Full Title: Prevalence of Muscular Dystrophies: A Systematic Literature Review

Short Title: Prevalence of Muscular Dystrophies

Alice Theadom[1], Miriam Rodrigues[2,3], Richard Roxburgh[2,] Shivanthi Balalla[1,] Chris Higgins[3], Rohit Bhattacharjee[1], Kelly Jones[1], Rita Krishnamurthi[1], Valery Feigin[1]

[1] National Institute for Stroke and Applied Neuroscience, Auckland University of Technology, Auckland, New Zealand

[2] Neurology Department, Auckland City Hospital, Auckland, New Zealand

[3] Muscular Dystrophy Association of New Zealand, Auckland, New Zealand

Words: 2370

Figures: 2

Tables: 3

Corresponding author:
Alice Theadom, PhD
Senior Research Fellow
National Institute for Stroke and Applied Neuroscience
AUT University, 90 Akoranga Drive
Private Bag 92006, Auckland, NZ,
Telephone: 0064 9 921 9999 X7805
Email: alice.theadom@aut.ac.nz
Fax: 0064 9 921 9620

ABSTRACT

Background: Determining prevalence of neuromuscular disorders for the general population is important to identify the scope of burden on society and enable comparisons with other health conditions. This systematic review aims to identify and collate the findings of studies published between 1960 and 2013 on the prevalence of all types of muscular dystrophies.

Summary: Relevant articles were identified through electronic database searches and manual searches of reference lists. There were 38 articles from across 19 countries that met the inclusion criteria. The total combined prevalence for all muscular dystrophies for studies classified as having a low risk of bias ranged between 19.8 and 25.1 per 100,000 person-years. Myotonic dystrophy (0.5-18.1 per 100,000), Duchenne muscular dystrophy (1.7-4.2) and facioscapulohumeral muscular dystrophy (3.2-4.6 per 100,000) were found to be the most common types of disorder. There was wide variation in study methodology, case ascertainment and verification procedures and populations studied, all of which may contribute to the wide prevalence range, in addition to the likely variation in prevalence by country.

Key Messages: Greater consistency in the conduct and reporting of neuroepidemiological studies is urgently needed to enable comparisons to be made between studies, countries and over time.

KEY WORDS

muscular dystrophy, myotonic dystrophy, epidemiology, prevalence, systematic review

INTRODUCTION

Muscular dystrophies are inherited disorders caused by mutations in a number of genes. These genetic mutations cause either a dysfunction in, or lack of, proteins that are essential for muscle cell stability, leading to progressive destruction and weakness in the muscles.[1, 2] The term muscular dystrophy encompasses a range of disorders including Duchenne, Becker, congenital, myotonic, Emery-Dreifuss, facioscapulohumeral, oculopharyngeal and limb-girdle muscular dystrophies.[1] Each disorder varies in severity, age of onset, pattern of inheritance and affected muscle groups and other organs.[3] Symptoms can include: muscle weakness and wasting; joint stiffness with reduced range of movement; recurrent chest infections and daytime somnolence when respiratory muscles are involved; shortness of breath and ankle swelling when cardiomyopathy occurs; faints, collapses and even sudden death when the cardiac conduction system is involved; facial weakness with drooping of the eyelids, pain and swallowing difficulties may also occur.[1] In myotonic dystrophy not only are muscle weakness and myotonia clinical features, but nearly every system including the endocrine system is affected.[4] Across the muscular dystrophies, symptoms commonly lead to difficulties with physical activity including walking and functioning in every-day life, reducing quality of life and placing a high strain on both the individual and their family.[5, 6]

Diagnosis of muscular dystrophies requires a comprehensive medical history, noting particularly the distribution of weakness, age of onset, family history and disease specific features. A physical examination needs to document the distribution of weakness and atrophy (face, distal or proximal or specific muscle groups), the presence of contractures and other specific features such as myotonia. These findings together with investigations such as serum

creatine phosphokinase, electromyography and muscle biopsy may direct testing towards a specific genetic diagnosis.[7] Prognosis varies across the muscular dystrophies with some patients experiencing mild, though usually progressive symptoms, while others experience severe disability and early mortality.[1] Advances have been made over the last decade in the treatment and management of the muscular dystrophies but there remains no cure. Current treatment aims to manage symptoms, slow progression and prevent complications.[1]

In order to ensure that information, resources and appropriate services are available to those affected by muscular dystrophies, accurate information on the prevalence of muscular dystrophies is needed to address both the common and disease-specific needs of the different disorders. Synthesising evidence in a systematic review helps to quantify both the burden and risk of disease across countries.[8] A systematic review of the prevalence of Duchenne and Becker muscular dystrophy has recently been undertaken, which has provided details of prevalence per 100,000 of the male population.[9] Whilst Duchenne and Becker muscular dystrophy occur predominantly in males, prevalence estimates need to also be available in relation to the general population to enable calculation of the scope of the burden for society. Data on the scope of burden can be critical in informing the allocation of research funds and development of new treatments. Additionally prevalence estimates are needed for all types of the muscular dystrophies. This systematic review aims to determine the prevalence of all muscular dystrophies within the general population.

METHODS

To determine the prevalence of muscular dystrophies, a systematic literature search of Medline, CINAHL, Psychology and behavioural sciences collection, ProQuest, Scopus, Web of Science between 01/01/1960 and 30/10/2013 was conducted. Search terms included; "muscular dystroph*" OR "myotonic dystrophy" AND "epidemiol*" OR "proportion" OR "prevalence" in the title or abstract. Hand searches of reference lists of identified articles were also conducted.

For inclusion into the systematic review, studies were required to present prevalence or data enabling calculation of crude prevalence (including number of cases identified and estimates of the denominator population) on muscular dystrophies and/or its various types. Only studies reporting on cases ascertained from a general population sample (e.g. not restricted by gender or ethnicity) were included to enable comparison with other disorders, and between populations, to ensure representativeness of the findings. Muscular dystrophy was defined as an inherited group of disorders caused by defects in the muscle membrane or supporting proteins leading to progressive weakness of the muscles.[1] Types of muscular dystrophies included in this review were dystrophinopathies (Duchenne, Becker and manifesting female carriers), myotonic dystrophy (both types 1 and 2), facioscapulohumeral, limb-girdle (all types), Emery-Dreifuss, oculpharyngeal and congenital (all types).[10-14] Spinal muscular atrophies and other neuromuscular disorders were not included in order to maintain a focus on disorders where the primary defect is in the muscle or its supporting membranes. Only abstracts and/or full articles published in English were considered for inclusion into the review.

Studies were excluded if they were published prior to 1960. This criteria was set as formal descriptions of many neuromuscular disorders were not established until the late 1950s and it would be difficult to make comparisons between earlier diagnoses and current diagnostic descriptions. Studies citing birth prevalence were also excluded as they more accurately reflect incidence of neuromuscular disorders among births, as opposed to prevalence in the general population. A founder effect occurs when there is a loss of genetic variation when new colonies are established from a few members of the original population resulting in extremely high prevalence.[15] Studies reporting a founder effect were therefore also excluded from the review to prevent prevalence estimates being skewed. Titles and abstracts for all citations were assessed for possible inclusion in the review. Full articles were obtained for studies meeting the inclusion criteria where possible. Duplicate publications reporting on the same data were removed.

Each identified study was classified as having a low, unclear (if insufficient information was available to determine risk) or high risk of under or over estimating prevalence. A study was assessed as having a high risk of bias for this review if the study population was restricted (e.g. <18 years), if cases were likely to be missed by the case ascertainment approaches used (e.g. household survey or reliance on clinician referrals) or if no verification of diagnosis was evident. Prevalence was calculated per 100,000 and checked for accuracy where possible, based on the data provided.

RESULTS

The search strategy elicited a total of 242 relevant citations from across all sources. There were 38 articles that met the inclusion criteria and from which data were extracted (see Figure 1).

INSERT FIGURE 1 HERE

The included studies reported data from 19 different geographical settings across the continents of North America, Asia, Africa, Oceania and Europe (see Figure 2). No studies were identified from South America. The included studies presented data on the prevalence of muscular dystrophies collected between 1966 and 2013. There were ten studies conducted in Italy,[16-25] seven from the UK,[26-32] three in Japan,[33-35] two in Sweden,[36, 37] and Canada,[38, 39] and one from China,[40] Croatia,[41] Egypt,[42] Libya,[43] Netherlands,[44] New Zealand,[45] Norway,[46] Portugal,[47] Russia,[48] Slovenia,[49] South Africa,[50] Spain,[51] Taiwan,[52] and the USA.[53]

INSERT FIGURE 2 HERE

Characteristics of the included studies including summaries of case ascertainment and diagnostic verification procedures and potential risk of bias rating are outlined in Table 1. Of the 38 included studies, 28 presented data based on searches of medical records at hospitals and/or specialist treatment centres; seven, data from searches of national/community databases; seven, data from referrals from treating practitioners, one, data from previous

research studies, and one, data from a door-to-door survey. Some studies focused specifically on certain types of muscular dystrophies whereas other included all muscular dystrophies. The method of case ascertainment was not able to be determined for six studies. Only ten studies reported using more than one method of ascertaining cases. Diagnosis was verified in 71% of studies by use of clinical investigations and/or genetic analysis. In the remaining studies it was not clear how the diagnosis was confirmed.

Fifteen studies (39.5%) were classified as having a low risk of bias based on the predetermined criteria; two of these, from the UK, covered all dystrophies,[26, 32]. For the separate conditions there were eight studies from four different countries that explored the prevalence of Duchenne[16, 22, 26, 28, 32, 38, 49, 54] and seven from four countries for Becker[22, 26, 28, 32, 38, 49, 54]. A further seven studies from five more ethnically diverse countries looked at myotonic dystrophy[23, 26, 30, 32, 41, 45, 52]; three studies from two countries studied facioscapulohumeral[20, 26, 32]; three studies from two countries studied limb-girdle [18, 26, 32], two studies from two countries reported on Emery-Driefuss[26, 32], two studies from two countries[26, 32] reported on manifesting carriers and one study reported on oculopharyngeal[26] and congenital muscular dystrophy.[32]

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Crude prevalence per 100,000 for all muscular dystrophies across the included studies ranged between 3.8 in Japan to 26.8 in Egypt (see Table 2). For studies classified as having low risk of bias, the prevalence estimates narrowed revealing a prevalence range between 19.8 and 25.1 per 100,000. Myotonic dystrophy was identified as the most prevalent muscular

dystrophy across countries within the general population. Only one study presented age-adjusted prevalence.[43] No studies reported prevalence by age or gender distribution. Data on the prevalence of each type of muscular dystrophy are presented in Table 2.

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DISCUSSION

The crude prevalence for all muscular dystrophies and the separate disorders was found to vary widely. However, when only the studies classified as having low risk of bias were considered there was closer agreement, yielding a best estimate of the combined prevalence of all muscular dystrophies of between 19.8 and 25.1 per 100,000, although it should be noted that both these studies were from the UK.

The prevalence range for the different types of muscular dystrophies varied substantially. For example, with myotonic dystrophy, in which studies with low risk of bias came from a wider range of countries, the prevalence range from 0.5 to 18.1 per 100,000. The lowest rates were seen in the Taiwanese (0.5) and Italian (2.0) populations and the highest in Croatia with studies in British populations (or their descendants) being midway (7.1 – 11.8). Prevalence for myotonic dystrophy was particularly wide ranging between 0.5 to 18.1 per 100,000, the reasons for which are unclear and require further investigation. Facioscapulohumeral muscular dystrophy showed a fairly consistent prevalence range of 3.2 to 4.6 but again only two countries were included as having studies that had a low risk of bias.

The low risk studies yielded estimates for Duchenne and Becker muscular dystrophy of 1.7 - 4.2 and 0.4 - 3.6 per 100 000 respectively. Whilst there are challenges in comparing findings

with other estimates based on the male population only, the findings for Duchenne appear lower than the prevalence of 4.78 per 100,00 males identified by Mah et al[9] This is likely a reflection of the exclusion of studies restricted to males or only exploring a limited age range from this review. The prevalence of Duchenne muscular may also not fully represent the burden of the condition due to the early mortality of people affected, often before 20 years of age[12].

Comparing the results with other neurological diseases, the overall rate for muscular dystrophy is clearly lower than for conditions such as multiple sclerosis (average prevalence of 67.83/100,000)[55] but more common than prevalence of dominantly hereditary cerebellar ataxias (2.7 per 100,000).[56] The impact for the affected person and their families can be devastating particularly as muscular dystrophy can be of early onset.[5, 6] Consequently it remains important to have accurate prevalence rates to ensure people affected by muscular dystrophies receive the support they need. Whilst there was insufficient data to explore change in prevalence over time, it should be acknowledged that advances in both the accuracy and availability of diagnostic tests may have increased prevalence reported in studies exploring prevalence over the last decade.

Whilst the wide range of prevalence across all included studies may reflect differences in population dispositions between populations, particularly for myotonic dystrophy. However, the assessment of study quality suggests that the findings are also likely to reflect differences between the epidemiological methods used and parameters for case inclusion. Whilst the reporting of epidemiological studies has improved over time, there are still a number of studies where information required to assess risk of bias was not clear or where

methodological approaches were used that were deemed to introduce possible bias in the study findings.

It was observed that a number of studies reported in their discussion that their results were likely to be an underestimate due to the use of case ascertainment methods used. Few studies used multiple case ascertainment methods which allow for capture-recapture analysis of ascertainment rates. Most studies restricted case ascertainment to a search of hospital records which is likely to miss patients who do not require further medical treatment. It was also difficult to determine in a number of studies whether cases that were believed to have a muscular dystrophy but were awaiting confirmation from a diagnostic test or clinical investigation were included in the prevalence estimates or not. A key finding of this review is that based on the wide variation in prevalence and between methodologies in previous research, standardised procedures for the conduct and reporting of epidemiological studies in this area are needed. There are no known guidelines for the conduct of epidemiological studies in neuromuscular conditions and therefore some recommendations for epidemiological studies in this field are proposed based on the findings of this systematic review (Table 3).

INSERT TABLE 3 HERE

Whilst studies were presented from a range of countries across the world, there were no studies identified that explored the prevalence of muscular dystrophies in South America. Additionally there was only one study conducted in Oceania, which focused on one type,

myotonic dystrophy, in a relatively low-populated area of New Zealand. This highlights gaps in the current research literature. Furthermore, only one of the included studies reported age-adjusted prevalence, with no studies reporting age-specific prevalence sufficient to derive pooled age-adjusted prevalence estimates. Although presenting breakdowns of estimates can be problematic for disorders that are relatively rare, it is important to adjust for differences in population characteristics e.g. countries with particularly high proportions of young people. Age adjusted prevalence could be provided in mid-decade age bands rather than five or 10 year age bands (more commonly reported in epidemiological studies) to increase the number of cases per band for these disorders. There is also a need for studies to describe how the area of the population studied reflects the overall population characteristics of the country as a whole to inform how representative the findings of the study can be. Prevalence by ethnicity is also recommended but may be restricted by low case numbers.

Although all efforts were made to identify and obtain all articles relevant to the systematic review, the authors acknowledge the possibility that not all studies were identified and that the findings do not reflect the early mortality or late onset of different types of disorders. The aim of this review was to determine the prevalence of all muscular dystrophies, the unique characteristics of disorders within the muscular dystrophies presents some challenges. For example, in order to enable comparisons with other neurological disorders, the review was limited to studies exploring prevalence within the general population. However, it is noted that for X-linked disorders such as Duchenne and Becker muscular dystrophy that occur mainly in males, this approach may have excluded some studies exploring prevalence in the male population only. It is suggested that for X-linked disorders that in addition to the recommendations outlined in Table 3, prevalence should be reported for both males only and total population to enable meaningful comparison with other disorders.

This review has provided an overview of prevalence of the muscular dystrophies, and also identified a number of challenges in conducting epidemiological studies within this field. A summary of recommendations for the conduct of future studies on the prevalence of muscular dystrophies are proposed in Table 3 to address some of the unique challenges that present within this field of neuroepidemiology.

CONCLUSION

The prevalence of muscular dystrophies as a group was found to be between 19.8 and 25.1 per 100,000 person years. Myotonic dystrophy (0.5-18.1 per 100,000), Duchenne muscular dystrophy (1.7-4.2 per 100,000) and facioscapulohumeral muscular dystrophy (3.2-4.6 per 100,000) were found to be the most common types of disorder. Wide diversity between case ascertainment and verification of diagnosis suggests the need for standards on conducting and reporting studies on the prevalence of muscular dystrophies to facilitate comparison between disorders, countries and over time.

ACKNOWLEDGEMENTS AND FUNDING

We thank the Neuromuscular Research Foundation Trust and Richdale Charitable Trust for funding this systematic review.

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Table 1. Characteristics of included studies in chronological order

First Author	Year	Country (Region)	Age (years)	Case ascertainment	Verification of diagnosis	Population denominator	Data provided	Full article available	Risk of Bias Rating
Okinaka [33]	1966	Japan (Fukoka and Niigata)	All	Search of clinical records and referrals from practitioners	Case definition unclear	Specified	All, M	Yes	Unclear
Danieli [17]	1977	Italy (North east)	All	Search of clinical records	Unspecified	Unclear	D	Abstract only	Unclear
Bertolotto [16]	1981	Italy (Turin)	All	Search of clinical records and community database	Clinical investigations	Specified	D	Yes	Low
Monckton [39]	1982	Canada (Alberta)	All	Search of clinical records	Unspecified	Specified	C	Abstract only	Unclear
Pinessi [23]	1982	Italy (Turin)	All	Search of clinical records	Clinical investigations	Specified	M	Yes	Low
Kurtzke [53]	1984	USA	All	Unspecified	Unspecified	Specified	All, M	Yes	Unclear
Yates [29]	1985	Scotland (Lothian region)	Onset >18 years	Search of clinical records	Clinical investigations	Specified	LG	Yes	High
Araki [35]	1987	Japan (Kumamoto)	All	Referrals requested from practitioners'	Clinical investigations	Specified	All, D B M, F, LG	Yes	High
Mostaccioulo [22]	1987	Italy	All	Search of clinical records	Clinical investigations	Specified	D, B	Yes	Low
Radhakrishnan [43]	1987	Libya (Benghazi)	All	Search of clinical records	Unspecified	Unclear	D, LG, F	Abstract only	Unclear
Tangsrud [46]	1988	Norway (Southern)	<18 years	Referrals from practitioners, search of clinical records and national databases	Clinical investigations	Specified	All, D, B, LG, F, C, M	Yes	High
MacMillan [27]	1991	UK (South Wales)	All	Search of clinical records	Unspecified	Specified	D, B,M, F	Yes	Unclear
Krivopus	1991	Russia	All	Unspecified	Unspecified	Unclear	D, F	Abstract	Unclear

k [48]		(Krasnodar territory)						only	
Bushby [28]	1991	UK (Northern Region)	All	Search of clinical records and referring clinicians	Clinical and genetic investigations	Specified	B, D	Yes	Low
Nakagawa [34]	1991	Japan (Okinawa)	All	Unspecified	Clinical investigations	Unclear	D, M, LG, C, F,	Abstract only	Unclear
Burcet [51]	1992	Spain (Mallorca)	All	Search of clinical records	Unspecified	Specified	M	Abstract only	Unclear
Merlini [19]	1992	Italy (Bologna)	<20 years	Search of clinical records	Clinical investigations	Specified	D, B, M, F	Yes	High
Ahlstrom [57]	1993	Sweden (Orebro)	All	Unspecified	Unspecified	Unclear	All	Abstract only	Unclear
Ballo [50]	1994	South Africa (Cape Town)	All	Referrals requested from practitioners/genetic clinics	Clinical investigations	Unclear	D	Yes	High
Hughes [32]	1996	Northern Ireland	All	Search of clinical records, national database and clinician referrals	Clinical investigations	Specified	All, D, B, M, E, C, F, LG, MC	Yes	Low
Mostacciuolo [21]	1996	Italy (four provinces of Veneto)	All	Unspecified	Unspecified	Unclear	C	Abstract only	Unclear
van der Kooi [44]	1996	Netherlands	All	Search of clinical records	Clinical investigations	Unclear	LG	Yes	Unclear
Peterlin [49]	1997	Slovenia	All	Search of clinical records	Clinical and genetic investigations	Specified	D, B	Yes	Low
Medica [41]	1997	Croatia (Istria)	All	Search of clinical records and community databases	Clinical investigations	Specified	M	Yes	Low
Magee [30]	1999	Northern Ireland	All	Search of clinical records and national databases	Clinical and genetic investigations	Referenced	M	Yes	Low
Siciliano [24]	1999	Italy (North west Tuscany)	All	Referrals from practitioners, search	Clinical and genetic investigations	Specified	D, B	Yes	Low

				of clinical records and previous research studies					
Darin [37]	2000	Sweden (western)	<16 years	Search of clinical records	Clinical investigations	Specified	All, D, B, E, C, F, LG	Yes	High
Chung [40]	2003	China (Hong Kong Island)	<19 years	Search of clinical records	Clinical investigations	Specified	All, D B M, E, C, F, LG	Yes	High
Hsiao [52]	2003	Taiwan	All	Search of clinical Records	Clinical and genetic investigations	Specified	M	Yes	Low
McKeever [31]	2003	Northern Ireland	All	Search of clinical records	Unspecified	Unclear	D	Abstract only	Unclear
El-Tallaway [42]	2005	Egypt (Assiut)	All	Household survey	Clinical investigations	Specified	All, D, B, E, C, F, LG	Yes	High
Fanin [18]	2005	Italy (North Eastern Region)	All	Search of clinical records	Clinical investigations	Specified	LG	Yes	Low
Sposito [25]	2005	Italy (Tuscany)	All	Unspecified	Clinical and genetic investigations	Unclear	F	Abstract only	Unclear
Ford [45]	2006	NZ (Otago)	All	Search of clinical records and community service database	Clinical and genetic investigations	Specified	M	Yes	Low
Santos [47]	2006	Portugal	<15 years	Referrals from practitioners	Unspecified	Referenced	D, B, LG, E, F, M	Abstract only	High
Mostacciuolo [20]	2009	Italy (Padova)	All	Search of clinical records	Clinical investigations	Specified	F	Yes	Low
Norwood [26]	2009	UK (Northern England)	All	Search of clinical records	Clinical and genetic investigations	Specified	All, D, B, M F,LG, E, O MC	Yes	Low
Mah [38]	2011	Canada	All	Search of clinical records	Clinical and genetic investigations	Specified	D, B	Yes	Low

*If separate rates were available for 6 or more conditions then these were used to calculate prevalence of all MDs

D = Duchenne, B = Becker, MC = manifesting female carriers, M = myotonic, E= Emery-Dreifuss, C= congenital, F = facioscapulohumeral, LG= limb-girdle, ED = Emery Dreifuss, O= Oculopharyngeal, C = Congenital

Table 2. Prevalence of types of Muscular Dystrophies per 100,000 from studies reporting prevalence for the general population

	North America		**Asia**			**Africa**			**Oceania**	**Europe**							**Total Prevalence Range per 100,000**	**Prevalence based on studies classified as having a low risk of bias**	
	USA [53]	Canada [38]	Taiwan [52]	Russia [48]	Japan [33-35]	Egypt [42]	South Africa [50]	Libya [43]	New Zealand [45]	Netherlands [44]	Italy [16-18, 20-23, 25, 54]	Spain [51]	Sweden [36]	Slovenia [49]	UK [26-28, 30-32]	Croatia [41]		Number of studies	Prevalence Range per 100,000
All MDs	8.0				3.8-13.7	26.8							20.0		19.8-25.1		3.8-26.8	2	19.8-25.1
D	-	1.7	-	1.2	5.7	7.7	1.0	6.0	-	-	1.7-3.4	-		2.9	3.5-4.3	-	1.0-7.7	8	1.7-4.2
B	-	0.4	-		0.4	3.8	0.1	-	-	-	1.3-2.4	-		1.2	1.6-3.6	-	0.1-3.8	7	0.4-3.6
MC	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.1-0.4	-	0.1-0.4	2	0.4
M	2.0	-	0.5	-	0.2-9.1	-	-	-	11.6	-	2.1	10.9		-	7.1-10.6	8.5-18.1	0.2-18.1	7	0.5-18.1
F	-	-	-	1.4	1.1-2.0	1.9	-	0.8	-	-	4.4-4.6	-		-	2.9-3.9	-	0.8-4.6	3	3.2-4.6
LG	-	-	-		1.6-5.2	5.7	-	3.7	-	0.8	0.9	-		-	1.1-2.3	-	0.8-5.7	3	0.9-2.3
ED	-	-	-	-	-	1.9	-	-	-	-	-	-		-	0.1-0.4	-	0.1-1.9	2	0.1-0.4
O	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0.1	-	0.1	1	0.1
C	-	-	-	-	1.1	3.8	-	-	-	-	0.7	-		-	0.6-0.9	-	0.6-3.8	1	0.6

D = Duchenne, B = Becker, MC = manifesting female carriers, M = myotonic, E= Emery-Dreifuss, C= congenital, F = facioscapulohumeral, LG= limb-girdle, ED = Emery Dreifuss, O= Oculopharyngeal, C = Congenital

Table 3. Suggested recommendations for the conduct of epidemiological studies on muscular dystrophies.

Domains	Core criteria
Standard definitions	• Muscular dystrophy and it types are defined • Requirements for meeting inclusion criteria are defined (including diagnostic standards and verification requirements)
Standard methods	• Multiple population-based case ascertainment methods used including searches of medical records, hospitals, referrals from specialists, self-referrals, community and national databases with duplicates removed after cross-checking • Well-defined population that is described by geographic location and population characteristics (e.g. age, sex and ethnicity distribution) , allowing at least 100,000 person-years of observation • Reliable data presented for estimating denominator (with population denominator specified e.g. population census data)
Standard data presentation	• Total prevalence for all muscular dystrophies presented as well as each disorder presented separately • Prevalence of cases that have been genetically verified and by clinical investigation presented separately. • Mid-decade age bands (e.g. 0-14, 15-24, 25-34, 35-64, 65+ years) used to present overall prevalence of muscular dystrophies • 95% confidence intervals presented

FIGURE LEGENDS

Figure 1. Study selection flowchart

Figure 2. Worldwide map of identified prevalence studies on muscular dystrophies

Figure 1.

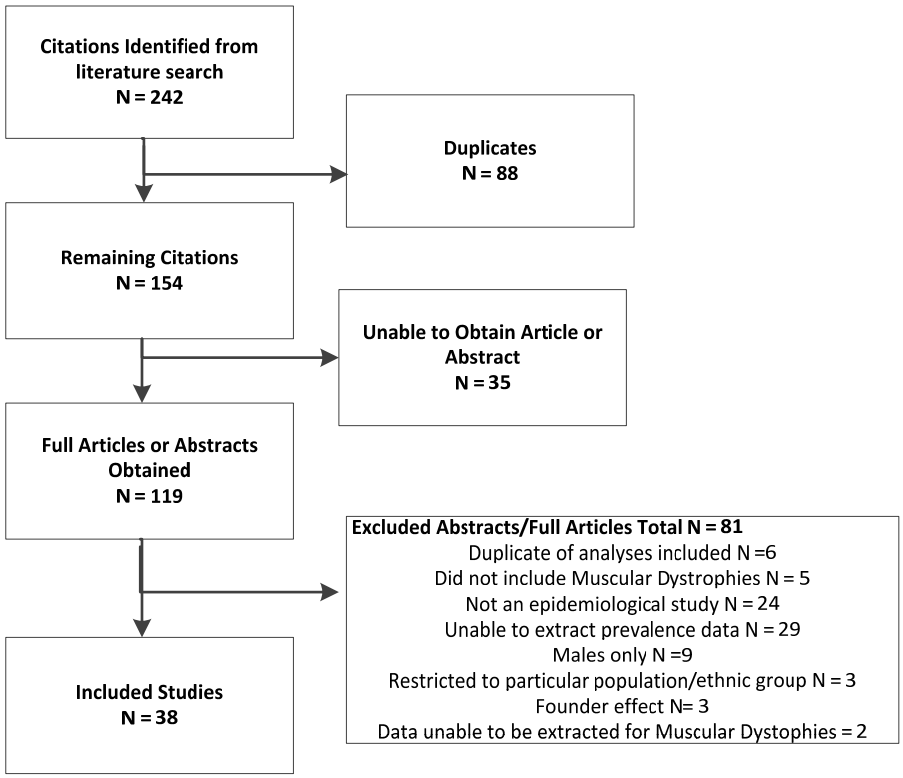

Figure 2.