Original Paper

Neuro
-epidemiology

Neuroepidemiology 2019;52:128–135
DOI: 10.1159/000494115

Received: August 20, 2018
Accepted: September 26, 2018
Published online: January 18, 2019

A Nationwide, Population-Based Prevalence Study of Genetic Muscle Disorders

Alice Theadom[a] Miriam Rodrigues[b, c] Gemma Poke[d] Gina O'Grady[e] Donald Love[f] Graeme Hammond-Tooke[g] Priya Parmar[h] Ronelle Baker[b] Valery Feigin[a] Kelly Jones[a] Braden Te Ao[i] Anna Ranta[j] Richard Roxburgh[c] On Behalf of the MDPrev Research Group

[a]National Institute for Stroke and Applied Neurosciences, Faculty of Health and Environmental Studies, Auckland University of Technology, Auckland, New Zealand; [b]Muscular Dystrophy Association of New Zealand, Auckland, New Zealand; [c]Department of Neurology, Auckland City Hospital, Auckland, New Zealand; [d]Genetic Health Service NZ, Capital and Coast District Health Board, Wellington, New Zealand; [e]Paediatric Neuroservices, Starship Children's Health, Auckland District Health Board, Auckland, New Zealand; [f]Diagnostic Genetics, LabPLUS, Auckland City Hospital, Auckland, New Zealand; [g]Department of Medicine, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand; [h]Department of Biostatistics and Epidemiology, Faculty of Health and Environmental Studies, Auckland University of Technology, Auckland, New Zealand; [i]Population Health, Faculty of Medicine and Health Sciences, University of Auckland, Auckland, New Zealand; [j]Department of Medicine, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand

Keywords
Prevalence · Neuromuscular · Muscular dystrophy · Population-based · Epidemiology

Abstract
Background: Previous epidemiological studies of genetic muscle disorders have relied on medical records to identify cases and may be at risk of selection biases or have focused on selective population groups. ***Objectives:*** This study aimed to determine age-standardised prevalence of genetic muscle disorders through a nationwide, epidemiological study across the lifespan using the capture-recapture method. ***Methods:*** Adults and children with a confirmed clinical or molecular diagnosis of a genetic muscle disorder, resident in New Zealand on April 1, 2015 were identified using multiple overlapping sources. Genetic muscle disorders included the muscular dystrophies, congenital myopathies, ion channel myopathies, GNE myopathy, and Pompe disease. Prevalence per 100,000 persons by age, sex, disorder, ethnicity and geographical region with 95% CIs was calculated using Poisson distribution. Direct standardisation was applied to age-standardise prevalence to the world population. Completeness of case ascertainment was determined using capture-recapture modelling. ***Results:*** Age standardised minimal point prevalence of all genetic muscle disorders was 22.3 per 100,000 (95% CI 19.5–25.6). Prevalence in Europeans of 24.4 per 100,000, (95% CI 21.1–28.3) was twice that observed in NZ's other 3 main ethnic groups; Māori (12.6 per 100,000, 95% CI 7.8–20.5), Pasifika (11.0 per 100,000, 95% CI

KARGER

E-Mail karger@karger.com
www.karger.com/ned

Assoc. Prof. Alice Theadom
National Institute for Stroke and Applied Neurosciences
Faculty of Health and Environmental Studies, Auckland University of Technology
AUT North Campus, Private Bag 92006, Auckland 1142 (New Zealand)
E-Mail alice.theadom@aut.ac.nz

5.4–23.3), and Asian (9.13 per 100,000, 95% CI 5.0–17.8). Crude prevalence of myotonic dystrophy was 3 times higher in Europeans (10.5 per 100,000, 9.4–11.8) than Māori and Pasifika (2.5 per 100,000, 95% CI 1.5–4.2 and 0.7 per 100,000, 95% CI 0.1–2.7 respectively). There were considerable regional variations in prevalence, although there was no significant association with social deprivation. The final capture-recapture model, with the least deviance, estimated the study ascertained 99.2% of diagnosed cases. ***Conclusions:*** Ethnic and regional differences in the prevalence of genetic muscle disorders need to be considered in service delivery planning, evaluation, and decision making.

Introduction

Genetic muscle disorders are a diverse group of hereditary disorders that present with muscle weakness, cause significant comorbidities and result in reduced daily functioning [1]. It has been shown that a substantial proportion of people living with a chronic illness are affected by a genetic muscle disease [2]. The wider impact on family members has also been found to be immense [3, 4]. Prevalence data provide a crucial foundation to identify the scope of the problem, the individuals most affected and the type and distribution of services required. Consequently, accurate and representative data on the prevalence of genetic muscle disorders are fundamental for evidence-based health care planning and as a basis of medical research [5].

In a UK study, crude prevalence of genetic muscle disorders including spinal muscular atrophy was reported to be 37/100,000 [2]. However, prevalence was not age-standardised to the world population and differences by sex and ethnic group remain unknown. Additionally, only patients known to the specialist neuromuscular centre were identified and consequently, patients who self-manage in the community not known to health care services would not have been accounted for. A recent study exploring prevalence of all neuromuscular disorders in the Republic of Ireland [6] utilised a community patient support service to assist in identifying cases; however, the study only included those aged 18 years or over. Previous epidemiological studies of genetic muscle disorders are consequently prone to selection and diagnostic biases [7]. This nationwide population-based study aimed to explore prevalence of genetic muscle disorders in New Zealand (NZ) by age, sex, ethnicity, region and disorder type.

Materials and Methods

This was a nationwide, epidemiological study of genetic muscle disease in children and adults using the capture-recapture method.

Study Population

The study population included people of all ages living in New Zealand (NZ, population = 4,242,048) as determined by the 2013 NZ population census [8]. Census data (where people can identify as being of more than one ethnicity) revealed 4 main ethnic groups in NZ: Europeans (74%), Māori (15%), Asian (12%) and Pasifika peoples (7%).

Procedures

The term "genetic muscle disorders" was used to encompass both non-dystrophic congenital myopathies and muscular dystrophies. On this basis, disorders of the anterior horn cell (such as spinal muscular atrophy) and neuromuscular junction were excluded. All types of muscular dystrophy (Duchenne, Becker, Facioscapulohumeral, Emery-Dreifuss, Limb-Girdle, Congenital, Myotonic, Oculopharyngeal and Distal), congenital myopathies and ion channel myopathies were included. Similar to Norwood et al. [2] metabolic myopathies were generally excluded except where the most usual presentation was of a progressive fixed muscle weakness (e.g., Pompe's disease) as the dominant feature. Duchenne and Becker muscular dystrophy are observed only in males; however, female carriers of the genetic mutation can also experience similar muscular weakness. These cases known as "manifesting carriers" were also included in the study to determine the full spectrum of impact of the condition.

The study aimed to identify all living children and adults with a confirmed diagnosis of a genetic muscle disorder on the point prevalence date of April 1, 2015. Cases needed to be a resident/citizen of NZ (operationalised as the adult or parent/guardian of a child case being registered on the electoral role at a NZ address or residing in the country for >6 months per year). A clinical diagnosis by the patient's treating neurologist was required for inclusion. Where available, supporting information on lab, neurophysiological, histological, histochemical and genetic test results was considered. Generally, the treating clinician's diagnosis was accepted though where information such as a positive genetic test in a known family member was available, the more specific diagnosis was accepted. In cases where a diagnosis was unclear, medical notes and test results were reviewed by a paediatric or adult neurologist. Cases where there was insufficient evidence to verify diagnosis were excluded. No additional investigations were undertaken by the research team.

Cases were ascertained using multiple overlapping sources. Keyword diagnostic searches were used to search neurologists' patient lists (including both private and publicly funded national health services). International Classification of Disease codes (ICD-10, including G71.0, G71.1, G71.2, G72.3) were used to search admission and discharge hospital records and the national Ministry of Health database. Searches by disorder identified cases from the NZ Muscular Dystrophy Association membership database, and the NZ Neuromuscular Disease Registry [9].

Additionally, national and regional disability services (including patient support organisations) contacted clients with the included conditions to inform them about the study and invite them to participate. National and local media coverage (including televi-

sion, newspaper and patient health or cultural magazines and a Facebook page) encouraged self-referrals into the study. Allied health professional organisations (e.g., physiotherapists, community nurses, occupational therapists and speech and language therapists) contacted their patients about the study and encouraged referrals. To facilitate the engagement of minority ethnic groups, a cultural liaison officer was employed to connect with culturally specific health and disability groups and health care services. A free phone number and social media accounts were set up to facilitate contact with the study team. Identified cases who agreed to be interviewed were also contacted and asked if there was anyone else in the family who had the condition. Interpreters were provided if required to facilitate participation in the study.

Searches were conducted by a member of staff of each organisation to protect patient confidentiality. Only demographic information (including date of birth, sex, ethnicity and region of residence) and details of diagnosis were obtained for each new case (no names and addresses were required). All people in New Zealand are given a unique National Health Index number and this enabled checking of all new cases against existing cases in the study database to exclude any duplicates and to link each case to information in the national death registry to confirm living status on the point prevalence date. Following case ascertainment, National Health Index numbers were removed from the main study database and kept in a separate password protected file for the purposes of cross-checking with medical records as required, while protecting patient confidentiality in the main database. To enable direct comparison with census data and to account for multiple associated ethnicities, all ethnicities the person associated with were recorded. Details of ethical approval and participant consent are outlined in the consent for publication section.

Statistical Analysis

Completeness of diagnosed case ascertainment was determined using capture-recapture techniques [10]. All sources of case notification were grouped based on the likely degree of overlap between them (e.g., linkage of health records within health care services) to ensure optimal uniqueness of the types of sources in the analysis. The final log-linear model assuming a Poisson distribution with the least deviance as an indicator of "goodness of fit" was selected to estimate the percentage of missing cases. NZ 2013 census data were used as the population denominator [8]. Direct standardisation was used to age-standardise prevalence to the world population for international comparability [11]. Prevalence by age, sex, region of residence and diagnostic subtype was calculated per 100,000 population with 95% CI using the Poisson distribution. Regional census data was used to explore if there were any associations between social deprivation and weekly income by regional prevalence.

Results

A total of 966 cases with a confirmed clinical and/or molecular diagnosis were identified. Crude prevalence was 22.7 per 100,000 person-years (95% CI 21.4–24.3). An additional 58 cases were identified as potentially eligible but were excluded because their diagnosis could not be verified. Of these, 23 (39.7%) people were identified by relatives as having the disorder but they did not wish that their details to be shared with the research team. They were not included, as there was no way of checking whether they might not have already been identified independently through another case ascertainment source. The remaining 35 (60.3%) were self-reported cases where there was insufficient clinical information and no molecular test results to verify diagnosis.

Capture-recapture analysis revealed a final model based on a 3-way interaction between (1) hospital records, genetic services and the national health database; (2) NZ Neuromuscular Disease Registry and (3) community services (which included self and family-referred cases) estimates that an absolute number of 7 diagnosed cases were likely to have been missed based on the case ascertainment approach undertaken. Divided by the total sample, this estimates that 99.2% of diagnosed cases were successfully captured by this study. Community services and the NZ Neuromuscular Disease Registry identified 71/966 (7.3%) unique cases not identified from health records (and consequently identifying patients who were not currently accessing health services).

As shown in Table 1, the most common genetic muscle disease in NZ was myotonic dystrophy, followed by the dystrophinopathies (54.7% Duchenne and 37.4% Becker) and facioscapulohumeral muscular dystrophy. These diagnoses made up 67.9% (656/966) of the overall prevalence of genetic muscle disorders. The proportion of cases with molecular confirmation varied considerably by diagnosis. Molecular confirmation of diagnosis was highest for the dystrophinopathies and myotonic dystrophy (both ~75%). The percentage of people with molecular confirmation was the lowest for limb-girdle muscular dystrophy. There were 24 patients who were identified as having genetic muscle disease but who could not be classified. In these cases, there was a diagnosis of "muscular dystrophy" in the medical record, but no further details were available.

The mean age of participants was 39.2 years (SD 20.3), ranging between 5 months to 90 years of age. The overall age-standardised minimal point prevalence was 22.3 per 100,000, (95% CI 19.5–25.6). The highest proportion of those living with these conditions was aged between 35 and 64 years (Table 2). Prevalence increased from 7.2 per 100,000 (95% CI 4.6–11.2) in those aged <5 years to 20.9 per 100,000 (95% CI 17.4–25.1) in the 5–14 years age group and then remained largely stable over the lifetime.

As shown in online supplementary Table 1 (for all online suppl. material, see www.karger.com/

Table 1. Crude prevalence of clinical and molecularly confirmed verified cases by disorder

Condition	Total prevalence			Cases with molecular diagnosis		
	number	prevalence per 100,000	95% CI	number	prevalence per 100,000	95% CI
Dystrophinopathies	190	4.47	3.87–5.17	142	3.35	2.83–3.96
Duchenne	104	2.45	2.01–2.98	87	2.05	1.65–2.54
Becker	71	1.67	1.32–2.12	45	1.06	0.78–1.43
Manifesting carriers	15	0.35	0.21–0.60	10	0.24	0.001–0.15
Facioscapulohumeral	123	2.90	2.15–3.47	71	1.67	1.32–2.12
Emery-Dreifuss	11	0.26	0.14–0.48	6	0.14	0.06–0.32
Limb-girdle	93	2.19	1.78–2.70	13	0.31	0.17–0.54
Congenital muscular dystrophy	27	0.64	0.43–0.94	8	0.19	0.09–0.39
Distal	9	0.21	0.10–0.42	3	0.07	0.02–0.23
Congenital myopathy	60	1.41	1.09–1.83	17	0.40	0.24–0.66
Central core disease	26	0.61	0.41–0.91	11	0.26	0.14–0.48
Nemaline	6	0.14	0.06–0.32	2	0.05	0.01–0.19
Congenital fibre type disproportion	5	0.12	0.04–0.29	1	0.02	0.001–0.15
Multiminicore	4	0.09	0.03–0.26	1	0.02	0.001–0.15
Centronuclear	1	0.02	0.001–0.15	0	–	–
Titin myopathy	1	0.02	0.001–0.15	0	–	–
Unclassified	17	0.40	0.24–0.66	0	–	–
Myotonic dystrophy	343	8.09	7.26–9.00	257	6.06	5.35–6.86
Type 1 (DM1)	327	7.71	6.91–8.60	246	5.80	5.11–6.58
Type 2 (DM2)	16	0.38	0.22–0.63	11	0.26	0.14–0.48
Other myopathies	11	0.26	0.14–0.48	4	0.09	0.03–0.26
GNE myopathy	2	0.05	0.01–0.19	1	0.02	0.001–0.15
Oculopharyngeal	2	0.05	0.01–0.19	1	0.02	0.001–0.15
Myofibrillar myopathy	5	0.12	0.04–0.29	0	–	–
Native American myopathy	2	0.05	0.01–0.19	2	0.05	0.01–0.19
Ion channel muscle sisease	65	1.53	1.19–1.97	29	0.68	0.47–1.00
Myotonia congenita	46	1.08	0.80–1.46	24	0.57	0.37–0.86
Periodic paralysis	15	0.35	0.21–0.60	5	0.12	0.04–0.29
Paramyotonia congenita	4	0.09	0.03–0.26	0	–	–
Pompe disease	10	0.24	0.12–0.45	2	0.05	0.01–0.19
Unspecified	24	0.57	0.37–0.86	0	–	–
Total	966	22.77	21.37–24.27	552	13.01	11.96–14.16

doi/10.1159/000494115), age-standardised prevalence in Europeans (24.4 per 100,000, 95% CI 21.1–28.3) was twice as high as the other 3 main ethnic groups of New Zealand; Māori (12.6 per 100,000, 95% CI 7.8–20.5), Pasifika (11.0 per 100,000, 95% CI 5.4–23.3), and Asian (9.18 per 100,000, 95% CI 5.0–17.8). Crude prevalence by ethnicity and sub-type is presented in Table 3. Ethnic disparity was most marked for myotonic dystrophy and was 3 times higher in Europeans (10.5 per 100,000, 95% CI 9.4–11.8) than in Māori and Pasifika (2.5 per 100,000, 95% CI 1.5–4.2 and 0.7 per 100,000, 95% CI 0.1–2.7 respectively). All 16 cases of myotonic dystrophy type 2 were of European ancestry. The observed ethnic difference in the prevalence of myotonic dystrophy type 1 and 2 means that for Māori, and Pasifika, myotonic dystrophy was less common than facioscapulohumeral muscular dystrophy and the dystrophinopathies. Among Māori, the prevalence of Becker muscular dystrophy (1.5 per 100,000, 95% CI 0.6–2.8) was higher than Duchenne muscular dystrophy (1.3 per 100,000, 95% CI 0.7–3.0). The prevalence of other genetic muscle disorders was comparable across all the 4 main ethnic groups of NZ.

Females had a lower crude prevalence of genetic muscle disorders (18.7 per 100,000, 95% CI 16.9–20.6) than males (27.0 per 100,000, 95% CI 24.8–29.4) particularly in those aged <34 years. This difference was due to the x-linked nature of Duchenne and Becker muscular dystrophy as, once these were removed (together with the 15

Table 2. Crude prevalence of genetic muscle disorders by age and gender

	Total population, *n*	Number of cases, %	Prevalence per 100,000	95% CI
Boys and men				
0–4 years	149,295	11 (2.0)	7.37	3.88–13.62
5–14 years	292,875	92 (16.52)	31.41	25.46–38.71
15–34 years	543,363	156 (28.0)	28.71	24.46–33.68
35–64 years	799,608	237 (42.5)	29.64	26.04–33.73
≥65 years	278,877	62 (11.1)	22.23	17.19–28.7
Total	2,064,018	557 (100.0)	26.99	24.81–29.35
Standardised	–	–	27.06	22.74–32.38
Girls and women				
0–4 years	142,746	10 (2.5)	7.01	3.56–13.35
5–14 years	280,716	29 (7.1)	10.33	7.05–15.05
15–34 years	557,772	98 (24.1)	17.57	14.34–21.51
35–64 years	868,644	213 (52.3)	24.52	21.39–28.1
≥65 years	328,158	58 (14.3)	17.67	13.54–23.02
Total	2,178,033	407 (100.0)	18.69	16.94–20.62
Standardised	–	–	17.71	14.41–22.00
Total sample				
0–4 years	292,041	21 (2.2)	7.19	4.57–11.20
5–14 years	573,591	120 (12.4)	20.92	17.42–25.11
15–34 years	1,101,132	254 (26.3)	23.07	20.36–26.13
35–64 years	1,668,252	449 (46.6)	26.91	24.51–29.55
≥65 years	607,032	120 (12.4)	19.77	16.46–23.72
Total	4,242,048	966 (100.0)	22.72	21.32–24.22
Standardised*	–	–	22.30	19.51–25.58

* Standardised to the WHO standard population.

Table 3. Crude prevalence of genetic muscle disorders across the four main ethnic groups of NZ

Condition	European		Māori		Pasifika		Asian	
	number	prevalence per 100,000 (95% CIs)	number	prevalence per 100,000 (95% CIs)	number	prevalence per 100,000 (95% CIs)	number	prevalence per 100,000 (95% CIs)
Dystrophinopathies	156	5.25 (4.48–6.16)	18	3.01 (1.84–4.86)	7	2.37 (1.04–5.11)	14	2.97 (1.69–5.11)
Duchenne MD	83	2.80 (2.24–3.48)	8	1.34 (0.62–2.75)	4	1.35 (0.43–3.72)	11	2.33 (1.23–4.31)
Becker MD	60	2.02 (1.56–2.62)	9	1.50 (0.73–2.97)	2	0.68 (0.12–2.73)	3	0.64 (0.16–2.03)
Manifesting carriers	13	0.44 (0.24–0.77)	1	0.17 (0.01–1.09)	1	0.34 (0.02–2.19)	0	0.001 (0.00–1.02)
FSHD	102	3.44 (2.81–4.19)	16	2.67 (1.58–4.45)	6	2.03 (0.82–4.65)	4	0.85 (0.27–2.33)
Emery-Dreifuss MD	11	0.37 (0.19–0.68)	0	0.00 (0.00–0.80)	0	0.00 (0.00–1.62)	0	0.00 (0.00–1.02)
Limb-girdle MD	73	2.46 (1.94–3.11)	11	1.84 (0.97–3.4)	7	2.37 (1.04–5.11)	5	1.06 (0.39–2.63)
Congenital MD	20	0.67 (0.42–1.06)	3	0.50 (0.13–1.60)	2	0.68 (0.12–2.73)	1	0.21 (0.01–1.38)
Distal MD	7	0.24 (0.10–0.51)	0	0.00 (0.00–0.80)	0	0.00 (0.00–1.62)	1	0.21 (0.01–1.38)
Congenital myopathy	46	1.55 (1.15–2.09)	9	1.50 (0.73–2.97)	5	1.69 (0.62–4.19)	5	1.06 (0.39–2.63)
Myotonic dystrophy	312	10.51 (9.39–11.76)	15	2.51 (1.46–4.24)	2	0.68 (0.12–2.73)	16	3.39 (2.01–5.64)
DM1	296	9.97 (8.88–11.19)	15	2.51 (1.46–4.24)	2	0.68 (0.12–2.73)	16	3.39 (2.01–5.64)
DM2	16	0.54 (0.32–0.90)	0	0.001 (0–00.80)	0	0.001 (0.00–1.62)	0	0.001 (0.00–1.02)
Other myopathies	8	0.27 (0.13–0.55)	1	0.17 (0.01–1.09)	1	0.34 (0.02–2.19)	0	0.001 (0.00–1.02)
Ion channel muscle disease	54	1.82 (1.38–2.39)	8	1.34 (0.62–2.75)	3	1.01 (0.26–3.23)	1	0.21 (0.01–1.38)
Pompe disease	7	0.24 (0.10–0.51)	2	0.33 (0.06–1.35)	0	0.001 (0.001–1.62)	1	0.21 (0.01–1.38)
Unspecified	21	0.71 (0.45–1.10)	0	0.00 (0.00–0.80)	1	0.34 (0.02–2.19)	3	0.64 (0.16–2.03)
Total	817	27.51 (25.67–29.48)	83	13.87 (11.11–17.28)	34	11.49 (8.01–16.25)	51	10.81 (8.13–14.33)

FSHD, facioscapulohumeral muscular dsystrophy; MD, muscular dystrophy.

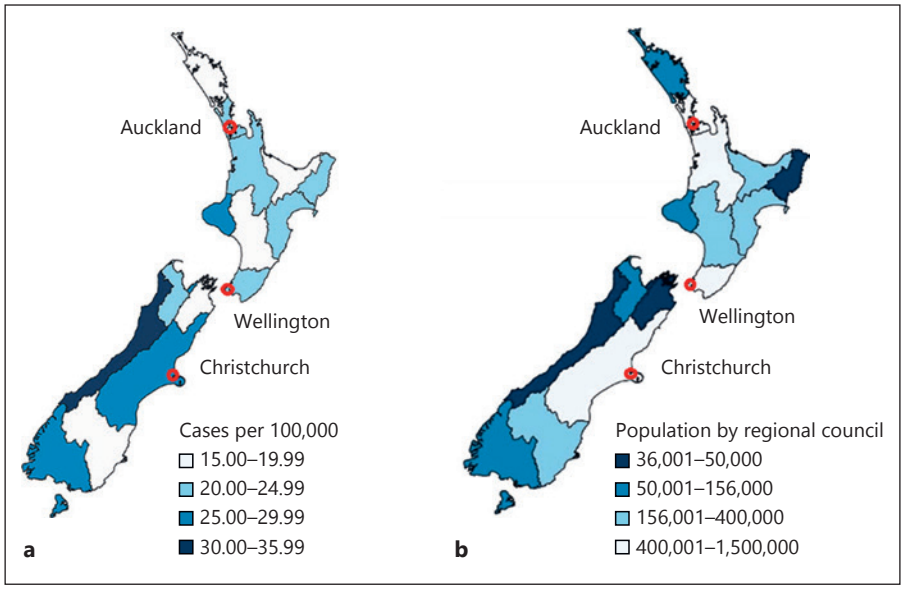

Fig. 1. Geographical distribution of cases by region (**a**) in comparison to general population density of (**b**).

manifesting female carriers), there were no sex differences in prevalence (males = 18.6 per 100,000 (95% CI 16.8–20.6) and females 18.0 per 100,000 (95% CI 16.3–19.9). Crude prevalence of clinically and molecularly verified cases by disorder type and age has been provided in online supplementary Tables 2a and b.

There was considerable variation in prevalence by geographical region as shown in Figure 1. Prevalence ranged between 17.8 per 100,000 in Northland to 34.2 per 100,000 in the West Coast of the South Island. There were no significant associations between regional prevalence and social deprivation (average weekly earnings, $r = 0.04$, $p = 0.88$), location of specialist health care services ($r = 0.19$, $p = 0.49$) or by population size ($r = 0.15$, $p = 0.59$, and as visually shown in Fig. 1).

Discussion

Age-standardised minimal prevalence of genetic muscle disorder in NZ was 22.3 per 100,000 person-years. The study revealed that people of European ancestry experienced higher prevalence of genetic muscle disorders compared with other ethnic groups. This was especially evident in myotonic dystrophy, which was 3 times higher in Europeans than in Māori and Pasifika. Prevalence remained relatively stable across the lifespan following 5 years of age, with peak prevalence in mid-adulthood. Wide regional variations in prevalence highlight the need to conduct national prevalence studies of genetic muscle disorders in order to ensure accuracy of prevalence data.

The overall crude prevalence of 22.7 per 100,000 is lower than the crude prevalence of 33.6 per 100,000 (with comparable diagnoses) identified in a study in the United Kingdom [2]. This difference in overall prevalence is likely to be due to the particularly low prevalence of dystrophinopathies (4.5 per 100,000 in NZ compared to 8.5 per 100,000 in England) and may also reflect ethnic differences in myotonic dystrophy. While there are methodological differences between the studies, for example, the Norwood et al. [2] study used data from a neuromuscular centre where generations of neuromuscular patients have been seen, compared with our study covering a number of less specialized, neurology services. We consider that the disparities in prevalence between our study and previous work reflect actual differences in prevalence between NZ and Europe, rather than being a reflection of case ascertainment limitations for a number of reasons. First, while lower prevalence of dystrophinopathies was observed, the prevalence of other disorders was comparable. Second, our case ascertainment procedures were more comprehensive than previous studies and the capture-recapture analysis indicated the estimated number of missed diagnosed cases was very low (<1%). Third, there were no significant associations between prevalence, social deprivation, rural or urban areas or presence of specialist neuromuscular centres suggesting case ascertainment was not affected by these factors.

It is also possible that the overall lower prevalence of genetic muscle disorders in NZ may be attributable to lower prevalence in Māori, Pasifika, and Asian peoples. In particular, ethnic differences in prevalence were ob-

served for myotonic dystrophy. The observed ethnic difference in the prevalence of myotonic dystrophy means that for Māori, and Pasifika, myotonic dystrophy was less common than facioscapulohumeral and the dystrophinopathies, a finding not previously described. Lower prevalence of myotonic dystrophy has been found in other ethnic minority groups in South Africa [12] and Israel [13]. However, these previous studies did not compare prevalence of myotonic dystrophy to other genetic muscle disorders. Ethnic differences were also observed within the dystrophinopathies, as for Māori the prevalence of Becker muscular dystrophy was higher than Duchenne muscular dystrophy. The observed ethnic differences could indicate barriers to diagnosis, inaccurate recording of ethnicity in the medical record or differential access to the health system as well as molecular differences. The use of total response ethnicity (where people were included in more than one ethnic group) in preference to allocating people into a single ethnic group (based on a prioritisation system), prevented concealment of any group diversity through optimising the sample size for ethnic minority groups. Previous work comparing ethnicity prioritisation versus total response ethnicity revealed no significant differences in prevalence estimates between the 2 approaches [14]. Classifying ethnicity in either way does not account for the strength of the ethnic affiliation and it is noted that a person may be over-represented through inclusion in multiple analyses [15]. Further research exploring genetic ancestry may help to explain the observed ethnic differences in this study.

Considerable regional variation in prevalence was observed across NZ. The proportions of genetic muscular disorder sub-types were similar across regions, making it unlikely there are significant founder effects for genetic muscle disorders in NZ, although a few large families with multiple affected members living in the same region could affect the findings. Regional variations may also potentially reflect differences in clinical diagnosis or case ascertainment procedures. Although if this was the case, it would be anticipated that the greatest case ascertainment would occur in the larger urban centres with specialist health care services. In this study, it was revealed that the highest prevalence was observed in the less densely populated region of the country (approximately 3.5 h away from the nearest specialist centre). Our findings have important implications for health care planning and highlight the importance of outreach services extending out from specialist centres to facilitate access to health care services and highlight the need to look at national prevalence due to wide regional variations.

Study Limitations

As we were unable to contact all identified cases in the study (e.g., contact details not shared from an external organisation in order to protect patient confidentiality or were no longer current) and not all participants agreed to be interviewed, we were not able to reliably connect all individual cases to family units. Additionally, although capture-recapture analysis showed that the multiple case ascertainment sources were effective in identifying clinically diagnosed patients, the study also identified a number of relatives of study participants who were exhibiting symptoms of the disorder but who had chosen not to seek a diagnosis. These cases, excluded from the prevalence figures, raise the likelihood that the prevalence of genetic muscle disorders may have been underestimated due to undiagnosed cases. The unique contribution of community-based sources to case ascertainment suggests that some people living with these conditions are not currently linked in with health care services in NZ. Previous evidence suggests that people may not seek a medical diagnosis due to the fact that there is little hope of a cure, they perceive little benefit from health services, or have symptoms that are relatively mild [16]. Furthermore, the reasons for choosing not to access services or for those experiencing difficulties with accessing services in addition to factors influencing uptake of molecular diagnosis need to be explored.

Conclusion

The prevalence of genetic muscle disorders was the lowest in infancy and then remained fairly constant over the life course. As the number of people living beyond 65 increases, it is likely that the number of affected individuals with genetic muscle disorders in NZ will increase, similar to projections made for motor neuron disease [17]. This is a particular concern given recent projections of a lack of specialist adult neurologists [18]. To facilitate health care access regional variations in prevalence need to be considered in health care planning.

Acknowledgements

We thank all study participants, clinicians and service providers who facilitated case ascertainment and our research team. We also thank Peter Edwards for his support with the design of the figure and Dr. Varsha Parag who assisted with the capture-recapture analysis.

MD-Prev Research Group Members include Alice Theadom, Ronelle Baker, Valery Feigin, Gina O'Grady, Graeme Hammond-

Tooke, Kelly Jones, Rita Krishnamurthi, Donald Love, Priya Parmar, Gemma Poke, Anna Ranta, Miriam Rodrigues, Richard Roxburgh, Jenny Stewart, and Braden Te Ao.

Ethics Statement

Subjects (or their parents or guardians) have given their written informed consent. This study was approved by the Northern Y Regional Ethics Committee of NZ (Reference: 14/NTB/118) and the Auckland University of Technology Ethics Committee (Reference: 14/296).

Disclosure Statement

The authors have no conflicts of interest to declare.

Funding Sources

The study was funded by the Health Research Council of New Zealand (Reference: 14/399) and the Brendel Trust.

References

1 Cardamone M, Darras BT, Ryan MM: Inherited myopathies and muscular dystrophies. Semin Neurol 2008;28:250–259.
2 Norwood FL, et al: Prevalence of genetic muscle disease in northern england: in-depth analysis of a muscle clinic population. Brain 2009;132:3175–3186.
3 Webb CL: Parents' persepctives on coping with duchenne muscular dystrophy. Child Care Health Dev 2005;31:385–396.
4 Boyer F, et al: Factors relating to carer burden for families of persons with muscular dystrophy. J Rehabil Med 2006;38:309–315.
5 Feigin VL, Howard G: The importance of epidemiological studies should not be downplayed. Stroke 2008;39:1–2.
6 Lefter S, Hardiman O, Ryan AM: A population-based epidemiologic study of adult neuromuscular disease in the republic of ireland. Neurology 2017;88:304–313.
7 Theadom A, et al: Prevalence of muscular dystrophies: a systematic literature review. Neuroepidemiology 2014;43:259–268.
8 Statistics NZ 2013 Census. http://www.stats.govt.nz/Census/2013-census.aspx (accessed 2016).
9 Rodrigues M, et al: The New Zealand neuromuscular disease registry. J Clin Neurosci 2012;19:1749–1750.
10 Hook EB, Regal RR: Capture-recapture methods in epidemiology: methods and limitations. Epidemiol Rev 1995;17:243–246.
11 Ahmad O, et al: Age Standardization of Rates: A New WHO Standard, in GPE Discussion Paper Series. Geneva, World Health Organization, 2000, p 31.
12 Goldman A, Ramsay M, Jenkins T: Ethnicity and myotonic dystrophy: a possible explanation for its absence in sub-Saharan Africa. Ann Hum Genet 1996;60:57–65.
13 Segel R, et al: Prevalence of myotonic dystrophy in Israeli Jewish communities: inter-community variation and founder premutations. Am J Med Genet A 2003;119A:273–278.
14 Ministry of Health, Presenting Ethnicity: Comparing Prioritised and Total Response Ethnicity in Desciptive Analyses of New Zealand Health Monitor Surveys. Wellington, Ministry of Health, 2008.
15 Didham R, Callister P: The effect of ethnic prioritisation on ethnic health analysis: a research note. N Z Med J 2012;125:58–66.
16 Dawson E, Savitsky K, Dunning D: Don't tell me, I don't want to know: understanding people's reluctance to obtain medical diagnostic information. J Appl Soc Psychol 2006;3:751–768.
17 Arthur KC, et al: Projected increase in amyotrophic lateral sclerosis from 2015 to 2040. Nat Commun 2016;7:12408.
18 Ranta AA, et al: New Zealand's neurologist workforce: a pragmatic analysis of demand, supply and future projections. N Z Med J 2015;128:35–44.