in 0.75mg/kg versus 0.30mg/kg	Glucocorticoid exposure
Mesa et al., 1991 (AR) [143]	Non-randomised controlled study (Level 3)	DFZ	28 patients with DMD (mean age: NR, range: 5–11 years)	Muscle Strength	Improvement in muscle strength as given by myometric evaluation	Glucocorticoid exposure
				Lower Extremity and Motor Function	Improved Scott functional score and STS	
Beenakker et al., 2005 (NL) [144]	RCT (Level 2)	PDN/PRED	17 patients with DMD (mean age: 6 years, range: NR)	Muscle Strength	Intermittent PDN/PRED improves total muscle force as given by myometric evaluation	Glucocorticoid exposure
				Lower Extremity and Motor Function	Intermittent PDN/PRED improves 9 metre run/walk and 4SC	
Griggs et al., 1991 (CA/US) [145]	RCT (Level 2)	PDN/PRED	99 patients with DMD (mean age: NR, range: NR)	Muscle Strength	Improved muscle strength as given by myometric evaluation and MMT. Improvements larger in 0.75mg/kg versus 0.30mg/kg	Glucocorticoid exposure
				Lower Extremity and Motor Function	9m run/walk test and STS improved in 0.75mg/kg; 4SC improved in both 0.75mg/kg and 0.30mg/kg	
				Respiratory Health and Function	Improved FVC versus PLC at both 0.3 and 0.75mg/kg	
Merlini et al., 2003 (IT) [146]	Case-control study (Level 4)	PDN/PRED	8 patients with DMD treated with PDN/PRED (mean age: 4 years, range: NR) or no treatment (mean age: 4 years, range: NR)	Muscle Strength	Improved muscle strength as given by myometric evaluation but only in the leg megascor	Glucocorticoid exposure
				Lower Extremity and Motor Function	Improved STS	
Pegoraro et al., 2011 (IT) [147]	Historically controlled cohort study (Level 4)	SPP1 genotype	262 patients with DMD (mean age: NR, range: NR)	Muscle Strength	G allele leads to weaker MRC scores and lower grip strength	DMD genetic modifiers
Fenichel et al., 2001 (NR) [148]	Randomised trial (Level 2)	OXAN vs PLC	51 patients with DMD (mean age: NR, range: 5–10 years)	Muscle Strength	Improved muscle strength score using an unspecified measure	OXAN treatment

(Continued)

Table 2. (Continued)

Author, year (country)	Study design (level of evidence)†	Interventions, DMD genetic modifiers, and/or DMD mutation types	Patient population	Disease progression outcome category	Disease progression outcome results	Identified prognostic indicator‡
Fenichel et al., 1997 (US) [149]	Case-series (Level 4)	OXAN	10 patients with DMD (mean age: NR, range: 6–9 years)	Muscle Strength	Improved muscle strength as given by manual muscle testing	OXAN treatment
Campbell et al., 2020 (*) [150]	Meta-analysis (Level 1)	ATA and PLC	342 patients with DMD (mean age: NR; range: 8.3–9.0)	Lower Extremity and Motor Function	Improved 6MWD, 4SC and 10WRT	ATA treatment
Cheshyre et al., 2020 (ENG) [151]	Case series (Level 4)	Dp140 deletion	320 patients with DMD (mean age: NR; range: NR)	Lower Extremity and Motor Function	Lower NSAA	DMD genetic modifiers
Clemens et al., 2020 (US and CAN) [152]	Randomised trial (Level 2)	Vitrolarsen (low dose and high dose)	16 patients with DMD (mean age: 7.4; range: NR)	Lower Extremity and Motor Function	Improved 10WRT, 6MWT, STS and NSAA	VIT treatment
Finkel et al., 2021 (NR) [153] Finkel et al., 2018 (NR) [154] Finkel et al., 2019 (NR) [155] Finkel et al., 2019 (NR) [156] Sweeney et al., 2019 (US) [157]	Randomised trial (Level 2)	EDASA and PLC	31 patients with DMD (mean age: 6.1; range: 4–7)	Muscle Strength	Improved lower leg muscle health as given by MRI transverse relaxation time constant	EDASA treatment
Parreira et al., 2010 (NR) [158]	Case series (Level 4)	DFZ and PDN/PRED	90 patients with DMD (mean age: NR, range: 5–12 years)	Muscle Strength	Delay in decline in muscle strength as given by MRC index	Glucocorticoid exposure
Willcocks et al., 2013 (NR) [159]	Follow-up study (Level 3)	DFZ and PDN/PRED	145 patients with DMD (mean age: NR, range: 5–14 years)	Muscle Strength	Delays decline in muscle as given by MRI and MRS transverse relaxation time constant	Glucocorticoid exposure
Goemans et al., 2020 (NR) [160]	Case series (Level 4)	DFZ	316 patients with DMD (median age: 7.9 years, range 4.4–19.4 years)	Lower Extremity and Motor Function	Delay loss of STS	Glucocorticoid exposure
Goemans et al., 2020 (NR) [161]	Historically controlled study (Level 4)	Glucocorticoid, height, weight, BMI	371 patients with DMD (mean age: NR; range: 8.81 and 9.36)	Lower Extremity and Motor Function	Glucocorticoid, including duration, height, weight and BMI predictive of 4SC	Glucocorticoid exposure, height, weight, BMI
Wilton et al., 2013 (US) [162]	Randomised trial (Level 2)	ETEP and PLC	NR patients with DMD (mean age: NR, range: NR)	Lower Extremity and Motor Function	Improvements in 6MWT	ETEP treatment

(Continued)

Table 2. (Continued)

Author, year (country)	Study design (level of evidence)†	Interventions, DMD genetic modifiers, and/or DMD mutation types	Patient population	Disease progression outcome category	Disease progression outcome results	Identified prognostic indicator‡
Signorovitch et al., 2017 (*) [163] Signorovitch et al., 2019 (*) [164] Signorovitch et al., 2019 (*) [165] Signorovitch et al., 2019 (*) [166]	MA (Level 1)	DFZ and PDN/PRED	231 patients with DMD (mean age: NR, range: NR)	Lower Extremity and Motor Function	DFZ improved NSAA, 6MWT, STS, and 4SC compared to PDN/PRED	Glucocorticoid exposure
Gupta et al., 2020 (UK) [167]	Case series (Level 4)	Glucocorticoids (drug NR)	465 patients with DMD (mean age: NR, range: NR)	Lower Extremity and Motor Function	Improved NSAA compared to steroid-naïve	Glucocorticoid exposure
Goemans et al., 2016 (NR) [168] Goemans et al., 2016 (NR) [169]	Open-label study (Level 2)	DRIS and natural history control	12 patients with DMD (mean age: 9.9 years, range: NR) or natural history control (mean age: 9.4 years, range: NR)	Lower Extremity and Motor Function	Improvement in 6MWT	DRIS treatment
Ricotti et al., 2013 (UK) [170] Ricotti et al., 2012 (UK) [75] Ricotti et al., 2011 (UK) [76] Ricotti et al., 2011 (UK) [77]	Case series (Level 4)	PDN/PRED	334–400 patients with DMD (mean age: NR, range: 3–15 years)	Lower Extremity and Motor Function	Improved NSAA in daily PDN-treated compared to intermittent PDN	Glucocorticoid exposure
Schreiber et al., 2018 (FR) [171] Schreiber et al., 2015 (FR) [172] Schreiber et al., 2016 (FR) [173]	Case-control study (Level 4)	DFZ and PDN/PRED	74–76 patients with DMD treated with DFZ and PDN/PRED (mean age: 8 years, range: 6–11 years) or no treatment (mean age: 8 years, range: 6–12 years)	Lower Extremity and Motor Function	Improved muscle function measure	Glucocorticoid exposure
Alfano et al., 2019 (US) [174]	Non-randomised controlled study (Level 3)	DFZ and PDN/PRED	148 patients with DMD (mean age: NR, range: 3–16 years)	Lower Extremity and Motor Function	Improved 10WRT and 100m walking ability	Glucocorticoid exposure
Goemans et al., 2016 (BE) [175]	Case series (Level 4)	DFZ and PDN/PRED	39 patients with DMD (mean age: 9 years, range: 4–16 years)	Lower Extremity and Motor Function	Improved 6MWD including duration of use; those with lower 6MWD showed larger declines Increased height and weight produced larger declines in 6MWD	Glucocorticoid exposure Height; and weight
Goemans et al., 2018 (BE) [176]	Case series (Level 4)	DFZ and PDN/PRED	81 patients with DMD (mean age: 10 years, range: NR)	Lower Extremity and Motor Function	Improved 4SC including duration of use	Glucocorticoid exposure
Mazzone et al., 2014 (NR) [177]	Non-randomised controlled study (Level 3)	DFZ and PDN/PRED	96 patients with DMD (mean age: NR, range: NR)	Lower Extremity and Motor Function	Improved 6MWT; baseline 6MWT >350m showed larger improvements	Glucocorticoid exposure

(Continued)

Table 2. (Continued)

Author, year (country)	Study design (level of evidence)†	Interventions, DMD genetic modifiers, and/or DMD mutation types	Patient population	Disease progression outcome category	Disease progression outcome results	Identified prognostic indicator‡
Shieh et al., 2018 (NR) [178] Shieh et al., 2018 (NR) [178] Darras et al., 2018 (NR) [179] [NR]	Meta-analysis (Level 1)	DFZ and PDN/PRED	147 patients with DMD (mean age: NR, range: NR)	Lower Extremity and Motor Function	Improved 6MWT favouring DFZ	Glucocorticoid exposure
Bushby et al., 2014 (*) [180] Mah et al., 2011 (*) [181] McDonald et al., 2013 (*) [182] McDonald et al., 2014 (*) [183] McDonald et al., 2014 (*) [184]	Randomised trial (Level 2)	ATA	174 patients with DMD (median age: 8 years, IQR: 5–20 years)	Lower Extremity and Motor Function	Low dose ATA improved 6MWT including larger improvements in baseline 6MWT <350m	ATA treatment
McDonald et al., 2017 (*) [185]	Randomised trial (Level 2)	ATA	230 patients with DMD treated with ATA (mean age: 9 years, range: 7–10 years) or PLC (mean age: 9 years, range: 8–10 years)	Lower Extremity and Motor Function	Improved 6MWT in 300–400m baseline 6MWT subgroup	ATA treatment
McDonald et al., 2019 (*) [186] McDonald et al., 2019 (*) [187] Bushby et al., 2016 (NR) [188]	Randomised trial (Level 2)	ATA	228 patients with DMD (mean age: NR, range: NR)	Lower Extremity and Motor Function	Preserved NSAA	ATA treatment
McDonald et al., 2017 (*) [189] McDonald et al., 2018 (*) [190] McDonald et al., 2018 (*) [191]	Randomised trial (Level 2)	ATA	168 patients with DMD (mean age: NR, range: NR)	Lower Extremity and Motor Function	Improved 6MWT, 4SC, and 10WRT	ATA treatment
Mercuri et al., 2019 (NR) [192] Muntoni et al., 2019 (NR) [193]	Non-randomised controlled study (Level 3)	ATA versus external natural history control	187 patients with DMD (mean age: NR, range: NR)	Lower Extremity and Motor Function Loss of Ambulation	Improved STS and 4SC Loss of Ambulation	ATA treatment
Brognia et al., 2019 (*) [194] Brognia et al., 2019 (*) [195]	Case series (Level 4)	Skip exons 44, 45, 51, and 53	92 patients with DMD (mean age: 8 years, range: NR)	Lower Extremity and Motor Function	Exon skipping impacts 6MWT	DMD mutation type

(Continued)

Table 2. (Continued)

Author, year (country)	Study design (level of evidence)†	Interventions, DMD genetic modifiers, and/or DMD mutation types	Patient population	Disease progression outcome category	Disease progression outcome results	Identified prognostic indicator‡
Komaki et al., 2020 (JP) [196]	Randomised trial (Level 2)	TAS-205 and PLC	36 patients with DMD (mean age: 8.3, range: NR)	Lower Extremity and Motor Function	High dose improves muscle volume index	TAS-205 treatment
Hoffman et al., 2019 (NR) [197]	Randomised non-controlled trial (Level 3)	VAM	48 patients with DMD (mean age: NR; range: 4–7 years)	Lower Extremity and Motor Function	Improved 10WRT, STS, 6MWT	VAM treatment
Smith et al., 2020 (*) [198]	Historically controlled study (Level 4)	VAM and external natural history control	122 patients with DMD (mean age: NR, range: 4–7 years)	Lower Extremity and Motor Function	Improved STS, 4SC, NSAA, 10WRT	VAM treatment
Koeks et al., 2017 (*) [199]	Case series (Level 4)	Glucocorticoid exposure	5345 patients with DMD (mean age: NR, range: NR)	Loss of Ambulation	Delay in loss of ambulation	Glucocorticoid exposure; DMD mutation type
				Scoliosis	Reduced scoliosis	
				Respiratory Health and Function	Reduced need for ventilation	
				Cardiac Health and Function	Reduced cardiomyopathy	
		Exon 45 deletion		Loss of Ambulation	Delay in loss of ambulation	
Voit et al., 2014 (*) [200]	Randomised trial (Level 2)	DRIS and PLC	53 patients with DMD (DRIS continuous: mean age: 7.2 years, range: NR and DRIS intermittent: mean age: 7.7 years) or PLC (mean age: 6.9 years, range: NR)	Lower Extremity and Motor Function	Improved STS versus PLC for both continuous and intermittent DRIS. 6MWD was improved in the continuous regimen versus PLC at week 25	DRIS treatment
McDonald et al., 2015 (NR) [201] McDonald et al., 2014 (NR) [202]	Randomised trial (Level 2)	DRIS	535 patients with DMD (mean age: NR, range: NR)	Lower Extremity and Motor Function	Improvement in 6MWT	DRIS treatment
Mayer et al., 2017 (*) [203]	Randomised trial (Level 2)	IDE and PLC	64 patients with DMD (mean age: NR, range: 10–19 years)	Respiratory Health and Function	Reduced decline in pulmonary function as given by FVC	IDE treatment

Note: Argentina (AR). Australia (AU). Belgium (BE). Canada (CA). China (CN). Denmark (DK). Egypt (EG). France (FR). Germany (DE). Holland (NL). India (IN). Italy (IT). Japan (JP). Korea (KR). Not reported (NR). Sweden (SE). Turkey (TR). United Kingdom (UK). United States of America (US). Angiotensin-converting enzyme (ACE). Angiotensin receptor blocker (ARB). Ataluren (ATA). Best standard of care (BSC). Beta2-adrenergic receptor (ADRB2). Beta blocker (BB). Body mass index (BMI). Cluster of differentiation 40 (CD40). Deflazacort (DFZ). Drisapersen (DRIS). Duchenne muscular dystrophy (DMD). Dystrophin protein 140 (Dp140). Edasalonexent (EDASA). End systolic volume (ESV). Eplerenone (EPL). Eteplirsen (ETEP). Forced expiratory volume in 1 second (FEV₁). Four Stair Climb (4SC). Idebenone (IDE). Interquartile range (IQR). Knee-ankle-foot-orthoses (KAFOS). Latent transforming growth factor beta-binding protein 4 (LTBP4). Left ventricular ejection fraction (LVEF). Left ventricular end diastolic dimension (LVEDd). Left ventricular end systolic dimension (LVESd). Left ventricular fractional shortening (LVFS). Left ventricular myocardial performance index (LVMPI). Manual muscle testing (MMT). Maximum expiratory pressure (MEP). Maximum inspiratory pressure (MIP). Maximum voluntary ventilation (MVV). Medical Research Council (MRC). Meridional wall stress (mWS). Meta-analysis (MA). NorthStar Ambulatory Assessment (NSAA). Not applicable (N/A). Optimal Medical Treatment (OMT). Peak cough flow (PCF). Peak expiratory flow rate (PEFR). Peak expiratory flow (PEF). Performance of Upper Limb (PUL). Placebo (PLC). Prednisone (PDN). Prednisolone (PRED). Quantitative muscle testing (QMT). Randomised controlled trial (RCT). Secreted phosphoprotein 1 (SPP1). Single nuclear polymorphisms (SNPs). Six-Minute Walk Test (6MWT). Supine-to-Stand (STS). Ten Metre Walk/Run Test (10WRT). Velocity of circumferential fibre shortening (VCFc). Vamolorone (VAM). Vitrolarsen (VIT).

† OCEBM Level of Evidence.

‡ Indicators with a significant impact on listed disease progression outcome measures.

* Multi-national.

<https://doi.org/10.1371/journal.pone.0265879.t002>

improves peak systolic radial strain in the LV inferolateral wall [Level 2] [111]. BMI is prognostic of cardiomyopathy [Level 4] [41]. Finally, mutations in exons 51 and 52, as well as latent transforming growth factor beta-binding protein 4 (LTBP4), have been shown to be significantly associated with improved or sustained cardiac health and function [Level 4]; [21, 22, 35]; mutations in exons 12, 14, 15, 16, and 17 with increased risk of cardiomyopathy [Level 4] [35]. and deletions in exon 53 with lower LVEF and higher contracture score compared with deletions not treatable by exon 53 skipping [Level 4] [91]. The ACTN3 null genotype is associated with earlier onset of cardiac dysfunction specifically, lower LV dilation-free rate [Level 4] [40].

3.2. Loss of independent ambulation

We identified 35 studies presenting evidence of prognostic indicators of disease progression in DMD measured in terms of loss of independent ambulation [11, 18–20, 38, 46, 51, 61–66, 68–91, 109, 126–130, 192, 193, 199]. In total, nine prognostic indicators were identified: age at diagnosis, age at onset of symptoms, ataluren treatment, DMD genetic modifiers, DMD mutation type, glucocorticoid exposure, eteplirsen treatment, height, and weight (Table 2). Prolonged independent ambulation was found in patients with later onset of symptoms [Level 2]; [83, 84] patients treated with glucocorticoids, including age at treatment initiation, duration of exposure, and pharmacological agent [Level 2]; [11, 18–20, 38, 46, 51, 61–64, 66, 70–82, 88, 199]; ataluren treatment [Level 2] [87, 109, 110, 192, 193]; eteplirsen treatment [Level 2] [126–130]; LTBP4 genotype [Level 2]; [65] lower limb surgery [Level 2] [89, 90] and mutations in exons 44 [Level 2] [11, 67, 73, 86, 88] and exons 3–7 [Level 2]; [11, 88] exon 8 [Level 4] [86, 88]; exon 45 [Level 4] [88, 199]; exon 53 [Level 4] [91]; and the minor allele at rs1883832 [Level 4] [85]. Earlier loss of ambulation was found in patients with TG/GG genotype at the rs28357094 secreted phosphoprotein 1 (SPP1) promoter [Level 2]; [63–66] exon 51 skipping and exon 49–50 deletions [Level 4] [88]; and deletions in the dystrophin gene [Level 4] [61]. Older age at diagnosis (>4 years) has been shown to be a predictor of later loss of ambulation [Level 5] [74]. Finally, greater weight and lower height have been shown to predict delayed time to loss of ambulation in patients treated with glucocorticoids [Level 4] [68, 69].

3.3. Lower extremity and motor function

We found 47 studies presenting evidence of prognostic indicators of disease progression in DMD measured in terms of lower extremity and motor function [47, 51, 71, 75–77, 79–82, 87, 92, 96, 101, 119–131, 136, 138, 140, 141, 143–146, 150–152, 160–186, 188–198, 200–202]. In total, twelve prognostic indicators were identified: ataluren treatment, BMI, DMD genetic modifiers, DMD mutation type, drisapersen treatment, eteplirsen treatment, glucocorticoid exposure, height, TAS-205 treatment, vamorolone treatment, vitrolarsen treatment, and weight (Table 2). Glucocorticoid treatment, including dose, duration of exposure, and regimen, have been shown to be significantly associated with improvement in motor function as measured using the Scott functional score [Level 2] [140, 143], the Vignos scale [Level 4] [71, 96], muscle function measure [Level 4] [171, 172], improvements in the NorthStar Ambulatory Assessment (NSAA) scale [Level 1] [75–77, 131, 163–167, 170], the 6-minute walk test (6MWT) including duration of glucocorticoid exposure [Level 1] [131, 163–166, 175, 177–179], 10 Meter Walk/Run Test (10WRT) [Level 2] [79–81, 92, 96, 138, 174], 100 metre walk/run test [Level 3] [174], 9 metre walk/run test [Level 2] [47, 141, 144, 145], unspecified walking test [Level 4] [71], Supine-to-Stand (STS) test [Level 1] [47, 51, 71, 82, 92, 96, 101, 131, 136, 138, 141, 143, 145, 146, 160, 163–166], and 4-Stairs Climb Test (4SCT) including duration of exposure [Level 1] [47, 71, 82, 92, 96, 101, 131, 138, 141, 144, 145, 161, 163–166, 176]. Ataluren treatment has been shown to be significantly associated with better performance in timed



Fig 2. Evidence of prognostic indicators of disease progression in DMD. Note: Numbers shown in the coloured squares refer to the number of studies reporting of the specific indicator. † Angiotensin-converting enzyme (ACE) inhibitors, beta blockers, and/or diuretics. ‡ Age at treatment initiation, dose, duration of exposure, pharmacological agent, and regimen. Duchenne muscular dystrophy (DMD).

<https://doi.org/10.1371/journal.pone.0265879.g002>

function tests, including the 4SCT [Level 2] [87, 150, 189–193], the STS test [Level 3] [87, 192, 193], the 10WRT [Level 2] [150, 189–191], the NSAA [Level 2] [186–188], and the 6MWT [Level 2]; [150, 180–185, 189–191] treatment with TAS-205 has been shown to increase muscle volume index [Level 2] [196]; treatment with vitrolarsen associated with improved 10WRT, 6MWT, STS and NSAA [Level 2] [152]; treatment with vamorolone improves 6MWT [Level 3] [197] STS [197, 198], 10WRT [197, 198], 4SCT and NSAA [Level 4] [198]; treatment with drisapersen improves STS and 6MWT [Level 2] [168, 169, 200–202]. Eteplirsen treatment improves 6MWT [Level 2] [119–130, 162]. Greater height and weight have been shown to be significantly associated with decline in the 6MWT [Level 4]; [175] similarly, height, weight BMI and glucocorticoid exposure including duration are predictive of 4SC [Level 4] [161]. Finally, skip exon mutations has been shown to be significantly associated with 6MWT performance [Level 4] and [194, 195] Dp140 deletions associated with lower NSAA scores [Level 4] [151].

3.4. Muscle strength

We found 26 studies presenting evidence of prognostic indicators of disease progression in DMD measured in terms of muscle strength [18, 47, 71, 79, 80, 91, 92, 100, 101, 135–149, 153–159]. In total, five prognostic indicators were identified: DMD genetic modifiers, DMD mutation type, edasalonexent, glucocorticoid exposure and oxandrolone (Table 2). Specifically, glucocorticoid treatment, including dose, duration of exposure, and regimen, have been shown to be associated with muscle strength as quantified by the Medical Research Council (MRC) muscle power assessment scale [Level 2] [18, 71, 100, 135, 136, 138, 158], quantitative muscle testing (QMT) [Level 2] [92, 139], muscle mass as given by creatine excretion [Level 2] [137, 139, 142], manual muscle testing (MMT) [Level 2] [92, 139, 142, 145], myometric evaluation [Level 2] [140–146], unspecified muscle strength testing [Level 2] [101, 137], grip and pinch strength [Level 2] [47, 140, 141], Lovett's test [Level 4]; [79, 80] and transverse relaxation time constant [Level 3] [159]. Edasalonexent improves the transverse relaxation time constant [Level 2] [153–157]. Oxandrolone improves muscle strength as given by MMT [Level 4] [149] and an unspecified measure [Level 2] [148]. Finally, GT/GG genotypes at the rs28357094 SPP1 promoter have been shown to be significantly associated with lower composite MRC scores and grip strength compared with the TT genotype [Level 4] [147]. and exon 53 deletions with lower pinch strength compared to all mutations not treatable by exon 53 skipping [Level 4] [91].

3.5. Respiratory health and function

We identified 35 studies presenting evidence of prognostic indicators of disease progression in DMD measured in terms of respiratory health and function [17–19, 21, 22, 28, 38, 47, 71, 77, 82, 92, 94–118, 132–134, 145, 199, 203]. In total, eight prognostic indicators were identified: ataluren treatment, DMD genetic modifiers, DMD mutation type, eteplirsen treatment, glucocorticoid exposure, idebenone treatment, ventilation support and weight (Table 2). Specifically, ataluren treatment has been shown to be significantly associated with improved forced vital capacity (FVC) [Level 2]; [103, 104, 109, 110] glucocorticoid treatment, including dose, duration of exposure, and regimen, with improved maximum inspiratory pressure (MIP) [Level 2] [92, 95, 96], maximum expiratory pressure (MEP) [Level 4] [94, 95], peak cough flow (PCF) [Level 4]; [94, 95] FVC [Level 2]; [17, 18, 21, 22, 38, 47, 71, 77, 82, 96–99, 101, 145] forced expiratory volume in 1 second (FEV₁) [Level 2] [96, 107], maximum voluntary ventilation (MVV) [Level 2], [92, 101, 102], FVC [Level 4] [107], reduced need for ventilation [Level 4] [199] and peak expiratory flow rate (PEFR) [Level 3] [96, 98–100, 107] and pulmonary function preservation [Level 4] [19]. Duration of glucocorticoid exposure has also been linked to declining FVC levels [Level 4] [28]. Eteplirsen has been shown to be associated with an attenuation in respiratory function [Level 4] [108, 118] and reduced decline in FVC [Level 2] [113–117] and MEP [Level 2] [116, 117]; and idebenone reduces the decline in respiratory function as given by FVC [Level 2] [203], FEV₁ [Level 2] [112] and PEF [Level 2] [111, 112, 133] as well as reducing bronchopulmonary adverse events [Level 2] [132]. Weight has been shown to be a significant predictor of need for full-time ventilation support [Level 4] [105]. Ventilation support has been shown to reduce the rate of decline of FVC [Level 4] [106]. Finally, Gly16 beta2--adrenergic receptor (ADRB2) polymorphism has been shown to be significantly associated with increased risk of requiring nocturnal ventilation support (compared with the Arg16 polymorphism) [Level 4] [105]; dystrophin protein 140 (Dp140)-related mutations with lower FVC [Level 4] [21, 22]; mutations in exon 44 with lower FVC, FEV₁ and PEF [Level 4] [107]; skip 51 and 53 mutations with decreased FEV₁, PEF and FVC [Level 4] [107]; splice site, skip 8 and skip 44 with increased FVC [Level 4] [107]; skip 8 and splice site mutations with increased FEV₁ and increased PEF [Level 4] [107]; nonsense mutation with decreased FEV₁

and FVC [Level 4] [107]; dominant G genotype at rs28357094 in the SPP1 promoter with reduced FVC and PEF [Level 4] [107]; additive T genotype at rs1883832 in the CD40 5' untranslated region with reduced FVC, FEV1 and PEF [Level 4] [107]; mutations in exon 8 with improved PEF [Level 4]; [21, 22]; cDMD deficit with worsened respiratory function [Level 3] [134]; and SPP1 and cluster of differentiation 40 (CD40) polymorphisms with reduced FVC and PEF, respectively [Level 4] [21, 22] with both mutations associated with NIV initiation [Level 4] [107].

3.6. Scoliosis

We identified 7 studies presenting evidence of prognostic indicators of disease progression in DMD measured in terms of risk of scoliosis [18, 46–50, 199]. In total, two prognostic indicators were identified: glucocorticoid exposure, and orthoses (Table 2). Specifically, glucocorticoid treatment, including duration of exposure, have been shown to significantly reduce the risk of developing scoliosis, including the degree of scoliosis and the need for spinal surgery [Level 3] [18, 46–50, 199]. Time in orthoses has been shown to be significantly related to scoliosis severity [Level 4] [50].

3.7. Survival

We identified 13 studies presenting evidence of prognostic indicators of disease progression in DMD measured in terms of survival [25, 42, 43, 49, 51–60]. In total, five prognostic indicators were identified: cardiac medication, glucocorticoid exposure, left ventricular assist devices, spinal surgery, and ventilation support (Table 2). Specifically, prolonged survival was found in patients treated with ACE inhibitors [Level 2] [42, 43] ACE inhibitors in combination with beta blockers, including timing of treatment initiation [Level 4]; [52] in patients treated with glucocorticoids (including duration of exposure) [Level 2]; [25, 49, 51] in patients receiving ventilation support [Level 4]; [53–59] and in those undergoing spinal surgery in combination with ventilation support [Level 4] [55].; and in those implanted with left ventricular assist devices in combination with cardiac medication [Level 4] [60].

3.8. Upper extremity function

We identified 5 studies presenting evidence of prognostic indicators of disease progression in DMD measured in terms of upper extremity function [51, 92, 93, 96, 140]. In total, two prognostic indicators were identified: glucocorticoid exposure (including pharmacological agent) and ATL1102 treatment (Table 2). Glucocorticoid treatment has been shown to significantly retain hand-to-mouth function as measured using the Brooke score [Level 2]; [51, 92, 96, 140] and deflazacort (DFZ) exposure significantly delays loss of hand-to-mouth function compared to prednisone (PDN) [Level 2] [51]. Treatment with ATL1102 improves upper limb function in non-ambulant boys as given by performance of upper limb (PUL) scores [Level 2] [93].

4. Discussion

In many disease areas, including DMD, RCTs are commonly unavailable, resulting in the need to indirectly compare treatment effects, for example, by pooling individual patient-level data from multiple sources. However, to derive reliable estimates, it is necessary to ensure that the samples considered are comparable with respect to factors significantly affecting the clinical progression of the disease. To help inform such analyses, the objective of this study was to review and synthesise the published evidence of prognostic indicators of disease progression in DMD. From our literature search, we identified 23 factors significantly affecting disease

progression outcomes in DMD, namely age at diagnosis, age at onset of symptoms, ataluren treatment, ATL1102, BMI, cardiac medication, DMD genetic modifiers, DMD mutation type, drisapersen, edasalonexent, eteplirsen, glucocorticoid exposure, height, idebenone, lower limb surgery, orthoses, oxandrolone, spinal surgery, TAS-205, vamorolone, vitlolarsen, ventilation support, and weight. Of these, two endogenous and two exogenous core prognostic indicators were designated, each supported by a high level of clinical evidence.

The most commonly examined prognostic indicator identified in the literature related to treatment with glucocorticoids—the cornerstone of the current pharmacological management of DMD. This core exogenous factor was found to significantly impact a wide range of disease progression outcomes, including loss of independent ambulation, lower extremity and motor function, muscle strength, respiratory health and function, survival, and upper extremity function (high level of evidence); cardiac health and function (moderate level of evidence); and possibly risk of developing scoliosis (low level of evidence). The body of evidence, spanning a total of 73 individual studies, encompassed various commonly reported features of glucocorticoid therapy, such as age at treatment initiation, dose, duration of exposure, pharmacological agent, and regimen.

The second exogenous core prognostic indicator of disease progression in DMD was cardiac medication, supported by data from a total of 13 studies of varying levels of evidence (Fig 2). As expected, this indicator only concerned cardiac health and function (with the exception of a single study of low evidence level showing an impact on survival). Even so, bearing in mind that cardiomyopathy has emerged as one of the leading causes of death in the aging DMD population in the presence of the routine use of mechanical ventilation support [12], the significance of this indicator should not be underestimated, in particular when comparing samples encompassing patients residing in more advanced stages of the disease.

The two endogenous core prognostic indicators of disease progression in DMD identified in our review were DMD genetic modifiers and DMD mutation type. Although more research is needed to quantify the impact of specific modifiers and mutations, emerging data show that these genetic aspects may play a non-trivial role in the overall progression of the disease. These findings underscore the importance of collecting genetic data from DMD patients as part of studies and patient registries.

Our study is subject to three specific limitations. First, our review did not cover grey literature, which means that evidence for some indicators of disease progression in DMD might have not been fully identified. However, given the comprehensive scope of our search and the limited body of clinical evidence disseminated in non-indexed journals, the impact of this limitation is expected to be negligible (in particular in terms of detecting novel prognostic indicators currently not included in our synthesis). Second, for interpretation of results, it is important to keep in mind that our study did not seek to assess the efficacy or effectiveness of current disease interventions, nor the sensitivity of specific indicators, but rather identify factors that have been shown to significantly alter the clinical progression of DMD (irrespective of magnitude). Although we only considered statistically significant factors, this means that it is not possible to discern the relative clinical importance, or relevance, of included indicators. Finally, the fact that we only reported statistically significant and not also non-significant results means that we were more likely to accept false positive than false negative conclusions of specific indicators. That being said, collating and synthesizing also non-significant results, of which a non-trivial proportion (β) would be expected to be false, were outside the scope of this review.

In conclusion, we identified a total of 23 prognostic indicators of disease progression in DMD, of which cardiac medication, DMD genetic modifiers, DMD mutation type, and glucocorticoid exposure were designated core indicators significantly affecting a wide range of

clinical outcomes. Our up-to-date summary of prognostic indicators in DMD should be helpful to inform the design of comparative analyses and future data collection initiatives in this patient population.

Supporting information

S1 Checklist. PRISMA 2009 checklist.
(PDF)

S1 Appendix. Search strings.
(DOCX)

Author Contributions

Conceptualization: Nermina Ferizovic, Jessica Summers, Igor Beitia Ortiz de Zárate, Christian Werner, Erik Landfeldt, Katharina Buesch.

Data curation: Nermina Ferizovic, Jessica Summers, Erik Landfeldt, Katharina Buesch.

Formal analysis: Nermina Ferizovic, Jessica Summers, Christian Werner, Erik Landfeldt, Katharina Buesch.

Funding acquisition: Nermina Ferizovic, Erik Landfeldt, Katharina Buesch.

Investigation: Nermina Ferizovic, Erik Landfeldt, Katharina Buesch.

Methodology: Nermina Ferizovic, Jessica Summers, Igor Beitia Ortiz de Zárate, Joel Jiang, Erik Landfeldt, Katharina Buesch.

Project administration: Nermina Ferizovic, Erik Landfeldt, Katharina Buesch.

Resources: Nermina Ferizovic, Erik Landfeldt, Katharina Buesch.

Software: Nermina Ferizovic, Erik Landfeldt, Katharina Buesch.

Supervision: Nermina Ferizovic, Erik Landfeldt, Katharina Buesch.

Validation: Nermina Ferizovic, Jessica Summers, Christian Werner, Joel Jiang, Erik Landfeldt, Katharina Buesch.

Visualization: Nermina Ferizovic, Erik Landfeldt, Katharina Buesch.

Writing – original draft: Nermina Ferizovic, Erik Landfeldt, Katharina Buesch.

Writing – review & editing: Nermina Ferizovic, Jessica Summers, Igor Beitia Ortiz de Zárate, Christian Werner, Joel Jiang, Erik Landfeldt, Katharina Buesch.

References

1. Emery AE. The muscular dystrophies. *Lancet*. 2002; 359(9307):687–95. [https://doi.org/10.1016/S0140-6736\(02\)07815-7](https://doi.org/10.1016/S0140-6736(02)07815-7) PMID: 11879882
2. Davies KE, Pearson PL, Harper PS, Murray JM, O'Brien T, Sarfarazi M, et al. Linkage analysis of two cloned DNA sequences flanking the Duchenne muscular dystrophy locus on the short arm of the human X chromosome. *Nucleic Acids Res*. 1983; 11(8):2303–12. <https://doi.org/10.1093/nar/11.8.2303> PMID: 6304647
3. Gao QQ, McNally EM. The Dystrophin Complex: Structure, Function, and Implications for Therapy. *Compr Physiol*. 2015; 5(3):1223–39. <https://doi.org/10.1002/cphy.c140048> PMID: 26140716
4. Flanigan KM, Dunn DM, von Niederhausern A, Soltanzadeh P, Gappmaier E, Howard MT, et al. Mutational spectrum of DMD mutations in dystrophinopathy patients: application of modern diagnostic techniques to a large cohort. *Hum Mutat*. 2009; 30(12):1657–66. <https://doi.org/10.1002/humu.21114> PMID: 19937601

5. Moat SJ, Bradley DM, Salmon R, Clarke A, Hartley L. Newborn bloodspot screening for Duchenne muscular dystrophy: 21 years experience in Wales (UK). *Eur J Hum Genet.* 2013; 21(10):1049–53. <https://doi.org/10.1038/ejhg.2012.301> PMID: 23340516
6. Parent Project Muscular Dystrophy. About Duchenne. Available from: <https://www.parentprojectmd.org/about-duchenne/> Accessed 05/01/2022.
7. van Ruiten HJA, Straub V, Bushby K, Guglieri M. Improving recognition of Duchenne muscular dystrophy: a retrospective case note review. *Archives of Disease in Childhood.* 2014; 99(12):1074. <https://doi.org/10.1136/archdischild-2014-306366> PMID: 25187493
8. Wong SH, McClaren BJ, Archibald AD, Weeks A, Langmaid T, Ryan MM, et al. A mixed methods study of age at diagnosis and diagnostic odyssey for Duchenne muscular dystrophy. *European journal of human genetics.* 2015; 23(10):1294–300. <https://doi.org/10.1038/ejhg.2014.301> PMID: 25626706
9. Blake DJ, Weir A, Newey SE, Davies KE. Function and Genetics of Dystrophin and Dystrophin-Related Proteins in Muscle. *Physiological Reviews.* 2002; 82(2):291–329. <https://doi.org/10.1152/physrev.00028.2001> PMID: 11917091
10. Ryder S, Leadley RM, Armstrong N, Westwood M, de Kock S, Butt T, et al. The burden, epidemiology, costs and treatment for Duchenne muscular dystrophy: an evidence review. *Orphanet Journal of Rare Diseases.* 2017; 12:79. <https://doi.org/10.1186/s13023-017-0631-3> PMID: 28446219
11. Bello L, Morgenroth LP, Gordish-Dressman H, Hoffman EP, McDonald CM, Cirak S, et al. DMD genotypes and loss of ambulation in the CINRG Duchenne Natural History Study. *Neurology.* 2016; 87(4):401–9. <https://doi.org/10.1212/WNL.0000000000002891> PMID: 27343068
12. Landfeldt E, Thompson R, Sejersen T, McMillan HJ, Kirschner J, Lochmüller H. Life expectancy at birth in Duchenne muscular dystrophy: a systematic review and meta-analysis. *Eur J Epidemiol.* 2020; 35(7):643–53. <https://doi.org/10.1007/s10654-020-00613-8> PMID: 32107739
13. Birnkrant DJ, Bushby K, Bann CM, Alman BA, Apkon SD, Blackwell A, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management. *Lancet Neurol.* 2018; 17(4):347–61. [https://doi.org/10.1016/S1474-4422\(18\)30025-5](https://doi.org/10.1016/S1474-4422(18)30025-5) PMID: 29395990
14. Brookhart MA, Schneeweiss S, Rothman KJ, Glynn RJ, Avorn J, Stürmer T. Variable selection for propensity score models. *Am J Epidemiol.* 2006; 163(12):1149–56. <https://doi.org/10.1093/aje/kwj149> PMID: 16624967
15. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ.* 2009; 339:b2700. <https://doi.org/10.1136/bmj.b2700> PMID: 19622552
16. OCEBM Levels of Evidence Working Group. The Oxford Levels of Evidence 2. 2021. <https://www.cebm.ox.ac.uk/resources/levels-of-evidence/ocebmllevels-of-evidence>. Accessed 31 Jan 2021. 2011
17. Biggar WD, Harris VA, Eliasoph L, Alman B. Long-term benefits of deflazacort treatment for boys with Duchenne muscular dystrophy in their second decade. *Neuromuscul Disord.* 2006; 16(4):249–55. <https://doi.org/10.1016/j.nmd.2006.01.010> PMID: 16545568
18. Houde S, Filiatrault M, Fournier A, Dubé J, D'Arcy S, Bérubé D, et al. Deflazacort use in Duchenne muscular dystrophy: an 8-year follow-up. *Pediatr Neurol.* 2008; 38(3):200–6. <https://doi.org/10.1016/j.pediatrneurol.2007.11.001> PMID: 18279756
19. Silversides CK, Webb GD, Harris VA, Biggar DW. Effects of deflazacort on left ventricular function in patients with Duchenne muscular dystrophy. *Am J Cardiol.* 2003; 91(6):769–72. [https://doi.org/10.1016/s0002-9149\(02\)03429-x](https://doi.org/10.1016/s0002-9149(02)03429-x) PMID: 12633823
20. Barber BJ, Andrews JG, Lu Z, West NA, Meaney FJ, Price ET, et al. Oral Corticosteroids and Onset of Cardiomyopathy in Duchenne Muscular Dystrophy. *The Journal of Pediatrics.* 2013; 163(4):1080–4.e1. <https://doi.org/10.1016/j.jpeds.2013.05.060> PMID: 23866715
21. Bello L D'Angelo G, Bruno C, Berardinelli A, Comi G, D'Amico A, et al. P.267 Modifiers of respiratory and cardiac function in the Italian Duchenne muscular dystrophy network and CINRG Duchenne natural history study. *Neuromuscular Disorders.* 2019; 29(Suppl 1):S145.
22. Bello L, D'Angelo G, Villa M, Fusto A, Vianello S, Merlo B, et al. Modifiers of respiratory and cardiac function in the Italian Duchenne muscular dystrophy Network and CINRG Duchenne Natural History Study. *Acta myologica Proceedings Of The XIX Congress Of The Italian Society of Myology: Bergamo, Italy.* 2019; 38(2):103–4.
23. Tandon A, Villa CR, Hor KN, Jefferies JL, Gao Z, Towbin JA, et al. Myocardial fibrosis burden predicts left ventricular ejection fraction and is associated with age and steroid treatment duration in duchenne muscular dystrophy. *J Am Heart Assoc.* 2015; 4(4):e001338. <https://doi.org/10.1161/JAHA.114.001338> PMID: 25814625

24. Zhang L, Liu Z, Hu K-Y, Tian Q-B, Wei L-G, Zhao Z, et al. Early myocardial damage assessment in dystrophinopathies using (99)Tc(m)-MIBI gated myocardial perfusion imaging. *Ther Clin Risk Manag*. 2015; 11:1819–27. <https://doi.org/10.2147/TCRM.S89962> PMID: 26677332
25. Schram G, Fournier A, Leduc H, Dahdah N, Therien J, Vanasse M, et al. All-cause mortality and cardiovascular outcomes with prophylactic steroid therapy in Duchenne muscular dystrophy. *J Am Coll Cardiol*. 2013; 61(9):948–54. <https://doi.org/10.1016/j.jacc.2012.12.008> PMID: 23352781
26. Markham LW, Kinnett K, Wong BL, Woodrow Benson D, Cripe LH. Corticosteroid treatment retards development of ventricular dysfunction in Duchenne muscular dystrophy. *Neuromuscul Disord*. 2008; 18(5):365–70. <https://doi.org/10.1016/j.nmd.2008.03.002> PMID: 18436445
27. Markham LW, Spicer RL, Khoury PR, Wong BL, Mathews KD, Cripe LH. Steroid therapy and cardiac function in Duchenne muscular dystrophy. *Pediatr Cardiol*. 2005; 26(6):768–71. <https://doi.org/10.1007/s00246-005-0909-4> PMID: 15990951
28. Kim S, Zhu Y, Romitti PA, Fox DJ, Sheehan DW, Valdez R, et al. Associations between timing of corticosteroid treatment initiation and clinical outcomes in Duchenne muscular dystrophy. *Neuromuscul Disord*. 2017; 27(8):730–7. <https://doi.org/10.1016/j.nmd.2017.05.019> PMID: 28645460
29. Aikawa T, Takeda A, Oyama-Manabe N, Naya M, Yamazawa H, Koyanagawa K, et al. Progressive left ventricular dysfunction and myocardial fibrosis in Duchenne and Becker muscular dystrophy: a longitudinal cardiovascular magnetic resonance study. *Pediatr Cardiol*. 2019; 40(2):384–92. <https://doi.org/10.1007/s00246-018-2046-x> PMID: 30564867
30. Kwon HW, Kwon BS, Kim GB, Chae JH, Park JD, Bae EJ, et al. The effect of enalapril and carvedilol on left ventricular dysfunction in middle childhood and adolescent patients with muscular dystrophy. *Korean Circ J*. 2012; 42(3):184–91. <https://doi.org/10.4070/kcj.2012.42.3.184> PMID: 22493613
31. Kajimoto H, Ishigaki K, Okumura K, Tomimatsu H, Nakazawa M, Saito K, et al. Beta-blocker therapy for cardiac dysfunction in patients with muscular dystrophy. *Circ J*. 2006; 70(8):991–4. <https://doi.org/10.1253/circj.70.991> PMID: 16864930
32. Thrush P, Viollet L, Flanigan K, Mendell J, Allen H. Natural history of cardiomyopathy in duchenne muscular dystrophy and the effects of angiotensin-converting enzyme inhibitor with or without beta-blocker. *Journal of the American College of Cardiology*. *Journal of the American College of Cardiology*. 2012; 59(Suppl 13):E820.
33. Thrush P, Viollet L, Flanigan K, Mendell J, Allen H. Natural history of cardiomyopathy in Duchenne muscular dystrophy and the effects of angiotensin-converting enzyme inhibitor with or without β -blocker (S15.003). *Neurology*. 2012; 78(Suppl 1):S15 003.
34. Viollet L, Thrush PT, Flanigan KM, Mendell JR, Allen HD. Effects of angiotensin-converting enzyme inhibitors and/or beta blockers on the cardiomyopathy in Duchenne muscular dystrophy. *Am J Cardiol*. 2012; 110(1):98–102. <https://doi.org/10.1016/j.amjcard.2012.02.064> PMID: 22463839
35. Jefferies JL, Eidem BW, Belmont JW, Craigen WJ, Ware SM, Fernbach SD, et al. Genetic Predictors and Remodeling of Dilated Cardiomyopathy in Muscular Dystrophy. *Circulation*. 2005; 112(18):2799–804. <https://doi.org/10.1161/CIRCULATIONAHA.104.528281> PMID: 16246949
36. Raman SV, Hor KN, Mazur W, Halnon NJ, Kissel JT, He X, et al. Eplerenone for early cardiomyopathy in Duchenne muscular dystrophy: a randomised, double-blind, placebo-controlled trial. *Lancet Neurol*. 2015; 14(2):153–61. [https://doi.org/10.1016/S1474-4422\(14\)70318-7](https://doi.org/10.1016/S1474-4422(14)70318-7) PMID: 25554404
37. Matsumura T, Tamura T, Kuru S, Kikuchi Y, Kawai M. Carvedilol can prevent cardiac events in Duchenne muscular dystrophy. *Intern Med*. 2010; 49(14):1357–63. <https://doi.org/10.2169/internalmedicine.49.3259> PMID: 20647648
38. van Ruiten HJA, Jimenez-Moreno AC, Elliot E, Mayhew A, James M, Marini-Bettolo C, et al. Impact of three decades of improvements in standards of care on clinical outcomes in Duchenne muscular dystrophy. *European Journal of Paediatric Neurology*. 2017; 21(Suppl 1):e235–e6.
39. Fayssoil A, Ognà A, Chaffaut C, Lamothe L, Ambrosi X, Nardi O, et al. Natural history of cardiac function in Duchenne and Becker muscular dystrophies on home mechanical ventilation. *Medicine (Baltimore)*. 2018; 97(27):e11381. <https://doi.org/10.1097/MD.00000000000011381> PMID: 29979426
40. Nagai M, Awano H, Yamamoto T, Bo R, Matsuo M, Iijima K. The ACTN3 577XX null genotype is associated with low left ventricular dilation-free survival rate in patients with Duchenne muscular dystrophy. *Journal of Cardiac Failure*. 2020; 26(10):841–8. <https://doi.org/10.1016/j.cardfail.2020.08.002> PMID: 32791185
41. Cheeran D, Khan S, Khara R, Bhatt A, Garg S, Grodin JL, et al. Predictors of death in adults with Duchenne muscular dystrophy-associated cardiomyopathy. *Journal of the American Heart Association*. 2017; 6(10):e006340. <https://doi.org/10.1161/JAHA.117.006340> PMID: 29042427
42. Duboc D, Meune C, Lerebours G, Devaux JY, Vaksman G, Bécane HM. Effect of perindopril on the onset and progression of left ventricular dysfunction in Duchenne muscular dystrophy. *J Am Coll Cardiol*. 2005; 45(6):855–7. <https://doi.org/10.1016/j.jacc.2004.09.078> PMID: 15766818

43. Duboc D, Meune C, Pierre B, Wahbi K, Eymard B, Toutain A, et al. Perindopril preventive treatment on mortality in Duchenne muscular dystrophy: 10 years' follow-up. *Am Heart J*. 2007; 154(3):596–602. <https://doi.org/10.1016/j.ahj.2007.05.014> PMID: 17719312
44. Ishikawa Y, Bach JR, Minami R. Cardioprotection for Duchenne's muscular dystrophy. *American Heart Journal*. 1999; 137(5):895–902. [https://doi.org/10.1016/s0002-8703\(99\)70414-x](https://doi.org/10.1016/s0002-8703(99)70414-x) PMID: 10220639
45. Ramaciotti C, Heistein LC, Coursey M, Lemler MS, Eapen RS, Iannaccone ST, et al. Left ventricular function and response to enalapril in patients with duchenne muscular dystrophy during the second decade of life. *Am J Cardiol*. 2006; 98(6):825–7. <https://doi.org/10.1016/j.amjcard.2006.04.020> PMID: 16950195
46. King WM, Rutten cutter R, Nagaraja HN, Matkovic V, Landoll J, Hoyle C, et al. Orthopedic outcomes of long-term daily corticosteroid treatment in Duchenne muscular dystrophy. *Neurology*. 2007; 68(19):1607–13. <https://doi.org/10.1212/01.wnl.0000260974.41514.83> PMID: 17485648
47. Balaban B, Matthews DJ, Clayton GH, Carry T. Corticosteroid treatment and functional improvement in Duchenne muscular dystrophy: long-term effect. *Am J Phys Med Rehabil*. 2005; 84(11):843–50. <https://doi.org/10.1097/01.phm.0000184156.98671.d0> PMID: 16244521
48. Alman BA, Raza SN, Biggar WD. Steroid Treatment and the Development of Scoliosis in Males with Duchenne Muscular Dystrophy. *J Bone Joint Surg Am*. 2004; 86(3):519–24. <https://doi.org/10.2106/00004623-200403000-00009> PMID: 14996877
49. Lebel DE, Corston JA, McAdam LC, Biggar WD, Alman BA. Glucocorticoid treatment for the prevention of scoliosis in children with Duchenne muscular dystrophy: long-term follow-up. *J Bone Joint Surg Am*. 2013; 95(12):1057–61. <https://doi.org/10.2106/JBJS.L.01577> PMID: 23783200
50. Kinali M, Main M, Eliahoo J, Messina S, Knight RK, Lehovsky J, et al. Predictive factors for the development of scoliosis in Duchenne muscular dystrophy. *Eur J Paediatr Neurol*. 2007; 11(3):160–6. <https://doi.org/10.1016/j.ejpn.2006.12.002> PMID: 17257866
51. McDonald CM, Henricson EK, Abresch RT, Duong T, Joyce NC, Hu F, et al. Long-term effects of glucocorticoids on function, quality of life, and survival in patients with Duchenne muscular dystrophy: a prospective cohort study. *The Lancet*. 2018; 391(10119):451–61.
52. Ogata H, Ishikawa Y, Ishikawa Y, Minami R. Beneficial effects of beta-blockers and angiotensin-converting enzyme inhibitors in Duchenne muscular dystrophy. *Journal of Cardiology*. 2009; 53(1):72–8. <https://doi.org/10.1016/j.jjcc.2008.08.013> PMID: 19167641
53. Rall S, Grimm T. Survival in Duchenne muscular dystrophy. *Acta Myol*. 2012; 31(2):117–20. PMID: 23097602
54. Jeppesen J, Green A, Steffensen BF, Rahbek J. The Duchenne muscular dystrophy population in Denmark, 1977–2001: prevalence, incidence and survival in relation to the introduction of ventilator use. *Neuromuscular Disorders*. 2003; 13(10):804–12. [https://doi.org/10.1016/s0960-8966\(03\)00162-7](https://doi.org/10.1016/s0960-8966(03)00162-7) PMID: 14678803
55. Eagle M, Bourke J, Bullock R, Gibson M, Mehta J, Giddings D, et al. Managing Duchenne muscular dystrophy—The additive effect of spinal surgery and home nocturnal ventilation in improving survival. *Neuromuscular Disorders*. 2007; 17(6):470–5. <https://doi.org/10.1016/j.nmd.2007.03.002> PMID: 17490881
56. Eagle M, Baudouin SV, Chandler C, Giddings DR, Bullock R, Bushby K. Survival in Duchenne muscular dystrophy: improvements in life expectancy since 1967 and the impact of home nocturnal ventilation. *Neuromuscul Disord*. 2002; 12(10):926–9. [https://doi.org/10.1016/s0960-8966\(02\)00140-2](https://doi.org/10.1016/s0960-8966(02)00140-2) PMID: 12467747
57. Gomez-Merino E, Bach JR. Duchenne muscular dystrophy: prolongation of life by noninvasive ventilation and mechanically assisted coughing. *Am J Phys Med Rehabil*. 2002; 81(6):411–5. <https://doi.org/10.1097/00002060-200206000-00003> PMID: 12023596
58. Kiény P, Chollet S, Delalande P, Le Fort M, Magot A, Pereon Y, et al. Evolution of life expectancy of patients with Duchenne muscular dystrophy at AFM Yolaine de Kepper centre between 1981 and 2011. *Annals of physical and rehabilitation medicine*. 2013; 56(6):443–54. <https://doi.org/10.1016/j.rehab.2013.06.002> PMID: 23876223
59. Ishikawa Y, Miura T, Ishikawa Y, Aoyagi T, Ogata H, Hamada S, et al. Duchenne muscular dystrophy: survival by cardio-respiratory interventions. *Neuromuscular Disorders*. 2011; 21(1):47–51. <https://doi.org/10.1016/j.nmd.2010.09.006> PMID: 21144751
60. Adorasio R, D'Amario D, Cantarutti N, Cicienia M, D'Amico A, Baban A, et al. P3446 Left-ventricular assist device as a destination therapy in Duchenne cardiomyopathy: are we ready to change the natural history? *European Heart Journal*. 2019; 40(Supplement_1).

61. Davidson ZE, Kornberg AJ, Ryan MM, Sinclair K, Cairns A, Walker KZ, et al. G.P.77 Deletions in the dystrophin gene predict loss of ambulation before 10years of age in boys with Duchenne muscular dystrophy. *Neuromuscular Disorders*. 2012; 22(9):835.
62. Bonifati DM, Witchel SF, Ermani M, Hoffman EP, Angelini C, Pegoraro E. The glucocorticoid receptor N363S polymorphism and steroid response in Duchenne dystrophy. *Journal of neurology, neurosurgery, and psychiatry*. 2006; 77(10):1177–9. <https://doi.org/10.1136/jnnp.2005.078345> PMID: 16980656
63. Bello L, Gordish-Dressman H, Morgenroth L, Henricson E, Duong T, Hoffman E, et al. Prednisone/prednisolone and deflazacort differ in long term outcomes on ambulation and side effects in the CINRG Duchenne Natural History Study (S50.001). *Neurology*. 2015; 84(Suppl 14):S50 001.
64. Bello L, Gordish-Dressman H, Morgenroth LP, Henricson EK, Duong T, Hoffman EP, et al. Prednisone/prednisolone and deflazacort regimens in the CINRG Duchenne Natural History Study. *Neurology*. 2015; 85(12):1048–55. <https://doi.org/10.1212/WNL.0000000000001950> PMID: 26311750
65. Bello L, Kesari A, Gordish-Dressman H, Cnaan A, Morgenroth LP, Punetha J, et al. Genetic modifiers of ambulation in the Cooperative International Neuromuscular Research Group Duchenne Natural History Study. *Ann Neurol*. 2015; 77(4):684–96. <https://doi.org/10.1002/ana.24370> PMID: 25641372
66. Bello L, Kesari A, Gordish-Dressman H, Punetha J, Henricson E, Duong T, et al. Loss of ambulation in the Cooperative International Neuromuscular Research Group (CINRG) Duchenne Muscular Dystrophy (DMD) cohort is synergistically influenced by glucocorticoid corticosteroid treatment and candidate genetic polymorphisms. *Journal of Neuromuscular Diseases 13th International congress on Neuromuscular Diseases*. 2014; 1(Suppl 1):S124.
67. Bello L, Morgenroth L, Gordish-Dressman H, Hoffman E, McDonald C, Cirak S. DMD genotypes and loss of ambulation in the CINRG Duchenne natural history study. *Neuromuscular Disorders*. 2016; 26:S119. <https://doi.org/10.1212/WNL.0000000000002891> PMID: 27343068
68. Goemans N, Signorovitch J, Sajeev G, Fillbrunn M, Wong H, Ward S, et al. P.202 A composite prognostic score for time to loss of walking ability in Duchenne muscular dystrophy (DMD). *Neuromuscular Disorders*. 2019; 29(Suppl 1):S108.
69. Goemans N, Signorovitch J, Sajeev G, Fillbrunn M, Wong H, Ward SJ, et al. PRO126 A composite prognostic score for time to loss of walking ability in Duchenne muscular dystrophy (DMD). *Value in Health*. 2019; 22(Suppl 3):S864.
70. Kim S, Campbell KA, Fox DJ, Matthews DJ, Valdez R. Corticosteroid Treatments in Males With Duchenne Muscular Dystrophy: Treatment Duration and Time to Loss of Ambulation. *Journal of Child Neurology*. 2015; 30(10):1275–80. <https://doi.org/10.1177/0883073814558120> PMID: 25414237
71. Schara U, Mortier J, Mortier W. Long-Term Steroid Therapy in Duchenne Muscular Dystrophy-Positive Results versus Side Effects. *J Clin Neuromuscul Dis*. 2001; 2(4):179–83. <https://doi.org/10.1097/00131402-200106000-00002> PMID: 19078632
72. van den Bergen JC, Ginjaar HB, van Essen AJ, Pangalila R, de Groot IJ, Wijkstra PJ, et al. Forty-Five Years of Duchenne Muscular Dystrophy in The Netherlands. *J Neuromuscul Dis*. 2014; 1(1):99–109. PMID: 27858664
73. van den Bergen JC, Ginjaar HB, Niks EH, Aartsma-Rus A, Verschuuren JJGM. Prolonged Ambulation in Duchenne Patients with a Mutation Amenable to Exon 44 Skipping. *J Neuromuscul Dis*. 2014; 1:91–4. PMID: 27858662
74. Wang RT, Silverstein Fadlon CA, Ulm JW, Jankovic I, Eskin A, Lu A, et al. Online self-report data for duchenne muscular dystrophy confirms natural history and can be used to assess for therapeutic benefits. *PLoS Curr*. 2014;6. <https://doi.org/10.1371/currents.md.e1e8f2be7c949f9fe81ec6fca1cce6a> PMID: 25635234
75. Ricotti V, Manzur A, Scott E, Muntoni F. Benefits and adverse effects of glucocorticoids in males with Duchenne muscular dystrophy: A UK perspective. *Developmental Medicine & Child Neurology*. 2012; 54(Suppl 1):14–5.
76. Ricotti V, Manzur A, Scott E, Muntoni F. 2FC2.6 Benefits and adverse effects of glucocorticoids in boys with Duchenne Muscular Dystrophy: A UK perspective. *European Journal of Paediatric Neurology*. 2011; 15(Suppl 1):S21.
77. Ricotti V, Manzur AY, Scott E, Muntoni F. P4.5 Benefits and adverse effects of glucocorticoids in boys with Duchenne Muscular Dystrophy. *Neuromuscular Disorders*. 2011; 21(9):705–6.
78. DeSilva S, Drachman DB, Mellits D, Kuncl RW. Prednisone treatment in Duchenne muscular dystrophy. Long-term benefit. *Arch Neurol*. 1987; 44(8):818–22. <https://doi.org/10.1001/archneur.1987.00520200022012> PMID: 3632394
79. Yilmaz O, Karaduman A, Topaloglu H. Prednisolone therapy in Duchenne muscular dystrophy prolongs ambulation and prevents scoliosis. *Eur J Neurol*. 2004; 11(8):541–4. <https://doi.org/10.1111/j.1468-1331.2004.00866.x> PMID: 15272899

80. Yilmaz O, Karaduman A, Aras O, Basoglu B, Topaloglu H. Prednisolone therapy in Duchenne muscular dystrophy prolongs ambulation and prevents scoliosis. *Neuromuscular Disorders*. 2004; 14(8–9):581. <https://doi.org/10.1111/j.1468-1331.2004.00866.x> PMID: 15272899
81. Tunca O, Kabakus O, Herguner A, Karaduman A, T H.. Alternate day prednisone therapy in Duchenne muscular dystrophy. 2001; 11:630.
82. Biggar WD, Gingras M, Fehlings DL, Harris VA, Steele CA. Deflazacort treatment of Duchenne muscular dystrophy. *J Pediatr*. 2001; 138(1):45–50. <https://doi.org/10.1067/mpd.2001.109601> PMID: 11148511
83. Ciafaloni E, McDermott M, Kumar A, Liu K, Pandya S, Westfield C, et al. Age at First Symptoms/Signs and Loss of Ambulation in Duchenne-Becker Muscular Dystrophy: Data from the MD STARNet (IN1-2.002). *Neurology*. 2013; 80(Suppl 7):IN1-2.002.
84. Ciafaloni E, Kumar A, Liu K, Pandya S, Westfield C, Fox DJ, et al. Age at onset of first signs or symptoms predicts age at loss of ambulation in Duchenne and Becker Muscular Dystrophy: Data from the MD STARnet. *J Pediatr Rehabil Med*. 2016; 9(1):5–11. <https://doi.org/10.3233/PRM-160361> PMID: 26966795
85. Bello L, Flanigan KM, Weiss RB, Dunn DM, Swoboda KJ, Gappmaier E, et al. Association study of exon variants in the NF- κ B and TGF β pathways identifies CD40 as a modifier of Duchenne muscular dystrophy. *The American Journal of Human Genetics*. 2016; 99(5):1163–71. <https://doi.org/10.1016/j.ajhg.2016.08.023> PMID: 27745838
86. Haber G, Conway KM, Paramsothy P, Roy A, Rogers H, Ling X, et al. Association of genetic mutations and loss of ambulation in childhood-onset dystrophinopathy. *Muscle & Nerve*. 2021; 63(2):181–91. <https://doi.org/10.1002/mus.27113> PMID: 33150975
87. Mercuri E, Muntoni F, Osorio AN, Tulinius M, Buccella F, Morgenroth LP, et al. Safety and effectiveness of ataluren: comparison of results from the STRIDE Registry and CINRG DMD Natural History Study. *Journal of comparative effectiveness research*. 2020; 9(5):341–60. <https://doi.org/10.2217/ce-2019-0171> PMID: 31997646
88. Wang RT, Barthelemy F, Martin AS, Douine ED, Eskin A, Lucas A, et al. DMD genotype correlations from the Duchenne Registry: Endogenous exon skipping is a factor in prolonged ambulation for individuals with a defined mutation subtype. *Hum Mutat*. 2018; 39(9):1193–202. <https://doi.org/10.1002/humu.23561> PMID: 29907980
89. Forst J, Forst R. Lower limb surgery in Duchenne muscular dystrophy. *Neuromuscul Disord*. 1999; 9(3):176–81. [https://doi.org/10.1016/s0960-8966\(98\)00113-8](https://doi.org/10.1016/s0960-8966(98)00113-8) PMID: 10382913
90. Forst R, Forst J. Importance of lower limb surgery in Duchenne muscular dystrophy. *Arch Orthop Trauma Surg*. 1995; 114(2):106–11. <https://doi.org/10.1007/BF00422837> PMID: 7734231
91. Servais L, Montus M, Guiner CL, Ben Yaou R, Annoussamy M, Moraux A, et al. Non-ambulant Duchenne patients theoretically treatable by exon 53 skipping have severe phenotype. *J Neuromuscul Dis*. 2015; 2(3):269–79. <https://doi.org/10.3233/JND-150100> PMID: 27858743
92. Escolar DM, Hache LP, Clemens PR, Cnaan A, McDonald CM, Viswanathan V, et al. Randomized, blinded trial of weekend vs daily prednisone in Duchenne muscular dystrophy. *Neurology*. 2011; 77(5):444–52. <https://doi.org/10.1212/WNL.0b013e318227b164> PMID: 21753160
93. Tachas G, Desem N, Button P, Coratti G, Pane M, Mercuri E, et al. DMD–THERAPY: P. 284 ATL1102 treatment improves PUL2. 0 in non-ambulant boys with Duchenne muscular dystrophy compared to a natural history control. *Neuromuscular Disorders*. 2020; 30:S129–S30.
94. Daftary AS, Crisanti M, Kalra M, Wong B, Amin R. Effect of long-term steroids on cough efficiency and respiratory muscle strength in patients with Duchenne muscular dystrophy. *Pediatrics*. 2007; 119(2):e320–4. <https://doi.org/10.1542/peds.2006-1400> PMID: 17272595
95. Abresch RT, McDonald CM, Henricson EK, Gustavo N, Hu F, Duong T, et al. P.11.11 Pulmonary function characteristics of boys with Duchenne Muscular Dystrophy by age groups, ambulatory status and steroid use. *Neuromuscular Disorders*. 2013; 23(9):801–2.
96. Henricson EK, Abresch RT, Cnaan A, Hu F, Duong T, Arrieta A, et al. The cooperative international neuromuscular research group Duchenne natural history study: glucocorticoid treatment preserves clinically meaningful functional milestones and reduces rate of disease progression as measured by manual muscle testing and other commonly used clinical trial outcome measures. *Muscle Nerve*. 2013; 48(1):55–67. <https://doi.org/10.1002/mus.23808> PMID: 23649481
97. McDonald CM, Gordish-Dressman H, Henricson EK, Duong T, Joyce NC, Jhavar S, et al. Longitudinal pulmonary function testing outcome measures in Duchenne muscular dystrophy: Long-term natural history with and without glucocorticoids. *Neuromuscul Disord*. 2018; 28(11):897–909. <https://doi.org/10.1016/j.nmd.2018.07.004> PMID: 30336970

98. Henricson E, McDonald C, Gordish-Dressman H, Abresch T, Cnaan A. Steroid use delays but does not prevent loss of pulmonary function in patients with Duchene muscular dystrophy (DMD). *Developmental Medicine & Child Neurology*. 2017; 59(Suppl 4):30.
99. McDonald C, Gordish-Dressman H, Henricson E, Abresch T, Cnaan A. Steroid Use Delays but Does Not Prevent Loss of Pulmonary Function in Patients with Duchene Muscular Dystrophy (DMD). *C105 Disorders of respiratory physiology and sleep in children*. 2017; 195:A6883.
100. Pradhan S, Ghosh D, Srivastava NK, Kumar A, Mittal B, Pandey CM, et al. Prednisolone in Duchenne muscular dystrophy with imminent loss of ambulation. *J Neurol*. 2006; 253(10):1309–16. <https://doi.org/10.1007/s00415-006-0212-1> PMID: 16786214
101. Fenichel GM, Mendell JR, Moxley RT, III, Griggs RC, Brooke MH, Miller JP, et al. A Comparison of Daily and Alternate-Day Prednisone Therapy in the Treatment of Duchenne Muscular Dystrophy. *Archives of Neurology*. 1991; 48(6):575–9. <https://doi.org/10.1001/archneur.1991.00530180027012> PMID: 2039377
102. Dubow J, Cunniff T, Wanaski S, Meyer J. Effect of Deflazacort and Prednisone Versus Placebo on Pulmonary Function in Boys with Duchenne Muscular Dystrophy Who Have Lost Ambulation (I4.009). *Neurology*. 2016; 86(Suppl 16):14.009.
103. Comi GP, Bertini E, Magri F, Luo X, McIntosh J, Ong T, et al. Respiratory function in ataluren-treated, nonambulatory patients with nonsense mutation Duchenne (nmDMD) muscular dystrophy from a long-term extension trial versus untreated patients from a natural history study. *Acta myologica: myopathies and cardiomyopathies*. 2017; 36(2):69.
104. McDonald CM, Tulinius M, Selby K, Kroger H, Luo X, McIntosh J, et al. Lung function in ataluren-treated, non-ambulatory patients with nonsense mutation Duchenne muscular dystrophy from a long-term extension trial versus untreated patients from a natural history study. *Sinapse*. 2016; 16(2):77.
105. Kelley EF, Cross TJ, Snyder EM, McDonald CM, Hoffman EP, Bello L, et al. Influence of $\beta 2$ adrenergic receptor genotype on risk of nocturnal ventilation in patients with Duchenne muscular dystrophy. *Respiratory Research*. 2019; 20(1):221. <https://doi.org/10.1186/s12931-019-1200-1> PMID: 31619245
106. Angliss ME, Sclip KD, Gauld L. Early NIV is associated with accelerated lung function decline in Duchenne muscular dystrophy treated with glucocorticosteroids. *BMJ open respiratory research*. 2020; 7(1):e000517. <https://doi.org/10.1136/bmjresp-2019-000517> PMID: 32079608
107. Bello L, D'Angelo G, Villa M, Fusto A, Vianello S, Merlo B, et al. Genetic modifiers of respiratory function in Duchenne muscular dystrophy. *Annals of clinical and translational neurology*. 2020; 7(5):786–98. <https://doi.org/10.1002/acn3.51046> PMID: 32343055
108. Iff J, Tuttle E, Gerrits C, Gupta D, Zhong Y. DMD–THERAPY: P. 291 Real-world evidence of eteplirsen treatment effects on Duchenne muscular dystrophy related health outcomes using claims data in the United States. *Neuromuscular Disorders*. 2020; 30:S131–S2.
109. McDonald C, Francesco M, Rance M, McIntosh J, Jiang J, Kristensen A, et al. Ataluren delays loss of ambulation and decline in pulmonary function in patients with nonsense mutation Duchenne muscular dystrophy. *Neuromuscular Disorders Presented at the 25TH International Congress of the World Muscle Society (WMS), 2020 (Virtual Congress)*. 2020; 30(S1):S132.
110. McDonald CM F.; Rance M.; Jiang J.; Kristensen A.; Penematsa V.; Bibbiani F.; et al. Ataluren delays loss of ambulation and decline in pulmonary function in patients with nonsense mutation duchenne muscular dystrophy. *Muscle and Nerve*. 2020; 62 (SUPPL 1):S53–S4.
111. Buyse GM, Goemans N, Van den Hauwe M, Thijs D, de Groot IJ, Schara U, et al. Idebeneone as a novel, therapeutic approach for Duchenne muscular dystrophy: results from a 12 month, double-blind, randomized placebo-controlled trial. *Neuromuscular Disorders*. 2011; 21(6):396–405. <https://doi.org/10.1016/j.nmd.2011.02.016> PMID: 21435876
112. Karafilidis J, Mayer H, Leinonen M, Buyse G. Comparison of Longitudinal Changes in Expiratory Respiratory Function Endpoints and Inspiratory Flow Reserve (IFR) in Patients with Duchenne Muscular Dystrophy (DMD). A47 NEUROMUSCULAR DISEASE AND RESPIRATION. *American Thoracic Society International Conference Abstracts: American Thoracic Society*; 2018. p. A1765-A.
113. Khan N, Eliopoulos H, Han L, Kinane TB, Lowes LP, Mendell JR, et al. Eteplirsen treatment attenuates respiratory decline in ambulatory and non-ambulatory patients with Duchenne muscular dystrophy. *J Neuromuscul Dis*. 2019; 6(2):213–25. <https://doi.org/10.3233/JND-180351> PMID: 30856119
114. Khan N, Han L, Kinane B, Gordish-Dressman H, Lowes L, McDonald C. Eteplirsen-treatment attenuates respiratory decline in ambulatory and non-ambulatory patients with duchenne muscular dystrophy: Comparison with natural history cohorts. *Neurology Conference: 71st Annual Meeting of the American Academy of Neurology, AAN*. 2019; 92(15(S1)).
115. Khan N, Han L, Kinane B, Gordish-Dressman H, Lowes L, McDonald C. Respiratory Function Decline in Eteplirsen-treated Patients Diverges From Natural History Comparators Over Time. *J Neuromuscul Dis*. 6(S1):S28.

116. Mendell J, Lowes L, Alfano L, Saoud J, Duda P, Kaye E. GP 112: Pulmonary function is stable through week 120 in patients with Duchenne muscular dystrophy (DMD) treated with exon-skipping drug eteplirsen in phase 2b study. *Neuromuscular Disorders*. 2014; 24(9):828–9.
117. Mendell J, Lowes L, Alfano L, Saoud J, Kaye E. Pulmonary function and safety results at week 120 of exon-skipping drug eteplirsen from the phase 2b study in patients with duchenne muscular dystrophy (DMD). *J Neuromuscul Dis*. 2014; 1:S136.
118. Mendell J, Lowes L, Alfano L, Duda P, Saoud J, Kaye E. Pulmonary function is stable in patients with duchenne muscular dystrophy (DMD) treated with exon-skipping drug eteplirsen in phase 2B study. *Annals of neurology*. 2014; 76:S237.
119. Mendell J, Rodino-Klapac L, Sahenk Z, Roush K, Bird L, Lowes L, et al. Overview of Eteplirsen Clinical Outcomes in Duchenne Muscular Dystrophy (DMD). *Annals of Neurology*. 2014; 76:S63.
120. Mendell JR, Rodino-Klapac L, Sahenk Z, Roush K, Bird L, Lowes L, et al. Eteplirsen in Duchenne Muscular Dystrophy (DMD): 144 week update on six-minute walk test (6MWT) and safety. *Annals of Neurology*. 2014; 76:S237.
121. Mendell JR, Rodino-Klapac L, Sahenk Z, Roush K, Bird L, Lowes L, et al. C-2. Eteplirsen, a Phosphorodiamidate Morpholino Oligomer (PMO) for the Treatment of Duchenne Muscular Dystrophy (DMD): 168 Week Update on Six-Minute Walk Test (6MWT), Pulmonary Function Testing (PFT), and Safety. *Molecular Therapy*. 2015; 23:S16.
122. Kaye E, Mendell J, Rodino-Klapac L, Sahenk Z, Roush K, Bird L, et al. Results at 96 Weeks of a Phase IIb Extension Study of the Exon-Skipping Drug Eteplirsen in Patients with Duchenne Muscular Dystrophy (DMD)(S6. 002). *Neurology*. 2014; 82(10(S1)).
123. Kaye E, Mendell J, Rodino-Klapac L, Sahenk Z, Lowes L, Alfano L, et al. Eteplirsen, a Phosphorodiamidate morpholino oligomer (PMO) for the treatment of Duchenne muscular dystrophy (DMD): Clinical update. *Neuromuscular Disorders*. 2015; 25:S263.
124. Kaye E, Mendell J, Rodino-Klapac L, Sahenk Z, Lowes L, Alfano L, et al. Eteplirsen, a phosphorodiamidate morpholino oligomer (PMO) for the treatment of duchenne muscular dystrophy (DMD). *Annals of Neurology*. 2015; 19:s105.
125. Kaye E, Mendell J, Rodino-Klapac L, Sahenk Z, Roush K, Lowes L, et al. Eteplirsen, a phosphorodiamidate morpholino oligomer (PMO) for the treatment of Duchenne muscular dystrophy (DMD): 3.2 year update on six-minute walk test (6MWT), pulmonary function testing (PFT), and safety. *European journal of paediatric neurology*. 2015; 19:S69.
126. Mendell JR, Khan N, Sha N, Eliopoulos H, McDonald CM, Goemans N, et al. Comparison of long-term ambulatory function in patients with Duchenne muscular dystrophy treated with eteplirsen and matched natural history controls. *J Neuromuscul Dis*. 2021; 8(4):469–79. <https://doi.org/10.3233/JND-200548> PMID: 33523015
127. Mendell J, Goemans N, Rodino-Klapac L, Sahenk Z, Lowes L, Alfano L, et al. Eteplirsen, a phosphorodiamidate morpholino oligomer (PMO) for duchenne muscular dystrophy (DMD): Longitudinal comparison to external controls on six-minute walk test (6MWT) and loss of ambulation (LOA). *Annals of Neurology*. 2016; 80(S20):S415.
128. Mendell J, Goemans N, Rodino-Klapac L, Lowes L, Alfano L, Berry K, et al. Eteplirsen, a Phosphorodiamidate Morpholino Oligomer (PMO) for Duchenne Muscular Dystrophy (DMD): Longitudinal Comparison to External Controls on Six-Minute Walk Test (6MWT) and Loss of Ambulation (LOA)(S42. 004). *Neurology*. 2017; 88(16S1).
129. Mendell J, Goemans N, Rodino-Klapac L, Sahenk Z, Lowes L, Alfano L, et al. Eteplirsen, a Phosphorodiamidate Morpholino Oligomer (PMO) for Duchenne Muscular Dystrophy (DMD): Clinical Update and Longitudinal Comparison to External Controls on Six-Minute Walk Test (6MWT)(S28. 001). *Neurology*. 2016; 86(16S1).
130. Mendell JR, Goemans N, Lowes LP, Alfano LN, Berry K, Shao J, et al. Longitudinal effect of eteplirsen versus historical control on ambulation in D uchenne muscular dystrophy. *Annals of neurology*. 2016; 79(2):257–71. <https://doi.org/10.1002/ana.24555> PMID: 26573217
131. McDonald CM, Sajeev G, Yao Z, McDonnell E, Elfring G, Souza M, et al. Deflazacort vs prednisone treatment for Duchenne muscular dystrophy: A meta-analysis of disease progression rates in recent multicenter clinical trials. *Muscle Nerve*. 2020; 61(1):26–35. <https://doi.org/10.1002/mus.26736> PMID: 31599456
132. Lawrence C, Warnock A, McDonald C, Mayer O, Meier T, Leinonen M, et al. Effect of idebenone on bronchopulmonary adverse events and hospitalizations in patients with Duchene muscular dystrophy (DMD). *Neuromuscular Disorders*. 2018; 28(S1):S16–S7.
133. Rummey C, Meier T, Leinonen M, Hasham S, Voit T, Mayer O. Comparison of home-based versus hospital-based spirometry measurements in duchenne muscular dystrophy. *J Neuromuscul Dis*. 2018; 5:S299–S300.

134. Kanazawa H, Takashima H, Fujishita S, Shibuya N, Tamura T. Correlation between clinical features and deletions of the gene for dystrophin in Duchenne muscular dystrophy. *Jpn J Med.* 1991; 30(1):1–4. <https://doi.org/10.2169/internalmedicine1962.30.1> PMID: 1865568
135. Hussein MR, Hamed SA, Mostafa MG, Abu-Dief EE, Kamel NF, Kandil MR. The effects of glucocorticoid therapy on the inflammatory and dendritic cells in muscular dystrophies. *Int J Exp Pathol.* 2006; 87(6):451–61. <https://doi.org/10.1111/j.1365-2613.2006.00470.x> PMID: 17222213
136. Angelini C, Pegoraro E, Turella E, Intino MT, Pini A, Costa C. Deflazacort in Duchenne dystrophy: study of long-term effect. *Muscle Nerve.* 1994; 17(4):386–91. <https://doi.org/10.1002/mus.880170405> PMID: 8170484
137. Fenichel GM, Florence JM, Pestronk A, Mendell JR, Moxley RT, Griggs RC, et al. Long-term benefit from prednisone therapy in Duchenne muscular dystrophy. *Neurology.* 1991; 41(12):1874–7. <https://doi.org/10.1212/wnl.41.12.1874> PMID: 1745340
138. Hu J, Ye Y, Kong M, Hong S, Cheng L, Wang Q, et al. Daily prednisone treatment in Duchenne muscular dystrophy in southwest China. *Muscle Nerve.* 2015; 52(6):1001–7. <https://doi.org/10.1002/mus.24665> PMID: 25809413
139. Rifai Z, Welle S, Moxley R, Lorenson M, Griggs RC. Effect of prednisone on protein metabolism in Duchenne dystrophy. *Am J Physiol.* 1995; 268(1 Pt 1):E67–74. <https://doi.org/10.1152/ajpendo.1995.268.1.E67> PMID: 7840185
140. Bäckman E, Henriksson KG. Low-dose prednisolone treatment in Duchenne and Becker muscular dystrophy. *Neuromuscul Disord.* 1995; 5(3):233–41. [https://doi.org/10.1016/0960-8966\(94\)00048-e](https://doi.org/10.1016/0960-8966(94)00048-e) PMID: 7633189
141. Connolly AM, Schierbecker J, Renna R, Florence J. High dose weekly oral prednisone improves strength in boys with Duchenne muscular dystrophy. *Neuromuscul Disord.* 2002; 12(10):917–25. [https://doi.org/10.1016/s0960-8966\(02\)00180-3](https://doi.org/10.1016/s0960-8966(02)00180-3) PMID: 12467746
142. Griggs RC, Moxley RT, Mendell JR, Fenichel GM, Brooke MH, Pestronk A, et al. Duchenne dystrophy: randomized, controlled trial of prednisone (18 months) and azathioprine (12 months). *Neurology.* 1993; 43(3 Pt 1):520–7. https://doi.org/10.1212/wnl.43.3_part_1.520 PMID: 8450994
143. Mesa LE, Dubrovsky AL, Corderi J, Marco P, Flores D. Steroids in Duchenne muscular dystrophy—deflazacort trial. *Neuromuscul Disord.* 1991; 1(4):261–6. [https://doi.org/10.1016/0960-8966\(91\)90099-e](https://doi.org/10.1016/0960-8966(91)90099-e) PMID: 1822804
144. Beenakker EA, Fock JM, Van Tol MJ, Maurits NM, Koopman HM, Brouwer OF, et al. Intermittent prednisone therapy in Duchenne muscular dystrophy: a randomized controlled trial. *Arch Neurol.* 2005; 62(1):128–32. <https://doi.org/10.1001/archneur.62.1.128> PMID: 15642859
145. Griggs RC, Moxley RT, Mendell JR, Fenichel GM, Brooke MH, Pestronk A, et al. Prednisone in Duchenne dystrophy. A randomized, controlled trial defining the time course and dose response. *Clinical Investigation of Duchenne Dystrophy Group. Arch Neurol.* 1991; 48(4):383–8. <https://doi.org/10.1001/archneur.1991.00530160047012> PMID: 2012511
146. Merlini L, Cicognani A, Malaspina E, Gennari M, Gnudi S, Talim B, et al. Early prednisone treatment in Duchenne muscular dystrophy. *Muscle Nerve.* 2003; 27(2):222–7. <https://doi.org/10.1002/mus.10319> PMID: 12548530
147. Pegoraro E, Hoffman EP, Piva L, Gavassini BF, Cagnin S, Ermani M, et al. SPP1 genotype is a determinant of disease severity in Duchenne muscular dystrophy. *Neurology.* 2011; 76(3):219–26. <https://doi.org/10.1212/WNL.0b013e318207afeb> PMID: 21178099
148. Fenichel GM, Griggs RC, Kissel J, Kramer TI, Mendell JR, Moxley RT, et al. A randomized efficacy and safety trial of oxandrolone in the treatment of Duchenne dystrophy. *Neurology.* 2001; 56(8):1075–9. <https://doi.org/10.1212/wnl.56.8.1075> PMID: 11320181
149. Fenichel G, Pestronk A, Florence J, Robison V, Hemelt V. A beneficial effect of oxandrolone in the treatment of Duchenne muscular dystrophy. *Neurology.* 1997; 48(5):1225. <https://doi.org/10.1212/wnl.48.5.1225> PMID: 9153447
150. Campbell C, Barohn RJ, Bertini E, Chabrol B, Comi GP, Darras BT, et al. Meta-analyses of ataluren randomized controlled trials in nonsense mutation Duchenne muscular dystrophy. *Journal of comparative effectiveness research.* 2020; 9(14):973–84. <https://doi.org/10.2217/cer-2020-0095> PMID: 32851872
151. Chesshyre M, Ridout D, Abbott L, Ayyar Gupta V, Maresh K, Manzur A, et al. The role of dystrophin brain isoforms on early motor development and motor outcomes in young children with Duchenne muscular dystrophy. *Developmental Medicine and Child Neurology.* 2020; 62(S1):P110.
152. Clemens PR, Rao VK, Connolly AM, Harper AD, Mah JK, Smith EC, et al. Safety, tolerability, and efficacy of viltolarsen in boys with Duchenne muscular dystrophy amenable to exon 53 skipping: a phase 2 randomized clinical trial. *JAMA neurology.* 2020; 77(8):982–91. <https://doi.org/10.1001/jamaneurol.2020.1264> PMID: 32453377

153. Finkel RS, Finanger E, Vandeborne K, Sweeney HL, Tennekoon G, Shieh PB, et al. Disease-modifying effects of edasalonexent, an NF- κ B inhibitor, in young boys with Duchenne muscular dystrophy: Results of the MoveDMD phase 2 and open label extension trial. *Neuromuscular Disorders*. 2021; 31(5):385–96. <https://doi.org/10.1016/j.nmd.2021.02.001> PMID: 33678513
154. Finkel R, Vandeborne KH, Sweeney HL, Finanger E, Tennekoon G, Shieh P, et al. MoveDMD@: Positive Effects of Edasalonexent, an NF- κ B Inhibitor, in 4 to 7-Year Old Patients with Duchenne Muscular Dystrophy in Phase 2 Study with an Open-Label Extension (S29. 006). *Neurology*. 2018; 90(15(S1)).
155. Finkel R, Vandeborne K, Sweeney HL, Finanger E, Tennekoon G, Shieh P, et al. Edasalonexent, an NF- κ B Inhibitor, Slows Longer-Term Disease Progression on Multiple Functional and MRI Assessments Compared to Control Period in 4 to 7-Year Old Patients with Duchenne Muscular Dystrophy (S51. 006). *Neurology*. 2019; 92(15(S1)).
156. Finkel R, Vandeborne K, Sweeney H, Finanger E, Tennekoon G, Shieh P, et al. O. 42Treatment of young boys with Duchenne muscular dystrophy with the NF- κ B inhibitor edasalonexent showed a slowing of disease progression as assessed by MRI and functional measures. *Neuromuscular Disorders*. 2019; 29:S208.
157. Sweeney H, Vandeborne K, Finkel R, Finanger E, Tennekoon G, Willcocks R, et al. MoveDMD, a Phase 2 with Open-Label Extension Study of Treatment of Young Boys with Duchenne Muscular Dystrophy with the NF- κ B Inhibitor Edasalonexent Showed a Slowing of Disease Progression as Assessed by MRI and Functional Measures. *J Neuromuscul Dis*. 2019; 6(S2):S53–S4.
158. Parreira SL, Resende MB, Zanoteli E, Carvalho MS, Marie SK, Reed UC. Comparison of motor strength and function in patients with Duchenne muscular dystrophy with or without steroid therapy. *Arq Neuropsiquiatr*. 2010; 68(5):683–8. <https://doi.org/10.1590/s0004-282x2010000500002> PMID: 21049175
159. Willcocks RJ, Forbes SC, Finanger EL, Russman BS, Lott DJ, Senesac CR, et al. P. 13.5 Magnetic resonance imaging and spectroscopy detect changes with age, corticosteroid treatment, and functional progression in DMD. *Neuromuscular Disorders*. 2013; 23(9):810.
160. Goemans N, McDonald C, Signorovitch J, Sajeev G, Fillbrunn M, Wong H, et al. DMD & BMD—CLINICAL: P. 55 Prognostic factors for loss of ability to rise from supine in Duchenne muscular dystrophy (DMD). *Neuromuscular Disorders*. 2020; 30:S63–S4.
161. Goemans N, Wong B, Van den Hauwe M, Signorovitch J, Sajeev G, Cox D, et al. Prognostic factors for changes in the timed 4-stair climb in patients with Duchenne muscular dystrophy, and implications for measuring drug efficacy: A multi-institutional collaboration. *PloS one*. 2020; 15(6):e0232870. <https://doi.org/10.1371/journal.pone.0232870> PMID: 32555695
162. Wilton S, editor An update on DMD exon skipping trials: Making more sense with splice switching antisense oligonucleotides. *Clinical and Experimental Pharmacology and Physiology*; 2013; Hangzhou, China: Cell Therapy and Stem Cell Biology.
163. Signorovitch JE, Sajeev G, McDonnell E, Yao Z. Deflazacort or Prednisone Treatment for Duchenne Muscular Dystrophy: A Meta-Analysis of Disease Progression Rates in Recent Multicenter Clinical Trials. *Value in Health*. 2017; 20(9):A718.
164. Signorovitch J, Schilling T, Sajeev G, Yao Z, McDonnell E, Elfring G, et al. Deflazacort or Prednisone Treatment for Duchenne Muscular Dystrophy: A Meta- Analysis of Disease Progression Rates in Recent Multicenter Clinical Trials (P1.6–066). *Neurology*. 2019; 92(Suppl 15):P1.6–066.
165. Signorovitch J, Sajeev G, Yao Z, McDonnell E, Elfring G, Trifillis P, et al. Deflazacort or prednisone treatment for duchenne muscular dystrophy: A meta-analysis of disease progression rates in two multicenter clinical trials. *Muscle and Nerve*. 2019; 60 (SUPPL 2):S13. <https://doi.org/10.1002/mus.26736> PMID: 31599456
166. Signorovitch J, Sajeev G, Yao Z, McDonnell E, Elfring G, Trifillis P, et al. Deflazacort or prednisone treatment for duchenne muscular dystrophy: A meta-analysis of disease progression rates in two multicenter clinical trials. *Annals of Neurology*. 2019; 86 (Supplement 23):S128–S9. <https://doi.org/10.1002/mus.26736> PMID: 31599456
167. Gupta VA, Abbott L, Chesshyre M, Main M, Baranello G, Scoto M, et al. DMD & BMD—CLINICAL: P.59 Functional progression in young DMD. *Neuromuscular Disorders*. 2020; 30 (Supplement 1):S65.
168. Goemans N, Tulinius M, Kroksmark A, Van Den Hauwe M, Lin Z, Wang SC, G. Longitudinal Effect of Drisapersen Versus Historical Controls on Ambulation in Duchenne Muscular Dystrophy. *J Neuromuscul Dis*. 2016; 3(S1):S137.
169. Goemans NM, Tulinius M, Van den Hauwe M, Kroksmark A-K, Buyse G, Wilson RJ, et al. Long-term efficacy, safety, and pharmacokinetics of drisapersen in Duchenne muscular dystrophy: results from an open-label extension study. *PloS one*. 2016; 11(9):e0161955. <https://doi.org/10.1371/journal.pone.0161955> PMID: 27588424

170. Ricotti V, Ridout DA, Scott E, Quinlivan R, Robb SA, Manzur AY, et al. Long-term benefits and adverse effects of intermittent versus daily glucocorticoids in boys with Duchenne muscular dystrophy. *J Neurol Neurosurg Psychiatry*. 2013; 84(6):698–705. <https://doi.org/10.1136/jnnp-2012-303902> PMID: 23250964
171. Schreiber A, Brochard S, Rippert P, Fontaine-Carbonnel S, Payan C, Poirot I, et al. Corticosteroids in Duchenne muscular dystrophy: impact on the motor function measure sensitivity to change and implications for clinical trials. *Developmental Medicine & Child Neurology*. 2018; 60(2):185–91. <https://doi.org/10.1111/dmcn.13590> PMID: 28990163
172. Schreiber-Bontemps A, Brochard S, Fontaine-Carbonnel S, Chabrier S, Gautheron V, Peudenier S, et al. Promoting the use of Motor Function Measure (MFM) as outcome measure in patients with Duchenne Muscular Dystrophy (DMD) treated by corticosteroids. *Annals of Physical and Rehabilitation Medicine*. 2015; 58(Suppl 1):e139–e40.
173. Schreiber A, Brochard S, Rippert P, Fontainecarbonel S, Peudenier S, Payan C, et al. The natural history of Duchenne muscular dystrophy with corticosteroids using the Motor Function Measure. *Developmental Medicine & Child Neurology*. 2016; 58(S6):22–6.
174. Alfano L, Miller N, Iammarino M, Moore-Clingenpeel M, Waldrop M, Flanigan K, et al. P.192 The 100 meter timed test: responsiveness to change, predicting loss of ambulation, and data-driven phenotypes. *Neuromuscular Disorders*. 2019; 29(Suppl 1):S105.
175. Goemans N, vanden Hauwe M, Signorovitch J, Swallow E, Song J, Collaborative Trajectory Analysis P. Individualized Prediction of Changes in 6-Minute Walk Distance for Patients with Duchenne Muscular Dystrophy. *PLOS ONE*. 2016; 11(10):e0164684. <https://doi.org/10.1371/journal.pone.0164684> PMID: 27737016
176. Goemans N, Vanden Hauwe M, Signorovitch J, Sajeev G, Yao Z, Jenkins M, et al. Development of a prognostic model for 1-year change in timed 4 stair-climb in duchenne patients. *J Neuromuscul Dis*. 2018; 5(Suppl 1):S196.
177. Mazzone ES, Pane M, Sivo S, Palermo C, Sormani MP, Messina S, et al. T.P.4: Long term natural history data in ambulant boys with Duchenne muscular dystrophy: 36month changes. *Neuromuscular Disorders*. 2014; 24(9):861.
178. Shieh P O'Mara E, Elfring G, Trifillis P, Santos C, Parsons J, et al. Meta-analyses of deflazacort vs prednisone/prednisolone in patients with nonsense mutation duchenne muscular dystrophy. *Muscle & Nerve*. 2018; 58(Suppl 1):S1–S20.
179. Darras B, Riebling P, O'Mara E, Elfring G, Luo X, Trifillis P, et al. Meta-Analysis of Deflazacort vs Prednisone/Prednisolone in Patients with Duchenne Muscular Dystrophy (P2.325). *Neurology*. 2018; 90(Suppl 15):P2.325.
180. Bushby K, Finkel R, Wong B, Barohn R, Campbell C, Comi GP, et al. Ataluren treatment of patients with nonsense mutation dystrophinopathy. *Muscle & nerve*. 2014; 50(4):477–87. <https://doi.org/10.1002/mus.24332> PMID: 25042182
181. Mah JK, Selby K, Campbell C, Reha A, Elfring G, Morsy M, et al. Safety and Efficacy of low-dose ataluren in boys with nonsense mutation dystrophinopathy. *Canadian Journal of Neurological Sciences / Journal Canadien des Sciences Neurologiques*. 2011; 38(Suppl 1):S21.
182. McDonald CM, Henricson EK, Abresch RT, Elfring GL, Barth J, Peltz SW, et al. P.11.19 Phase 2b, dose-ranging study of ataluren (PTC124®) in nonsense mutation Duchenne muscular dystrophy—results of a post hoc analysis of change in %-predicted 6-min walk distance. *Neuromuscular Disorders*. 2013; 23(9):804.
183. McDonald CM, Reha A, Elfring GL, Peltz SW, Spiegel R. T.P.5: Timed function tests and other physical function outcomes in Ataluren-treated patients with nonsense mutation Duchenne Muscular Dystrophy (nmDMD). *Neuromuscular Disorders*. 2014; 24(9):861.
184. McDonald CM, Reha A, Elfring GL, Peltz SW, Spiegel RJ. Timed function tests and other physical function outcomes in ataluren-treated patients with nonsense mutation duchenne muscular dystrophy (nmDMD). 2014; 76(Suppl 18):S236–S7.
185. McDonald CM, Campbell C, Torricelli RE, Finkel RS, Flanigan KM, Goemans N, et al. Ataluren in patients with nonsense mutation Duchenne muscular dystrophy (ACT DMD): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2017; 390(10101):1489–98. [https://doi.org/10.1016/S0140-6736\(17\)31611-2](https://doi.org/10.1016/S0140-6736(17)31611-2) PMID: 28728956
186. McDonald C, Wei L-J, Elfring G, Schilling T, Trifillis P, McIntosh J, et al. Preservation of Function over time as Measured by North Star Ambulatory Assessment in Ambulatory Boys with Nonsense Mutation Muscular Dystrophy Treated with Ataluren (S51.004). *Neurology*. 2019; 92(Suppl 15):S51.004.
187. McDonald C, Wei L, Elfring G, Trifillis P, Able R, Souza M, et al. Preservation of function over time as measured by North Star ambulatory assessment in ambulatory boys with nonsense mutation muscular dystrophy treated with ataluren. *Muscle and Nerve*. 2019; 60 (SUPPL 1):S58.

188. Bushby K, Kirschner J, Luo X, Elfring G, Kroger H, Riebling P, et al. Results of North Star Ambulatory Assessments (NSAA) in the Phase 3 Ataluren Confirmatory Trial in Patients with Nonsense Mutation Duchenne Muscular Dystrophy (ACT DMD) (115.008). *Neurology*. 2016; 86(16 Supplement):115.008.
189. McDonald CM, Riebling P, Souza M, Elfring GL, McIntosh J, Ong T, et al. Use of ≥ 5 -second threshold in baseline time to stand from supine to predict disease progression in Duchenne muscular dystrophy. *European Journal of Paediatric Neurology*. 2017; 21(Suppl 1):e237.
190. McDonald CM, Souza M, Elfring GL, McIntosh J, Werner C, Trifillis P, et al. Use of a ≥ 5 -second threshold in baseline time to stand from supine to predict disease progression in Duchenne muscular dystrophy. *Neuromuscular Disorders*. 2018; 28(Suppl 1):S12.
191. McDonald CM, Souza M, Elfring GL, Trifillis P, McIntosh J, Peltz SW, et al. Use of a ≥ 5 -second threshold in baseline time to stand from supine to predict progression in DMD. *J Neuromuscul Dis*. 2018; 5(Suppl 1):S199.
192. Mercuri E, Buccella F, Desguerre I, Kirschner J, Muntoni F, Nascimento Osorio A, et al. Timed-function test data in patients with duchenne muscular dystrophy from the strategic targeting of registries and international database of excellence (STRIDE) registry and the CINRG natural history study: A matched cohort analysis. *Annals of Neurology*. 2019; 86 (Supplement 23):S126–S7.
193. Muntoni F, Buccella F, Desguerre I, Kirschner J, Mercuri E, Nascimento Osorio A, et al. Age at loss of ambulation in patients with duchenne muscular dystrophy from the stride registry and the CINRG natural history study: A matched cohort analysis. *Annals of Neurology*. 2019; 86 (Supplement 23):S127.
194. Brogna C, Coratti G, Pane M, Ricotti V, Messina S, D'Amico A, et al. Long-term natural history data in Duchenne muscular dystrophy ambulant patients with mutations amenable to skip exons 44, 45, 51 and 53. *PLOS ONE*. 2019; 14(6):e0218683. <https://doi.org/10.1371/journal.pone.0218683> PMID: 31237898
195. Brogna C, Coratti G, Pane M, Ricotti V, Messina S, Bruno C, et al. P.148 Long-term natural history data in Duchenne muscular dystrophy ambulant patients with mutations amenable to skip exons 44, 45, 51 and 53. *Neuromuscular Disorders*. 2019; 29(Suppl 1):S91.
196. Komaki H, Maegaki Y, Matsumura T, Shiraishi KA, H., Nakamura A, Kinoshita S, et al. Early phase 2 trial of TAS-205 in patients with Duchenne muscular dystrophy. *Annals of Clinical and Translational Neurology*. 2020; 7(2):181–90. <https://doi.org/10.1002/acn3.50978> PMID: 31957953
197. Hoffman EP, Schwartz BD, Mengle-Gaw LJ, Smith EC, Castro D, Mah JK, et al. Vamorolone trial in Duchenne muscular dystrophy shows dose-related improvement of muscle function. *Neurology*. 2019; 93(13):E1312–E23. <https://doi.org/10.1212/WNL.00000000000008168> PMID: 31451516
198. Smith EC, Conklin LS, Hoffman EP, Clemens PR, Mah JK, Finkel RS, et al. Efficacy and safety of vamorolone in Duchenne muscular dystrophy: An 18-month interim analysis of a non-randomized open-label extension study. *PLoS Med*. 2020; 17(9):e1003222. <https://doi.org/10.1371/journal.pmed.1003222> PMID: 32956407
199. Koeks Z, Bladen CL, Salgado D, Van Zwet E, Pogoryelova O, McMacken G, et al. Clinical outcomes in Duchenne muscular dystrophy: a study of 5345 patients from the TREAT-NMD DMD global database. *J Neuromuscul Dis*. 2017; 4(4):293–306. <https://doi.org/10.3233/JND-170280> PMID: 29125504
200. Voit T, Topaloglu H, Straub V, Muntoni F, Deconinck N, Campion G, et al. Safety and efficacy of drisapersen for the treatment of Duchenne muscular dystrophy (DEMAND II): an exploratory, randomised, placebo-controlled phase 2 study. *Lancet Neurol*. 2014; 13(10):987–96. [https://doi.org/10.1016/S1474-4422\(14\)70195-4](https://doi.org/10.1016/S1474-4422(14)70195-4) PMID: 25209738
201. McDonald C, Goemans N, Voit T, Wilson R, Wardell C, Campion G. Drisapersen: An overview of the EXON51 skipping antisense oligonucleotide clinical program to date in duchenne muscular dystrophy (DMD). *Neurology Conference: 67th American Academy of Neurology Annual Meeting, AAN*. 2015; 84(S14).
202. McDonald C, Mercuri E, Goemans N, Voit T, Wilson R, Wardell C, et al. Drisapersen: An overview of the clinical programme to date in Duchenne Muscular Dystrophy (DMD). *Neuromuscular Disorders*. 2014; 24(9–10):922.
203. Mayer OH, Leinonen M, Rummey C, Meier T, Buyse GM. Efficacy of Idebeneone to Preserve Respiratory Function above Clinically Meaningful Thresholds for Forced Vital Capacity (FVC) in Patients with Duchenne Muscular Dystrophy. *J Neuromuscul Dis*. 2017; 4(3):189–98. <https://doi.org/10.3233/JND-170245> PMID: 28869486