Estimating the economic cost of adults living with genetic muscle disorders in New Zealand: A cost-of-illness study

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Abstract

Aim: The primary aim of this research was to determine the costs associated with genetic muscle disorders (GMDs) among adults in New Zealand. This study also aimed to highlight the main cost drivers for GMDs and their subgroups in New Zealand, and determine the clinical, socioeconomic and healthcare system factors that predict the level of treatment cost.

Methods: A prevalence-based cost-of-illness model was developed using a bottom-up and retrospective approach from a societal perspective. Population-based data containing electronic hospital records and self-reported health service usage from the Genetic Muscle Disorder Prevalence study were utilised in this research. Multivariable linear regression analyses were conducted to determine which variables predicted higher direct and total costs for people with GMDs.

Results: Eight hundred and nine cases were eligible in the data set; 490 (61%) provided consent to be included in this cost-of-illness study. The mean age was 45.6 years, ranging from 16 to 90 years. The most common GMD in the study was myotonic dystrophy with 202 patients (41%). Total direct healthcare costs per person were NZ$29,762 (95%CI $24,354-$35,224) and formal care was the largest cost component (67%) of direct healthcare costs. The total direct non-healthcare costs per person was NZ$33,090 (95%CI 28,207-$38,517) and informal care was the largest cost component (74%) of this category. Indirect costs were estimated as temporary productivity loss due to missed workdays or reduced work hours. Fifty-four (11%) of the cohort reported this productivity loss which was valued at NZ$11,466 (95%CI $7,695-$16,141). The total per person per annum cost of GMDs in New Zealand was estimated at NZ$64,114 (95% CI $57,045-$73,777). When informal care was excluded, the total one-year per person cost reduced to NZ$39,789 (95%CI $34,717-$46,983). The main cost drivers of GMDs and for the six common subtypes of GMDs were formal and informal care, followed by medical aids and hospital admissions. Variables of high predictors of cost were being in employment, having a manual or electric wheelchair, the need for ventilatory support and having at least one co-morbid condition.

Conclusion: This study has highlighted that the economic burden of GMDs among adults in New Zealand is substantial. Consistent with previous literature, informal care was found to be a large driver of costs and a significant area of unmet need. Quantifying this high cost stresses the importance and need of providing adequate support for informal caregivers of people with GMDs.

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Glossary

ACC	Accident Compensation Corporation
BMD	Becker muscular dystrophy
DMD	Duchenne muscular dystrophy
DM	Myotonic dystrophy
FSHD	Facioscapulohumeral muscular dystrophy
GMDs	Genetic muscle disorders
ION	Ion channel muscle disease
LGMD	Limb-girdle muscular dystrophy
MD	Muscular dystrophy
MD-Prev	Genetic muscular disorder prevalence study
MOH	Ministry of Health
PHARMAC	Pharmaceutical Management Agency
WTA	Willingness to accept
WTP	Willingness to pay

Chapter 1. Introduction

Genetic muscle disorders (GMDs) are the most common form of neuromuscular disorders and are characterised by weakness in and degeneration of the muscles (Cardamone et al., 2008; Mercuri & Muntoni, 2013). This group of disorders encompasses both muscular dystrophies and myopathies which are caused by genetic mutations or changes in the muscle, muscle membrane or supporting proteins (Cardamone et al., 2008). People with GMDs can experience high levels of disability and commonly have increased risk of early mortality, medical complications, and a life with impaired mobility, although for some the symptoms are relatively mild. There is also a broader impact for families/whānau with two disability-adjusted life years lost for families for every year a person is affected (Access Economics Pty Limited, 2007).

The economic burden of GMDs has not been widely researched nationally or globally. Previous literature has mainly focused on the more prevalent disorders within GMDs such as Duchenne muscular dystrophy and myotonic dystrophy, leaving the economic burden of the many other GMDs not estimated. The present study aimed to conduct a cost-of-illness study from a societal perspective to estimate the costs associated with GMDs for adults in New Zealand (NZ) using population-based prevalence and outcomes data (Theadom et al., 2019). This chapter describes GMDs as a public health issue and explores the different aspects of the disorders within GMDs, such as symptoms, severity, and prevalence. This research utilised data from a population-based, cross-sectional study that identified all living children and adults with GMDs in NZ therefore a summary of this study was provided. Lastly, this chapter outlines the aims and objectives of this research and the structure of the thesis.

1.1 Genetic Muscle Disorders as a Public Health Issue

GMDs are a rare, diverse group of hereditary neuromuscular disorders made up of muscular dystrophies and myopathies. They primarily present with muscle weakness and degeneration of the muscles, which varies in distribution and severity (Cardamone et al., 2008; Mercuri & Muntoni, 2013). Muscular dystrophies are diseases of the muscle membrane and supporting proteins, while myopathies are caused by genetic defects in muscle contractile apparatus (Cardamone et al., 2008). Symptoms, age of onset, and prognosis can vary across disorders, but muscle weakness, motor delay, and respiratory dysfunction are consistent symptoms seen across both muscular dystrophies and myopathies (Cardamone et al., 2008).

Due to the severity of symptoms and comorbidities associated with GMDs, patients often require multidisciplinary care and treatment management (Bushby et al., 2010b). This care should include the monitoring of disease progression and preventative care of symptoms, which require access to a

number of health professionals such as neurologists, orthopaedists, and rehabilitation specialists (Bushby et al., 2010b). Currently, there are no cures for GMDs, so in many cases there is a reliance on medications and therapies to help manage symptoms and improve the length and quality of life (Emery, 2002; Lovering et al., 2005). Due to the rarity of these disorders, many treatments are not funded or subsidised by the government and create more barriers to healthcare for this population (Lovering et al., 2005). In most severe cases of GMDs, wheelchairs and medical devices such as gastronomy tubes, hoists, or ventilators are required to assist with daily living activities (Bushby et al., 2010a; Loutfi Sami et al., 1997). Therefore, the costs of treatment and everyday care can be significant and a factor that prevents access to receiving this care.

The symptoms of GMDs can also significantly impact all areas of a person's life and reduce access to employment, education, and social activities (Graham et al., 2011). For instance, bodily pain among people with muscle diseases was shown to impact physical and social functioning due to restricted activity and reduced motivation (Graham et al., 2011). Fatigue was experienced at high levels for people with muscle diseases where it was associated with poorer quality of life and physical functioning (Graham et al., 2011). Notably, literature indicates that fatigue and pain were the main factors influencing work performance and creating barriers to employment for people with GMDs (Frank, 2016; Lindsay et al., 2015; Mulroy, 2019). So although GMDs are relatively rare, their impact and costs are substantial for the affected individual, their families, and society (Access Economics Pty Limited, 2007).

1.2 The Epidemiology and Clinical Manifestations of Genetic Muscle Disorders

1.2.1 Muscular dystrophies

Muscular dystrophies (MD) are inherited disorders caused by genetic mutations of the muscle membrane and supporting proteins, leading to progressive destruction of and weakness in the muscles (McNally & Pytel, 2007; Mercuri & Muntoni, 2013). There are a range of disorders encompassed by the term muscular dystrophy, and these include the dystrophinopathies (Duchenne and Becker), myotonic, congenital, Emery-Dreifuss, facioscapulohumeral, oculopharyngeal, distal, and limb-girdle muscular dystrophies. To diagnose muscular dystrophies, a comprehensive medical history and physical examination is needed, accompanied by clinical testing to determine the specific genetic diagnosis (Emery, 2002). A systematic review of muscular dystrophies found that the combined population prevalence across 19 countries ranged between 19.8 and 25.1 per 100,000 (Theadom et al., 2014). The onset of symptoms in muscular dystrophies varies from birth to adulthood and primarily presents with muscle weakness due to degeneration of the muscles, which also varies in distribution and severity (Cardamone et al., 2008; Carter et al., 2018; Emery, 2002; Mercuri & Muntoni, 2013).

Dystrophinopathies include Duchenne and Becker muscular dystrophy and they are caused by mutations of the dystrophin gene (Cardamone et al., 2008; Emery, 2002). Duchenne muscular dystrophy (DMD) is the most common and most severe form of muscular dystrophy and is an X-linked disease that occurs predominantly in males (Emery, 2002). A systematic review and meta-analysis of worldwide prevalence estimates reported that the pooled prevalence of DMD was 4.78 per 100,000 males, and the incidence ranged from 10.71 to 27.78 per 100,000 (Mah et al., 2014). Age of onset is often around five years of age and, if untreated, loss of ambulation occurs quickly, so that life expectancy drops to 19 years of age (Bushby et al., 2010a; Emery, 2002). Muscle weakness is mainly proximal and progressive, often leading to delayed motor milestones and the use of a wheelchair by age 12 (Emery, 2002; Shieh, 2013). Respiratory, orthopaedic, and cardiac-related complications can occur and some degree of mental impairment is common (Bushby et al., 2010a; Emery, 2002). Pneumonia compounded with cardiac complications such as congestive heart failure and arrhythmias are frequent causes of death for people with DMD (Cardamone et al., 2008; Emery, 2002). A recent meta-analysis on the life expectancy in DMD indicated that the median life expectancy was 22 years (Broomfield et al., 2021). However, with the advancement of treatments and care, some studies reported that there was an increased life expectancy; where patients had ventilatory support and were born after 1990, the pooled median life expectancy was 29.9 years with a range of 26.5 to 30.8 years (Broomfield et al., 2021; Landfeldt et al., 2020).

Becker muscular dystrophy (BMD) is also an X-linked disease and a milder allelic variant of DMD, so the course of the disorder is more benign (Cardamone et al., 2008; Emery, 2002). For diagnosis, a muscle biopsy is often helpful for patients with BMD (McNally & Pytel, 2007). Symptoms begin at around 5 to 15 years of age, where calf pain, myalgia and cramps are common (Bushby & Gardner-Medwin, 1993). The pattern of muscle weakness and wasting is similar to that of DMD (Bushby & Gardner-Medwin, 1993; Cardamone et al., 2008; Emery, 2002). Loss of ambulation can occur when patients are adolescents, and the age of wheelchair confinement is later for those with BMD at approximately 17 years of age (Bushby & Gardner-Medwin, 1993; Cardamone et al., 2008). Death often occurs around the fourth or fifth decade and is usually due to respiratory failure or cardiomyopathy (Cardamone et al., 2008; Emery, 2002). A systematic review found that the pooled prevalence of BMD across 167 studies was 1.53 per 100,000 males (Mah et al., 2014). In England, the prevalence was reported to be 2.38 per 100,000 (Bushby et al., 1991).

Myotonic dystrophy (DM) is classified into two subtypes: myotonic dystrophy type 1 or dystrophia myotonica 1 (DM1), and myotonic dystrophy type 2 (DM2) (Cardamone et al., 2008). Both types are progressive multisystem genetic disorders (Turner & Hilton-Jones, 2014). DM1 is the most common form of muscular dystrophy that affect adults (Cardamone et al., 2008; Takahashi & Matsumura, 2018). It is caused by a mutation in the dystrophia myotonica protein kinase gene (Turner & Hilton-Jones, 2014). The age of onset for adult DM1 can be around the second to fourth decades, and common clinical characteristics are myotonia and paradoxical weakness and wasting (Cardamone et

al., 2008; Turner & Hilton-Jones, 2014; Yum et al., 2017). The multisystem aspect includes cardiac, endocrine, ocular, and central nervous system involvement (Cardamone et al., 2008; Turner & Hilton-Jones, 2014). As a result, patients with DM1 may experience respiratory failure, cardiomyopathy, cataracts, infertility, cognitive dysfunction, gastrointestinal dysfunction, and sleep disorders (Cardamone et al., 2008; Takahashi & Matsumura, 2018; Turner & Hilton-Jones, 2014).

DM2 shares many of the multisystemic features of DM1, but DM2 is less common and causes milder phenotypes (Turner & Hilton-Jones, 2014). The age of onset is later than DM1, and may present around the fourth to seventh decades (Shieh, 2013). Common clinical characteristics include myalgia, stiffness, mild grip myotonia, myotonia of the proximal legs, and exercise-induced fatigue (Yum et al., 2017). Patients with DM2 often experience a milder degree of cataracts, cardiac conduction abnormalities, cardiomyopathy, cognitive impairment, and endocrine abnormalities (Shieh, 2013; Takahashi & Matsumura, 2018). For patients with DM1 or DM2, management should monitor and screen the multisystem involvement. For instance, treatments are monitoring ventilatory function and any swallowing difficulties, and yearly ECGs to screen for any cardiac conduction abnormalities and cardiomyopathy (Shieh, 2013; Turner & Hilton-Jones, 2014; Yum et al., 2017).

Limb-girdle muscle disease (LGMD) is a collection of progressive muscle diseases with proximal muscle weakness of the hip and shoulder girdles (Cardamone et al., 2008; Thompson & Straub, 2016). Seven are dominantly inherited and 12 recessively inherited, where the autosomal dominant forms are quite rare and less severe than the recessive types (Cardamone et al., 2008; Thompson & Straub, 2016). The age of onset and severity can vary, but the recessive forms often have earlier onset and more rapid progression (Cardamone et al., 2008). Cardiac involvement among most types of LGMDs can occur, where cardiomyopathy and cardiac arrhythmias should be monitored (Cardamone et al., 2008; Shieh, 2013). Most childhood-onset LGMDs are associated with predominant weakness and calf hypertrophy (Shieh, 2013). Adult patients often have increased hip and shoulder girdle weakness, resulting in limited mobility and often wheelchair confinement, but ambulation can be maintained (Cardamone et al., 2008; Mercuri & Muntoni, 2013; Shieh, 2013). A study in Northern England estimated the prevalence of LGMDs to be approximately 2.27 per 100,000, while a study in Ireland similarly reported a prevalence of 2.88 per 100,000 (Lefter et al., 2017; Norwood et al., 2009).

Facioscapulohumeral muscular dystrophy (FSHD) is a dominantly inherited disease due to a partial deletion on chromosome 4 (Cardamone et al., 2008). Prevalence studies of neuromuscular disorders in Northern England and Ireland reported the prevalence to be 3.95 per 100,000 and 2.59 per 100,000, respectively (Lefter et al., 2017; Norwood et al., 2009). Onset is usually in adulthood and there is variation in the distribution of weakness, where the pattern of weakness is often asymmetric (Shieh, 2013). Disease progression is generally slow, where a functional decline of the arms and legs has been noted, but ambulation is usually maintained (Shieh, 2013; Stübgen & Stipp, 2010). FSHD is associated with retinal involvement, and hearing loss can also occur (Mercuri & Muntoni, 2013).

Cardiac and respiratory complications are rare but may occur years after disease onset (Shieh, 2013). Regular ophthalmological monitoring for exudative retinal telangiectasia, an eye disease that causes loss of central vision, should be part of treatment for patients with FSHD (Shieh, 2013; Stübgen & Stipp, 2010).

1.2.2 Myopathies

Myopathies are caused by genetic defects in the contractile apparatus of muscle. The term myopathy encompasses a range of disorders, including ion channel muscle disease, congenital myopathies, Pompe disease, inclusion body myopathy, and myofibrillar myopathy. As this present study analysed ion channel diseases and Pompe disease, the clinical manifestations of these diseases were of primary focus and explored below.

Ion channel muscle diseases (ION) are disorders caused by mutations in the genes encoding ion channel subunits in the skeletal muscle (Maggi et al., 2021). The disorders in this group include myotonia congenita, paramyotonia congenita, and periodic paralysis. Myotonia congenita is an autosomal dominant or recessive mutation that causes muscle stiffness and onset in the first decade (Maggi et al., 2021; Shieh, 2013). The prevalence study for all neuromuscular diseases in Ireland found the prevalence of myotonia congenita to be 0.32 per 100,000 (Lefter et al., 2017). The clinical manifestations include myotonia with the warm-up phenomenon, which is when myotonia occurs after a period of rest (Trip et al., 2007). This myotonia can be decreased with continued exercise (Shieh, 2013; Trip et al., 2007). This disorder predominantly affects limb muscles and can be lower or upper limbs depending on whether it is a dominant or recessive mutation (Maggi et al., 2021; Shieh, 2013).

Paramyotonia congenita is an autosomal dominant mutation that also causes muscle stiffness, and the age of onset is usually in the first decade (Maggi et al., 2021; Shieh, 2013). However, exercise and cold temperatures both can trigger myotonia and episodic muscle weakness (Maggi et al., 2021; Shieh, 2013). Fixed muscle weakness can occur in the later stages of the disease (Maggi et al., 2021). A study in Ireland estimated that paramyotonia congenita's prevalence is 0.15 per 100,000 (Lefter et al., 2017).

There are different forms of periodic paralysis, such as hyperkalemic, hypokalemic, thyrotoxic periodic paralysis and Andersen-Tawil syndrome (Maggi et al., 2021; Shieh, 2013). Lefter's study in Ireland estimated the prevalence of periodic paralysis at 1.72 per 100,000 (Lefter et al., 2017). Onset is often in infancy or childhood for hyperkalemic and hypokalemic periodic paralysis. Andersen-Tawil syndrome can begin from early childhood to adulthood and throtoxic periodic paralysis begins in early adulthood (Maggi et al., 2021). The clinical characteristics of periodic paralysis include episodic flaccid muscle weakness and the duration varies depending on the type (Maggi et al., 2021; Shieh, 2013). For hyperkalemic periodic paralysis, muscle weakness is correlated with elevated potassium

levels, whereas for hypokalemic periodic paralysis, weakness is correlated with low potassium levels (Maggi et al., 2021; Shieh, 2013). Andersen-Tawil syndrome is also manifested as a potassium-sensitive periodic paralysis in which facial and skeletal malformations and cardiac arrhythmias can occur (Maggi et al., 2021; Shieh, 2013). Thyrotoxic periodic paralysis is seen predominantly in Asian men, where episodic flaccid paralysis is associated with hyperthyroidism and hypokalemia (Maggi et al., 2021; Shieh, 2013). Treatment for periodic paralysis can include beta blockers, acetazolamide, or potassium which is given to patients during attacks (Maggi et al., 2021; Shieh, 2013).

Pompe disease is an inherited metabolic myopathy that is caused by a deficiency leading to lysosomal glycogen storage (van der Ploeg & Reuser, 2008). The deficiency is of the enzyme acid alpha-glucosidase, which is needed for the degradation of lysosomal glycogen (Kanters et al., 2011). The clinical features and onset of Pompe disease vary significantly. The classic infantile form of Pompe disease presents in the first months of life and is on the severe end of the spectrum with rapid progression (van der Ploeg & Reuser, 2008). The common symptoms include difficulty feeding, respiratory infections, hypertonia, and failure to thrive (van der Ploeg & Reuser, 2008). The late-onset form of Pompe disease has a slower progression, and most patients are adults (van der Ploeg & Reuser, 2008). This form mainly affects skeletal muscles, leading to mobility and respiratory dysfunction and many patients become wheelchair-confined or ventilatory-dependent (van der Ploeg & Reuser, 2008). Cardiac involvement is sporadic (van der Ploeg & Reuser, 2008). Common symptoms include fatigue, muscle cramps, and sleep disorders such as excessive daytime sleeping and night-time hyperventilation (van der Ploeg & Reuser, 2008). An Australian study found that the birth prevalence of Pompe disease was approximately 1 per 7,700 live births (Meikle et al., 1999). In the Netherlands, prevalence was estimated to be 14 per 100,000 live births (Meikle et al., 1999). Pompe disease is the first inheritable muscle disorder that has an approved therapy available. Enzyme replacement therapy targets the skeletal muscles and is often treatment for early onset patients (van der Ploeg & Reuser, 2008).

1.3 The Parent Study

The New Zealand Muscular Dystrophy Association identified that research on neuromuscular conditions was a priority and accurate and representative data on the prevalence and impact of GMDs was urgently needed in NZ (Theadom et al., 2019). To address this, a population-based, cross-sectional study (Genetic Muscular Disorder Prevalence [MD-Prev] study) was conducted in 2015 to identify the prevalence and outcomes of all living children and adults with GMDs in NZ (Theadom et al., 2019). Notably, previous prevalence studies worldwide had methodological limitations, which likely underestimated the results (Theadom et al., 2014). These limitations regard the case ascertainment methods and use of a broad case definition, which likely did not capture the target population. Additionally, most studies' case ascertainment was restricted to one source of

clinical, administrative records, which likely missed patients who did not require further medical treatment (Theadom et al., 2014).

The MD-Prev study addressed these limitations of selection and diagnostic biases by utilising the 'capture-recapture' method to ascertain all cases living in NZ with a confirmed diagnosis of a GMD (Hook & Regal, 1995; Theadom et al., 2019; Theadom et al., 2014). The capture-recapture method uses multiple overlapping sources to ascertain cases, and in the MD-Prev study, cases were identified from hospital and neurologist's patient lists, the Ministry of Health database, the New Zealand Muscular Dystrophy Association membership database, and the NZ Neuromuscular Disease Registry (Hook & Regal, 1995; Theadom et al., 2019). Alongside this approach, a clinical diagnosis had to be confirmed by the patient's treating neurologist, and for cases where diagnosis was unclear, test results and medical notes were reviewed by a paediatric or adult neurologist (Theadom et al., 2019).

Respondents completed a questionnaire regarding different areas of resource utilisation associated with their muscular dystrophy conditions within the past 12 months. For instance, they were asked about formal and informal care provision, medication use, and medical aids or home modifications required to assist in daily activities (Theadom et al., 2019). Ultimately, the robust methods and nationwide sample used in the MD-Prev study provided a data source with sufficient information on resource utilisation to estimate the societal costs of people living with GMDs in NZ.

Results from the prevalence study identified a total of 966 cases with a confirmed clinical and/or molecular diagnosis, ranging between 5 months to 90 years of age (Theadom et al., 2019). The most common GMD in NZ was myotonic dystrophy, followed by the dystrophinopathies (Duchenne and Becker muscular dystrophy), and then facioscapulohumeral muscular dystrophy (Theadom et al., 2019). The reported age standardised prevalence of GMDs in NZ was 22.3 per 100,000 person years (Theadom et al., 2019).

1.4 The Economic Burden of Genetic Muscle Disorders

A study estimating the global economic burden of neuromuscular disorders concluded that costs were high per person primarily driven by the need for extensive on-going informal care compared to other common disorders of the brain (Gustavsson et al., 2011; Lefter et al., 2017; Norwood et al., 2009; Ryder et al., 2017). As mentioned above, the impairments caused by GMDs significantly impact the patient's quality of life and their need for respite care, informal care, and high-cost treatment and therapies. Although there are several disorder specific cost-of-illness studies for some GMDs, there is scant economic evidence for GMDs among adults. In addition, there are methodological limitations consistently seen among previous studies which reduced the reliability and comparability of results. These limitations were related to selection biases, the lack of diagnosis verification and case

ascertainment issues, which have been further detailed in the literature review in Chapter Two. It should be noted that some of the variability of these costs across countries are attributed to differences in the health and cost-sharing systems which results in differences in the price of treatments and services and the differences in the volume of care (Lorenzoni & Koechlin, 2017).

The existing economic evidence notes that when compared to common disorders of the brain, such as multiple sclerosis or Parkinsons disease, neuromuscular conditions had the greatest average cost per patient at €30,052 (approx. NZ$5,305) and the highest indirect cost at €17,278 (approx. NZ$28,865) (Gustavsson et al., 2011). However, this estimate only included a subset of the large range of neuromuscular conditions due to the lack of relevant economic studies. This implies that the total economic burden of neuromuscular conditions would be higher if all disorders were included (Gustavsson et al., 2011).

In Australia, a study that took a societal perspective reported that the total annual cost per person with DMD was AU$46,669 (approximately NZ$49,956) (Teoh et al., 2016). The authors indicated that people with DMD had higher average health expenditures when compared with the Australian mean (Teoh et al., 2016). Particularly, the 5 to 14 and 15 to 24 age groups had mean health expenditures that were over 10 times that of the per capita mean (Teoh et al., 2016). However, the age of the population of Teoh et al.'s (2016) study ranged from 1 to 33 years, which does not include all those older individuals diagnosed with DMD and may underestimate overall DMD costs in Australia (Teoh et al., 2016).

A study in the United States reported the total per-capita costs for DMD and myotonic muscular dystrophy as US$50,952 (approx. NZ$76,080) and US$32,236 (approx. NZ$48,134), respectively (Larkindale et al., 2014). A limitation seen in this study was regarding potential selection bias, as participants were selected from a database of members of only one national private health insurance plan (Larkindale et al., 2014). This selection of data likely would have excluded those patients who are not a member with that health insurance plan and those who do not have health insurance at all.

A European study looking at the societal costs of DMD found that the average annual cost per person ranged from €7,657 (approx. NZ$12,811) in Hungary to €58,704 (approx. NZ$98,220) in France (Cavazza et al., 2016). The researchers were able to differentiate between direct healthcare and non-healthcare costs, as well as productivity losses, and found that non-healthcare costs contributed to 64% to 89% of total costs across diverse European countries (Cavazza et al., 2016). Informal care was reported to be the main driver of direct non-healthcare costs, which is a consistent finding in previous literature (Cavazza et al., 2016; Larkindale et al., 2014). However, Cavazza et al.'s study obtained participants from one registry only for each country, which likely did not capture all people with DMD and is therefore not a representative sample of those populations (Cavazza et al., 2016; Larkindale et al., 2014).

In Germany, a study on the burden of DMD and BMD found that the mean annual costs were €78,913 (approx. NZ$131,931) and €39,060 (approx. NZ$65,302) respectively (Schreiber-Katz et al., 2014). Similarly, informal care costs were the highest cost driver of total direct non-medical costs, estimated to be €21,279 (approx. NZ$35575) for DMD and €7,636 (approx. NZ$12,766) for BMD (Schreiber-Katz et al., 2014). Productivity losses contributed the highest to the total annual burden for both groups, which is also consistently seen across the literature (Gustavsson et al., 2011; Larkindale et al., 2014; Schreiber-Katz et al., 2014).

Although there are some existing studies on the costs of GMDs, these focus predominantly on DMD, BMD, and myotonic dystrophy. Total costs are significant, and with high informal care costs and productivity losses associated with GMDs across countries. It is important to note that these cost estimates may be underestimated due to methodological limitations. Case ascertainment was often limited to one source, such as hospital administrative data, patient registries, or health insurance plan databases, which potentially introduced selection bias in these studies (Cavazza et al., 2016; Larkindale et al., 2014; Schreiber-Katz et al., 2014; Teoh et al., 2016). These limitations suggest that cases would likely have been missed and therefore selection was not representative of the whole population of interest. There is currently no published literature about the costs of any GMDs in NZ. Overall, the global and national economic burden of a range of different or even numerous GMDs is very limited. Methodological limitations in the available research suggests an underestimation of costs associated with GMDs.

1.5 Rationale for a Cost-of-Illness Study of Genetic Muscle Disorders in New Zealand

Based on current knowledge, there are no studies that have estimated the costs for people living with GMDs in NZ. With limited global and national evidence, there is a clear need for research to fill this knowledge gap and address any methodological issues from previous studies. Methodological limitations were surrounding case ascertainment issues that introduced selection bias so that studies were not representative of the target population. To address these issues, the opportunity to use the available national data from a ‘parent’ study - the MD-Prev research (Theadom et al., 2019) - was present. The MD-Prev study also addressed previous limitations and robustly collected prevalence-based national data using the capture-recapture method (Theadom et al., 2019). This method most likely ascertained cases accurately and provided a representative sample of people with GMDs in NZ. One study has indicated the importance of accurate and representative population data for fundamental evidence-based health care planning and informing the strategic allocation of resources (Hill & Phillips, 2006). Therefore, this current study drew upon data collected from the parent MD-Prev study to estimate the societal costs of GMDs among adults in NZ.

As there is currently no research in NZ on the cost of GMDs, there was no baseline that could be used for comparisons or for economic evaluations. Without this fundamental knowledge, cost-effective health care services and treatments cannot be provided, so there was a clear need to conduct a cost-of-illness study of the cost of GMDs among adults in NZ. Estimating these costs can illustrate this group's current access to healthcare and indicate barriers or areas of unmet need. Exploring these cost estimates would also identify areas of high cost and what factors drive these high costs. Accordingly, these estimates can indicate costs that can be reduced or areas where individuals and their families require more support, such as informal care as noted by previous literature (Cavazza et al., 2016; Larkindale et al., 2014). Estimating baseline costs of GMDs also provides health care providers with information to anticipate the resources required to treat patients with GMDs appropriately. Accurate cost estimates are also critical for decision makers to provide cost effective health care services and treatments to improve treatment outcomes (Drummond, 1992; Hodgson & Meiners, 1982). Lastly, the limited international evidence provides an opportunity for NZ to be a key contributor to international research on GMDs. There is a clear need for a baseline of cost estimates for people affected by GMDs in NZ and internationally. Through exploring the economic burden of GMDs, we can better understand this health issue and provide cost effective health services and treatments to improve the health and wellbeing of people with GMDs.

1.6 Research Aims and Objectives

This study aimed to determine the costs associated with GMDs among adults in New Zealand. The research objectives were:

- To estimate, from a societal perspective, the annual direct (healthcare and non-healthcare) and indirect (productivity loss) cost of GMDs among adults in New Zealand in 2021
- To identify the main cost drivers for GMDs and the subgroups of GMDs in New Zealand
- To determine the clinical, socioeconomic, and health care system factors that indicate whether patients incur a level of treatment cost

1.7 Structure of this Thesis

This thesis is presented in five chapters. Chapter 1 introduces GMDs as a public health issue and provides a background on the known health and economic burdens. Chapter 2 is a literature review of published research on the costs of GMDs. This review explores the methodologies used and identifies the known estimated costs of different GMDs. Chapter 3 details the cost-of-illness model used, the sources of data and unit costs, and the methods used to quantify the various cost outcomes. The key

findings of this research are then presented in Chapter 5. Chapter 6 provides a discussion of the results, a consideration of the research's strengths and limitations, and recommendations for future investigation.

Chapter 2. Literature Review

This chapter provides a review of the published literature on annual direct and indirect costs of muscular dystrophies using a systematic approach. The literature review aimed to identify existing cost estimates as well as existing methodologies to inform the present study.

2.1 Search Strategy

To determine the direct and indirect costs of GMDs, an electronic database search was conducted on May 21st, 2021, using EMBASE, Medline and Scopus. These three databases were chosen as they provided an in-depth coverage of diverse sets of journals and all research is peer-reviewed (Thomas & Hodges, 2010). The search was conducted for all original research (full text) articles published in the English language since 2000. The search strategy for the databases is set out in Appendix A and the search terms included 'muscular dystroph*', 'neuromuscular disease*', 'genetic muscle disorder*', 'myotonic dystroph*', 'cost-of-illness' in the title or abstract. A language limit was applied on all three databases to include only studies published in English. The titles and abstracts for all relevant citations were assessed for possible inclusion in the review. The full articles were obtained for studies meeting the inclusion criteria and any duplicate articles were removed. In addition, a manual search was completed of the reference lists of relevant articles.

Studies for inclusion were required to present at least one cost outcome associated with genetic muscle disorders or its various types with a confirmed diagnosis. The types of GMDs included in this review were dystrophinopathies (Duchenne, Becker and manifesting female carriers), myotonic dystrophy (type 1 and 2), facioscapulohumeral, limb-girdle, Emery Dreifuss, oculopharyngeal, congenital and Pompe's disease. Studies were included where data were obtained from adult patients (age 16 and over). Only original research published in a peer reviewed journal was included. Studies that reported on a treatment or intervention were excluded, as were case studies, randomised controlled trials and observational studies.

The costs reported from the literature were adjusted to NZ dollar currency using the EPPI Cost Converter tool (Cochrane Methods Economics, n.d.). This calculator is a tool recommended by the Campbell and Cochrane Economics Methods Group for cost adjustments. The calculator converts one cost estimate of one currency and price year to its equivalent value in a different currency and price year, accounting for general inflation using a Gross Domestic Product deflator index and differences in the current price levels between countries using conversion rates based on Purchasing Power Parities for gross domestic product (GDP) (Cochrane Methods Economics, n.d.). The reported costs in the included studies were converted to 2021 New Zealand dollars.

2.2 Findings

The literature search identified a total of 535 relevant citations from the three databases; EMBASE presented 334 citations, Medline presented 107 citations, and Scopus presented 94 citations. One hundred and forty-five duplicate publications were removed. The titles and abstracts of the remaining 380 citations were screened and led to 341 citations being excluded. From the remaining 49 citations, the full articles of 12 citations could not be obtained, leaving 37 full articles to review. Following full-text review, a total of six studies met the inclusion criteria. Tables summarising characteristics, methodologies, and cost data of the included studies can be found in the Appendix B.

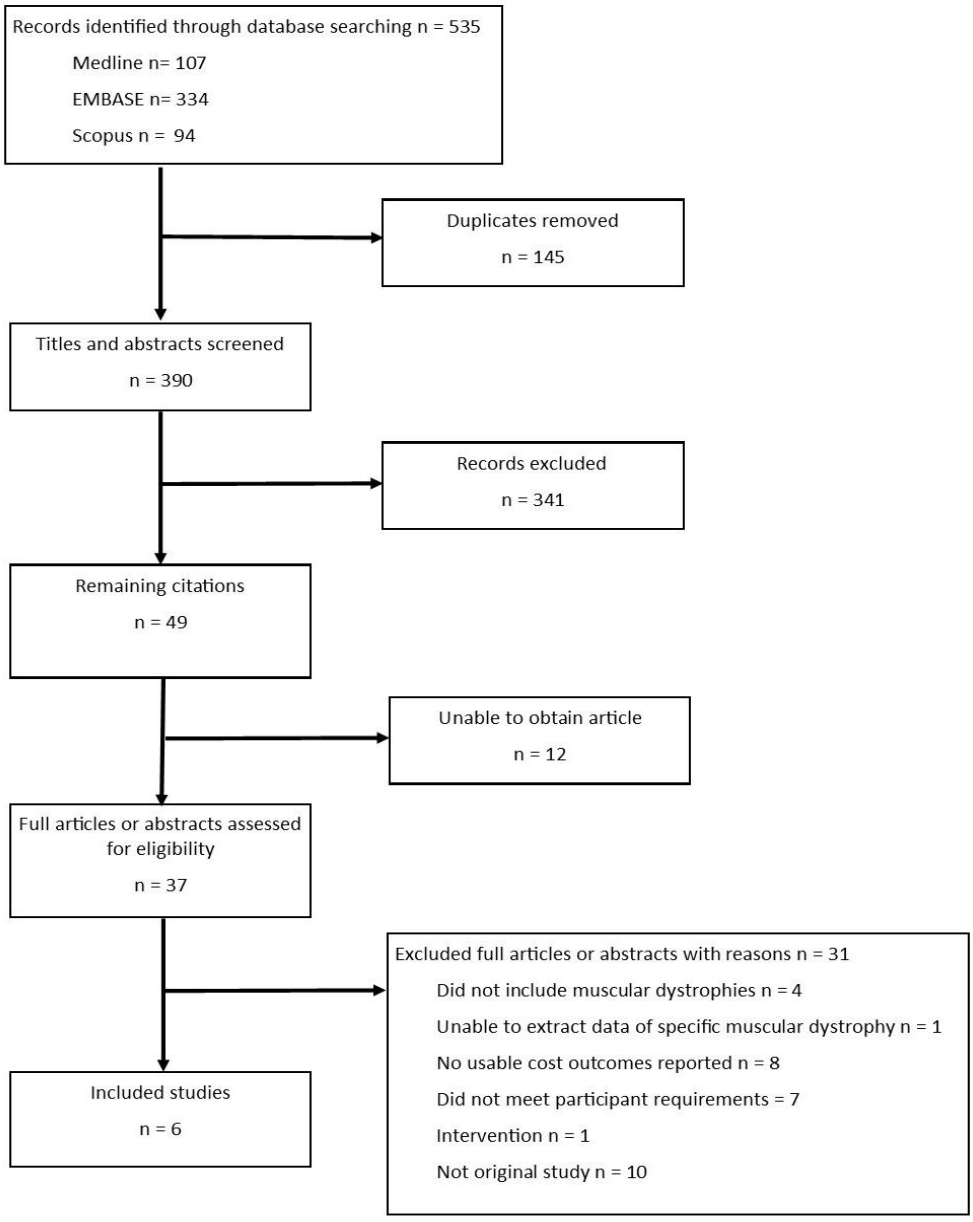

Figure 1. Flowchart of study selection

From the included studies, none were conducted in New Zealand; two studies were conducted in the United States (Ouyang et al., 2008; Ouyang et al., 2019), two in the Netherlands, one in Germany (Schepelmann et al., 2010), and one in Australia (Teoh et al., 2016). Sample sizes varied across studies, ranging from 80 (Kanters et al., 2011) to 1,891 (Ouyang et al., 2019). The age range for studies also varied, where some studies ranged from 0-29 years of age (Ouyang et al., 2008), 1-33 (Teoh et al., 2016) and others started older at 15-83 years of age (Schepelmann et al., 2010), 18-61+ (Ouyang et al., 2019), 18-80 (Blokhuis et al., 2021), and 25-76 (Kanters et al., 2011). Different types of GMDs were explored, where two studies focused on facioscapulohumeral muscular dystrophy (FSHD) (Blokhuis et al., 2021; Schepelmann et al., 2010), one reported on Pompe disease (Kanters et al., 2011), another reported on both type 1 and type 2 myotonic dystrophy (Ouyang et al., 2019), one reported on Duchenne muscular dystrophy (Teoh et al., 2016), and one reported on muscular dystrophies in general (Ouyang et al., 2008). Only aggregated cost estimates were able to be extracted for the 25-34 age group in the study by Teoh et al. (2016) as it was primarily focused on children with Duchenne muscular dystrophy.

Four studies identified participants from muscular dystrophy registries (Blokhuis et al., 2021), referral and specialised centres (Kanters et al., 2011; Schepelmann et al., 2010) or muscular dystrophy charities, disability providers or support organisations (Teoh et al., 2016). These four studies collected data through questionnaires that asked respondents about resource use related to their illness (Blokhuis et al., 2021; Kanters et al., 2011; Schepelmann et al., 2010; Teoh et al., 2016). The other two studies used administrative data and identified patients through accessing databases that contained hospital records (Ouyang et al., 2019) or paid medical and prescription drug claims (Ouyang et al., 2008).

Regarding the perspectives taken for the cost analysis, four studies took a societal perspective and therefore calculated both direct medical costs and indirect costs (Blokhuis et al., 2021; Kanters et al., 2011; Schepelmann et al., 2010; Teoh et al., 2016). These four studies did not explicitly define the approach used for quantifying medical costs, but they align with the resource-based approach. Informal care costs were also assessed under the societal perspective. The approaches taken to calculate these costs varied; one study stated the use of the proxy good method (Blokhuis et al., 2021), one used the shadow price method (Kanters et al., 2011), one did not specify the approach (Kanters et al., 2011), and the last study also did not define an approach but calculated it as the loss of productivity of primary caregivers at the full wage rate (Schepelmann et al., 2010). The methods for defining and calculating productivity loss as an indirect cost varied. Two studies primarily used the ‘friction cost’ method as well as the ‘human capital’ approach for sensitivity analyses (Blokhuis et al., 2021; Kanters et al., 2011). One study used the human capital approach (Schepelmann et al., 2010), while the remaining study measured indirect costs as the productivity loss of the working caregiver, rather than the productivity loss of the patient (Teoh et al., 2016).

Of the two remaining studies that took a different perspective for the cost analysis, one took a 'health care payer' perspective (Ouyang et al., 2008) and therefore only reported on medical costs (e.g., hospital admissions). The other study did not state which perspective was taken and reported only one usable cost, which was the hospitalisation cost for the specific age group (Ouyang et al., 2019).

The overview of the costs found in these studies is shown in Table B.3 in Appendix B. Total annual costs per patient ranged from NZ$41,651 to NZ$117,654 (Blokhuis et al., 2021; Kanters et al., 2011; Ouyang et al., 2008; Schepelmann et al., 2010; Teoh et al., 2016). One study did not report an annual cost per patient (Ouyang et al., 2019). Direct medical costs per patient ranged from NZ$4,305 to NZ$29,719 (Blokhuis et al., 2021; Kanters et al., 2011; Schepelmann et al., 2010; Teoh et al., 2016). Indirect costs per patient ranged from NZ$1,565 to NZ$39,702 (Blokhuis et al., 2021; Kanters et al., 2011; Schepelmann et al., 2010; Teoh et al., 2016). It should be noted again that variations in cost can be attributed to differences in the health system and national variations in wage and income levels.

The ability of these studies to report costs per patient varied and there was variation in which cost categories contributed the most to the total cost. Two studies reported the direct medical costs contributing the most to annual per patient costs (Blokhuis et al., 2021; Kanters et al., 2011). In the study by Blokhuis et al. (2021), home care made up the largest component of direct medical care costs, and similarly in the study by Kanters et al. (2011), home care was the largest cost component. One study had indirect costs contribute the most, where informal care was the largest cost component (Schepelmann et al., 2010), and another had direct non-medical costs contribute the most but did not indicate which component was the largest (Teoh et al., 2016).

Formal care or home care was a large direct medical cost identified in many studies. Blokhuis et al. (2021) did not specify the method of calculating formal care but did state they used the Dutch health care reference prices. They reported that 19% of the cohort received formal home care and this came to an estimated per person cost of NZ$17,356 (Blokhuis et al., 2021). Kanters et al. (2011) did not specify how home care was calculated but that it was valued with wage rates from the Dutch costing manual. They reported that home care on average cost NZ$15,232 and this cost component contributed the most to total costs and medical costs. In comparison, Schepelmann et al. (2010) stated that formal care costs were the payments by health insurance for home care. Their study found that 14% of the patients with FSHD received formal care and this care was for only two hours per week, which estimated a total per person cost of NZ$1,076.

Interestingly, a pattern seen in two studies by Blokhuis et al. (2021) and Kanters et al. (2011) was that patients received more informal care and for longer compared to other studies, yet informal care costs were estimated to be lower than that of formal care. In the study by Blokhuis et al. (2021), 42% of the patients with FSHD received informal care, which was higher than the utilisation of formal care. Informal care was provided on average, 22 hours a week and only totalled to NZ$14,515 (Blokhuis et

al., 2021). Kanters et al. (2011) estimated that 85% of their cohort utilised informal care and on average received 19 hours informal care per week. The total reported cost per person was NZ$12,473, which was the second largest cost component for this study. However, the results from Schepelmann et al. (2010)'s study did not show this pattern, where informal care was received on average for five hours a week and had a cost of NZ$16,975, which was significantly higher compared to the formal care cost of NZ$1,076.

Productivity losses varied from NZ$1,565 to NZ$39,703 (Blokhuis et al., 2021; Kanters et al., 2011; Schepelmann et al., 2010; Teoh et al., 2016). The wide range could be due to variation in wage rates and income across nations as well as differences in methods used to calculate productivity costs. The participation in the work force for the study by Blokhuis et al. (2021) was 42% and around half of the employed patients reported a health-related reduction of productivity. The total productivity loss for this study was NZ$10,091 (Blokhuis et al., 2021). Kanters et al. (2011) reported that 39% of patients with Pompe disease were employed and 52% indicated a reduction of work hours. The friction cost method was used in the Kanters et al. (2011) study to estimate a productivity loss of NZ$5,245 which was nearly half of the productivity loss reported by Blokhuis et al. (2021). The study by Schepelmann et al. (2010) only reported the combined proportion of people who indicated a temporary disability due to facioscapulohumeral muscular dystrophy, myasthenia gravia and amyotrophic lateral sclerosis, which was 8%.; the productivity loss due to temporary disability was NZ$6,157, while the cost of premature retirement was NZ$22,447 to give a total of NZ$22,727. In contrast, Teoh et al. (2016) measured the productivity loss of the parent, as this study focused on the costs for children with Duchenne muscular dystrophy. Parents in employment noted a mean loss of 11.7 workdays for the whole study cohort, which translated to an average of NZ$1,565 per working parent per year for the 25-34 year-old age group (Teoh et al., 2016).

Of the studies that reported on direct medical costs, two disaggregated these costs to at least 15 different cost outcomes by age group (Blokhuis et al., 2021; Kanters et al., 2011) and one study disaggregated these costs to 11 different cost outcomes by age group (Schepelmann et al., 2010). The remaining three studies did not further disaggregate the direct medical costs (Ouyang et al., 2008; Ouyang et al., 2019; Teoh et al., 2016). Overall, the most consistently reported costs across all studies were the costs of hospitalisations, outpatient care, and medication.

2.3 Literature Review Interpretation

The costs associated with GMDs and methods used to analyse these costs varied considerably across the reviewed studies. Notably, the available data extracted for this review was very limited and emphasises the gap in research about the economic burden of GMDs. The main finding extracted from these articles was that the annual per person cost associated with muscular dystrophies ranged from NZ$41,651 to NZ$117,654 (see Table B.3 in Appendix B). The large variance in this cost may

reflect the variability of methods used for analysis and definitions of cost outcomes among the studies. Additionally, the difference in GMDs studied can explain the variability of annual costs per person. For instance, the cost of Duchenne muscular dystrophy will differ from the cost of myotonic muscular dystrophy due to the differences in the nature and progression of the disease, leading to differences in costs. Although the many contributing cost variables make it difficult to make confident conclusions regarding these costs, it does generally illustrate the magnitude of the burden. However, it further highlights the lack of research for the cost of GMDs overall.

Another key finding was that participants from four studies were identified from only one source. For instance, Blokhuis et al. (2021) identified patients who were members of one FSHD registry, and Kanters et al. (2011) identified patients from only one referral centre. This finding suggests the potential for selection biases and underestimated costs, as these studies may not have accounted for those patients out in the community who self-manage their GMDs. In contrast, Teoh et al. (2016) sourced data from a range of muscular dystrophy charities, advocacy groups and patient organisations, and Schepelmann et al. (2010) identified data from specialised centers randomised through the German Network of Muscle Disorders. However, Teoh et al. (2016) and Schepelmann et al. (2010) did not look at hospital records, which may also suggest selection biases, as some patients may access only secondary care for their GMDs. Diagnosis verification was limited and only stated in studies by Ouyang et al. (2008), Ouyang et al. (2019), and Schepelmann et al. (2010).

All studies but one (Ouyang et al., 2019) explicitly stated the perspective used for the cost analysis. Despite four studies using the same societal perspective, the definitions of cost outcomes and methods used to calculate the costs differed. Kanters et al. (2011) reported on only medical and non-medical costs, which presumably placed informal care and productivity loss under non-medical costs. Blokhuis et al. (2021) defined the cost outcomes as direct medical costs, direct non-medical costs, and indirect costs. Notably, defining cost features differently may explain the inconsistencies seen in the proportion of costs that contributed to the annual per person cost of muscular dystrophies. In addition, the method of calculating informal care and productivity loss varied across all studies, which may have also contributed to this inconsistency. Thus it may not be feasible to directly compare costs across studies. Lastly, among the studies that took a societal perspective, the sample sizes ranged from 80 (Kanters et al., 2011) to 172 (Blokhuis et al., 2021). The smaller sample sizes in these studies may have resulted in costs being skewed higher in some cases, which contributed to the variability in costs.

Of the studies that calculated formal and informal care costs, both cost components were significant contributors of cost for different types of GMDs worldwide. Notably, the two studies by Blokhuis et al. (2021) and Kanters et al. (2011) indicated higher formal care costs compared to informal care costs, which is inconsistent with previous literature that indicates typically higher informal care costs for neuromuscular diseases (Cavazza et al., 2016; Gustavsson et al., 2011; Schepelmann et al., 2010). However, this difference could be explained by the country the Blokhuis et al. (2021) and Kanters et

al. (2011) studies were conducted in. Both of these studies were completed in The Netherlands which has a different health care and cost-sharing system compared to other countries (Blokhuis et al., 2021; Kanters et al., 2011). So, although Blokhuis et al. (2021) and Kanters et al. (2011) studied different GMDs, the finding was consistent and suggests that The Netherlands has sufficient support for formal care provision and therefore reports lower informal care costs.

Lastly, the range of GMDs that these studies reported on was limited. Ouyang et al. (2008) was the only study that reported on more than one type of GMD and explored both congenital hereditary muscular dystrophies and hereditary progressive muscular dystrophies. Although Schepelmann et al. (2010) studied three types of muscular dystrophies, only FSHD met the inclusion criteria for the present literature review. Despite the vast amount of research on the different types of GMDs, few studies have explored the economic burden of these illnesses.

In conclusion, there is limited evidence internationally on the cost of GMDs and the available data reflects inconsistent definitions of cost outcomes and methods of calculating these costs. This review has illustrated the need for identifying cases and collecting data from multiple sources and for a consistent approach to defining and calculating costs for better comparability of results across studies. Additionally, using resource data collected from a larger, population-based sample may lead to a more accurate and representative estimate of costs associated with GMDs. This larger sample removes the potential for selection biases seen in previous literature and underestimation of costs, particularly as accurate information is needed for health providers, advocacy groups, and patients themselves to understand the economic burden of GMDs in NZ.

Chapter 3. Methods

Section 3.1 contains the research aims and objectives. Section 3.2 explains the source of the data used in this research and Section 3.3 describes the cost-of-illness model. Sections 3.4, 3.5 and 3.6 outline the varying types of costs assessed and the methods of calculation. Section 3.7 describes how the results have been presented, and Section 3.8 discusses the statistical and sensitivity analyses of the research.

3.1 Research Aims and Objectives

This study aimed to determine the costs associated with GMDs among adults in New Zealand. The research objectives were:

- To estimate, from a societal perspective, the annual direct (healthcare and non-healthcare) and indirect (productivity loss) cost of GMDs among adults in New Zealand in 2021
- To identify the main cost drivers for GMDs and the subgroups of GMDs in New Zealand
- To determine the clinical, socioeconomic, and health care system factors that indicate whether patients incur a level of treatment cost

3.2 Data Source

The present research drew upon data from the larger prevalence and impact MD-Prev study that aimed to identify all living children and adults with GMDs in New Zealand. That population-based, cross-sectional study used the capture-recapture method to ascertain cases of living in New Zealand with a diagnosis of a GMD (Theadom et al., 2019). Notably, by using this method alongside diagnostic confirmation, the study addressed the limitations of selection and diagnostic biases found in previous epidemiological studies of muscular dystrophies (Theadom et al., 2019). Cases were identified from a range of sources including hospital and neurologists' patient lists, the Ministry of Health database, the New Zealand Muscular Dystrophy Association membership database, and the NZ Neuromuscular Disease Registry (Theadom et al., 2019). Respondents completed a questionnaire regarding different areas of resource utilisation associated with their muscular dystrophy conditions within the past 12 months. For instance, they were asked about formal and informal care provision and equipment required to undertake daily activities (Theadom et al., 2019). Ultimately, the robust methods and nationwide sample used in the MD-Prev study had provided a data source for this current study with sufficient information on resource utilisation to estimate the costs of GMDs among adults in New Zealand.

3.2.1 Case Definition

The full list of the included GMDs can be found in Appendix C. Cases needed to be a resident or citizen of NZ and aged over 16 years at the time of the assessment. Diagnostic confirmation was required for inclusion, and could be from the patient's treating neurologist, genetic test results, or from medical notes and test results reviewed by a neurologist (Theadom et al., 2019). Cases were identified using multiple overlapping sources to reduce the possibility of missing cases (Theadom et al., 2019). Cases were ascertained with an International Classification of Disease code (ICD-10, including G771.0, G71.1, G71.2, G72.3) in the admission and discharge hospital records and the national Ministry of Health database (Theadom et al., 2019). Cases were also identified through the NZ Muscular Dystrophy Association membership database and the NZ Neuromuscular Disease Registry if cases had a disorder that was in the list of included GMDs (Rodrigues et al., 2012; Theadom et al., 2019).

3.3 Cost-of-Illness Model

The goal of cost-of-illness studies is to quantify and describe the costs attributable to a particular disease (Drummond, 1992; Jo, 2014). This type of assessment is frequently done by identifying cost-generating components and attributing a monetary value, which is often referred to as the 'opportunity cost'. The three main cost components in cost-of-illness studies are direct, indirect, and intangible costs (Drummond, 1992).

Notably, measuring these costs is important to gain accurate knowledge about the burden of illness and provide a baseline for comparisons with other disease burdens (Drummond, 1992). The estimates from cost-of-illness studies can be further used in cost-benefit and cost-effectiveness analyses to evaluate new treatments and help decision makers in setting priorities and allocating resources (Hodgson & Meiners, 1982). These cost analyses can also be useful for communications with the public and policy makers on the importance of GMDs in New Zealand (Clabaugh & Ward, 2008).

The cost-of-illness model took a prevalence-based, bottom-up, retrospective approach from a societal perspective. There are two types of epidemiological data that can be used in cost-of-illness studies - prevalence-based or incidence-based approaches (Tarricone, 2006). The incidence-based approach estimates the lifetime costs of new cases diagnosed each year, whereas the prevalence-based approach estimates the total costs over a specific period, usually a year (Costa et al., 2012; Jo, 2014). In this present study, a prevalence-based approach was more appropriate than an incidence-based approach, as this research aimed to draw the attention of decision makers to the underestimated

economic burden of GMDs in NZ (Drummond et al., 2015; Tarricone, 2006). Additionally, using this approach illustrates to decision makers the overall burden and indicates major cost components where cost containment policies could be applied (Drummond et al., 2015; Tarricone, 2006). The available data was collected within a 12-month period, which was best suited to a prevalence-based approach (Jo, 2014).

When examining costs, two approaches are available to determine the methods to estimate the economic costs - the top-down approach, and the bottom-up approach (Drummond et al., 2015; Tarricone, 2006). The top-down approach measures the proportion of healthcare resource consumption of a given disease (Drummond et al., 2015; Jo, 2014; Tarricone, 2006). This approach uses aggregated expenditure data and divides this with the number of people with the disease to estimate the costs per person (Drummond et al., 2015; Jo, 2014). With the bottom-up approach, costs per person are estimated by first identifying cases and then assessing their individual cost (Drummond et al., 2015; Gustavsson et al., 2011; Tarricone, 2006). After measuring the individual resource consumption, a unit cost is multiplied by the number of persons for the resource (Drummond, 1992; Gustavsson et al., 2011; Jo, 2014). The advantage of this approach is that studies are more complete in terms of what resources are available and utilised by a population and are more accurate in terms of the selection of persons (Gustavsson et al., 2011).

There are also two temporal relationships between the initiation of the study and the data collection - the retrospective or prospective approach (Drummond, 1992; Tarricone, 2006). In retrospective cost-of-illness studies, all relevant resource use has already occurred, and data collection refers to the data that has been recorded (Jo, 2014; Tarricone, 2006). In prospective cost-of-illness studies, the relevant resource use has yet to be consumed when the study is initiated, so data collection requires a significant amount of time to follow-up with patients (Drummond, 1992; Jo, 2014; Tarricone, 2006). The retrospective approach provides benefits in being efficient in measuring the burden of illness and less time-consuming and expensive (Tarricone, 2006). Retrospective studies can only be conducted with sufficient data available (Tarricone, 2006). However, as robust data was available from the MD-Prev study, that provided the opportunity to carry out a retrospective cost-of-illness study.

The perspective of analysis is important to clarify, as it defines what cost outcomes are encompassed within a study (Drummond et al., 2015). This cost-of-illness study was developed using a societal perspective and measured the costs to society. The impacts of GMDs do not lie solely on an individual or organisation, so taking this broader societal perspective considered all the direct and indirect costs associated with GMDs (Jo, 2014). If a health care system perspective was used, only the direct medical costs would be analysed, excluding all the associated costs to the individual and family such as informal care (Jo, 2014).

The cost components assessed in the present study were categorised into the direct and indirect costs associated with GMDs for all members in the given society. Direct costs consist of healthcare

costs and non-healthcare costs. The direct healthcare costs are the medical care expenditures for diagnosis, treatment, continued care, and rehabilitation (Hodgson & Meiners, 1982; Jo, 2014). The direct non-healthcare costs refer to non-medical expenditures due to the illness, such as informal care which is detailed further below (Hodgson & Meiners, 1982; Jo, 2014). Indirect costs are the losses in output due to a reduction or cessation of productivity because of the illness (Hodgson & Meiners, 1982; Jo, 2014).

This study analysed the listed GMDs together and conducted subgroup analyses for different subtypes of GMDs. The inclusion criterion for the subgroup analyses was that the subtype had to have a sample size larger than 30 cases. The reason for this was to have sufficient data to analyse, limit the amount of uncertainty when conducting bootstrapping and protect participant privacy with smaller sample sizes. Therefore, the GMDs included for disaggregation were myotonic dystrophy, facioscapulohumeral muscular dystrophy, Limb-girdle muscular dystrophy, Ion channel muscle disease, and dystrophinopathies. However, as research has separated dystrophinopathies in cost-of-illness studies, an exception was made for Duchenne and Becker muscular dystrophy in order to be consistent with previous literature. All costs were expressed in 2021 New Zealand dollars.

This study was conducted according to the guidelines of the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) (Husereau et al., 2013). A completed CHEERS checklist can be found in Appendix D. Ethics approval was obtained from the University of Auckland Human Participants Ethics Committee (Reference number UAHPEC22577). All participants provided written informed consent before participating in the assessment.

3.4 Direct Healthcare Costs

Direct healthcare costs were all calculated using the resource-based approach, which applies a common unit cost to each health service or resource consumed. A table of all the unit costs used in this research and their data sources can be found in the Appendix E. The resources included as direct healthcare costs were hospital admissions, outpatient and community care, medication and supplements, formal care, and ventilatory support.

3.4.1 Hospital Admission Costs

Individual hospitalisation data was obtained from the Ministry of Health (MOH) database for those participants who consented to the MD-Prev study. Muscular dystrophy-related hospitalisations were matched individually using unique National Health Index numbers and these admissions were confirmed using ICD-10 codes (G71.0, G71.1, G71.2, G72.3) (Theadom et al., 2019). The cost of hospitalisations was determined using a weighted discharge value (i.e., Weighted Inlier Equivalent

Separations [WIES]) for all National Minimum Dataset events by the MOH (Ministry of Health, 2021b). For hospital admissions, including emergency visits, the WIES cost weight for the 2020/21 financial year was multiplied with the national price (NZ$5,545.26) (Ministry of Health, 2021b). This WIES cost weight includes the medical costs of ward stays, medications, tests, and nursing and other ward staff labour.

In some instances, participants indicated they were admitted to hospital but had no hospitalisation data that matched the data source provided by the MOH. As the MD-Prev study collected the length of stay information, the number of days was multiplied with the 'same day stay' or 'one day stay' WIESNZ cost of NZ$4,040.28 (nzdrg70 code B06C – "Procs for Cerebral Palsy, Muscular Dystrophy, Neuropathy, sameday") (Ministry of Health, 2021b).

3.4.2 Surgery

Participants indicated on the MD-Prev questionnaires whether they underwent any surgeries, what the specific surgery was for, and the length of stay at hospital. For those that did not have any hospitalisation data but noted they had a surgery related to their GMD, the WIESNZ nzdrg70 code that aligned with the specific surgery was used to calculate their surgery costs. This list of nzdrg70 codes used and the cost weight can be found in Table E.3 in Appendix E.

3.4.3 Outpatient and Community Care Costs

This sub-category of direct healthcare costs assessed the costs associated with support from allied health professionals. The MD-Prev data source provided each patient's number of therapy visits (e.g., speech and language therapist, physiotherapist, occupational therapist, dietician, general practitioner, medical specialist, psychologist, and visiting nurse) in the past 12 months. Using this information, the frequency of visits per health professional consultation over 12 months was multiplied by the resource unit cost (e.g., cost per hour for the therapist) sourced from the Accident Compensation Corporation (ACC) (ACC, 2021) and the Pharmaceutical Management Agency's (PHARMAC) Cost Resource Manual (PHARMAC, 2020a).

3.4.4 Prescribed Medication and Complementary Therapies

Information regarding the quantity of prescribed medication related to peoples GMDs was obtained from the MD-Prev study self-reported questionnaires. Using the cost estimates for medications from the PHARMAC schedule, a unit cost of NZ$5 was used to multiple this cost by the quantity of medications for each participant (PHARMAC, 2020b). Some participants received complementary treatments or

therapies, for which the annual number or frequency of visits to these services were recorded. The cost per visit was sourced from either ACC or PHARMAC's Cost Resource Manual and multiplied by the frequency of visits (ACC, 2021; PHARMAC, 2020a).

3.4.5 Formal Care

Formal care is defined as paid home help care and/or personal care provided at patients' homes by professional caregivers. The number of hours of support received each week (e.g., personal care, transport, organising activities, housework, and nursing care) was identified from the MD-Prev data source and was multiplied by the resource unit cost (e.g., cost per hour for provision of care). This unit cost was valued at NZ$28.00 per hour and was sourced from a previous study that looked at the costs of formal care within the NZ context (Te Ao et al., 2022).

3.5 Direct Non-healthcare Costs

Direct non-healthcare costs are expenditures that do not involve the purchasing of medical services but are costs occasioned by the disease or illness (Hodgson & Meiners, 1982; Jo, 2014). They included medical aids, home modifications, automobile modifications, travel expenses, and informal care. The unit costs used for these calculations can be found in the unit cost tables in Appendix E.

3.5.1 Medical Aids and Home Modifications

People with GMDs require a range of medical aids and home modifications to assist in activities of daily living. These were identified in the MD-Prev study and included equipment such as walking sticks, height-adjustable beds, railings in the toilet or bedroom, and ventilation support machines. The unit costs of each item were sourced from the Mobility Centre, PHARMAC, the New Zealand Respiratory and Sleep Institute, and through personal communications with the New Zealand Muscular Dystrophy Association. These are all listed in Table E.1 in Appendix E.

3.5.2 Travel Expenses

From the MD-Prev study data source, the support required for travel was recorded and included the average number of kilometres travelled for each journey. The cost of travel was calculated as the product of the average number of kilometres travelled by the rate per kilometre. The rate used was 79 cents per kilometre (Tier 1) and was sourced from the vehicle expense rate stated by Inland Revenue for the 2020-2021 income year (Inland Revenue, 2021).

3.5.3 Non-funded Medication and Supplements

The weekly expenditure for non-funded medication, herbal or vitamin supplements, and nutritional supplements related to their GMDs were also recorded in the MD-Prev study. The annual cost of non-funded medication and supplements was calculated by multiplying the weekly expenses by 52 to cover the 12-month period.

3.5.4 Informal Care

Informal care is defined as the unpaid care provided at home by non-professionals (e.g., family and friends) to help maintain or enhance patient independence (Cavazza et al., 2016; Hodgson & Meiners, 1982; Koopmanschap, 1998; Koopmanschap et al., 2008). The cost of informal care was calculated using the proxy good method, also known as the replacement cost approach. The proxy good method values the number of hours of care provided by non-professional caregivers (e.g., personal care, transport, organising activities, housework, and nurse care) and multiplies it by a wage rate of a close market substitute (Koopmanschap et al., 2008; van den Berg et al., 2004). This method assumes that if this care was not provided by a non-professional caregiver, it would likely be substituted by a professional caregiver (Cavazza et al., 2016; Hodgson & Meiners, 1982; Koopmanschap, 1998; Koopmanschap et al., 2008). The wage rate can differ for different tasks where, for instance, personal and nurse care is valued at the market wage of a professional nurse, while housework is valued at the market wage of a professional house worker (van den Berg et al., 2004). In this present study, the proxy good method was used based on the provided data. Therefore, the unit cost for informal care was NZ$28.00 as shown in Table E.2 Appendix E. This method allowed for the ability to compare between formal and informal care costs of GMDs in this study.

3.6 Indirect Costs

Indirect costs measure the loss of productivity, which values the effect of the illness on the patient's ability to work (Costa et al., 2012). Information regarding employment status and age of onset of muscular dystrophies was recorded from the MD-Prev study self-reported questionnaire. There are three major methods of measuring productivity loss - the human capital approach, friction cost method, and willingness to pay (WTP) method. The WTP method measures the value of people's eagerness to pay in order to reduce or avoid health risks (Gafni, 1991). However, this approach is rarely used as there are many difficulties in the practical application (Jefferson, 1996). These difficulties are due to the extensive surveys that depend on how the hypothetical questions about the person's willingness are constructed and the meaning placed on the answers given (Jefferson, 1996).

Therefore, the present study focused on calculating productivity loss using the human capital approach and the friction cost method.

3.6.1 Human Capital Approach

The human capital approach values future economic production over the expected remaining lifetime for someone of a given age if they were to continue working in full health (Jo, 2014; Pike & Grosse, 2018). The rationale for using this approach is that the withdrawal of an individual's labour due to their GMD results in the potential loss to society of that individual's future production (Pike & Grosse, 2018). Therefore, in the case of permanent disablement due to GMDs at a specific age, the indirect cost is calculated as the product of the remaining years from this age to the age of retirement assuming the average annual income (van den Hout, 2010). For the present research, the recorded age for those individuals in paid employment at the time of conducting the MD-Prev study was used to calculate the number of remaining working years. The retirement age was defined as 65 years of age as this was the average age of retirement for adults in New Zealand (New Zealand Government, 2020). The average annual income was sourced from the 2018 New Zealand census data (Statistics New Zealand, 2020a). Discounting was applied at 3.5% for future cost projections, as recommended by PHARMAC (PHARMAC, 2020b).

An advantage of using the human capital approach is that it quantifies the relative economic productivity loss due to illness or premature death of the individual, regardless of whether they are in paid employment. Although the human capital approach is the most frequently used method of calculating indirect costs, one major criticism is that it can overestimate productivity losses and calculates the potential costs rather than actual costs (Koopmanschap, 1998; Koopmanschap et al., 1995; van den Hout, 2010).

3.6.2 Friction Cost Method

The friction cost method is an alternative and commonly used method for calculating productivity loss (Koopmanschap, 1998; van den Hout, 2010). This approach values the temporary loss of earnings to the individual and depends on the time span employers need to restore the initial production level (Koopmanschap et al., 1995). Essentially, this method assumes that an individual will be replaced after a certain amount of time required to hire and train a new employee, known as the friction period (Koopmanschap et al., 1995). Aligned with previous studies, a friction period of three months was used (Koopmanschap et al., 1995). Patients with GMDs often experience muscle weakness and loss of muscle function or ambulation which can force a reduction or cessation in working hours due to their disability (Hodgson & Meiners, 1982). Therefore, two variables were used to apply the friction cost method. These were (i) if participants reported a reduction in work hours and (ii) if participants

reported missed work days (Theadom et al., 2019). The advantage of this method is that it quantifies the economic loss to society for those people with GMDs who were in paid employment (Jo, 2014; Koopmanschap et al., 1995). The productivity losses using this method will be smaller compared to the losses estimated by the human capital approach, but would more likely reflect the real production losses for society (Drummond, 1992; Koopmanschap et al., 1995). The productivity loss estimated using the friction cost method was used in the total one-year cost per person.

3.7 Presentation of Main Results

The three main cost categories of direct healthcare costs, direct non-healthcare costs, and indirect costs were presented separately. The mean number of visits, length of stay, or hours per day were also recorded mainly for direct healthcare costs and unpaid informal care. The total annual cost per person was calculated as the sum of the mean annual direct and indirect costs. However, the total results were presented as two separate totals, one including informal care and one excluding informal care. Previous literature has highlighted that informal care is a large driver of cost for people with GMDs and is an area of unmet need (Cavazza et al., 2016; Schepelmann et al., 2010; Teoh et al., 2016). Therefore, in order to determine if informal care was also a large driver in this study, the total one-year cost per person was presented with and without informal care. The total costs for the country were estimated, along with the cost drivers for GMDs in general and for the six subtypes of GMDs that were analysed.

3.8 Statistical Analysis

The data was analysed with SPSS Statistics version 27. The Mann-Whitney non-parametric test was conducted with non-parametric bootstrapping of 1,000 samples to produce results that were presented as mean annual total cost per person with 95% confidence intervals. The method that was used to handle any missing data was the ‘complete case analysis’, also known as ‘listwise deletion’ (Jamshidian & Mata, 2007; Pigott, 2001). This method only utilises those cases in a data set with complete information (Jamshidian & Mata, 2007; Pigott, 2001).

Additionally, multivariable linear regression analyses were conducted to determine which variables predicted higher costs for people with GMDs. The main demographic and socioeconomic variables, including sex, age, ethnicity, subtype of GMDs, income and employment, were analysed as independent variables. Other independent variables included the need for ventilation, satisfaction with healthcare, and whether the person had a manual wheelchair and/or an electric wheelchair. These factors were included as research has previously used wheelchair use and ventilatory support as a proxy for mobility and disease severity for people with GMDs (Teoh et al., 2016). Satisfaction with

healthcare was a unique variable that was collected in the MD-Prev study and from what is currently known has not been included in a regression analyses in past studies (Theadom et al., 2019) .

To account for uncertainties in the data or methodology, sensitivity analyses were conducted. The analysis explores the level of confidence associated with the results by changing key variables used in the analysis (Bland, 2015). One-way sensitivity analyses test single variables across a range of values and examine the impact on the results (Bland, 2015). As the methods for calculating indirect costs are contested in the literature, a one-way sensitivity analysis was generated to compare the human capital approach and friction cost method. Additionally, the discounting of long-term productivity costs was examined by using three different rates. The discount rate of 3.5% was the base case, as recommended by PHARMAC, and this study further examined the discount rates at 0% and 6% to account for any uncertainties regarding the long-term productivity cost of GMDs (PHARMAC, 2020a).

Chapter 4. Results

The aim of this chapter is to utilise GMD data from the population-based MD-Prev study in combination with electronic hospital records and self-reported health service usage to estimate the societal cost of GMD in one year for New Zealand in 2021. The preliminary results were published in the February 2021 issue of the Muscular Dystrophy Association's *In Touch* magazine, as provided in Appendix F.

4.1 Sample Characteristics

A total of 809 adult cases were eligible for this study and of those, 490 (61% [490/809]) provided consent to be included in this cost analysis. Written informed consent was obtained in the parent study from all study participants which included consent to analyse the economic data. The overall characteristics of the study population are presented in Table 1. As shown, the mean age of the sample was 45.6 ± 16.3 years (ranging from 16 to 90 years). There was a similar number of males (n = 255, 52%) and females (n = 235, 48%). The ethnicity that participants most associated with was New Zealand European (n = 424, 87%), then Māori (n = 34, 7%), Asian (n = 12, 3%), and Pacific Islander (n = 5, 1%). The most common GMD was myotonic muscular dystrophy, and this accounted for 41% [202/490] of the diagnoses. This was followed by facioscapulohumeral muscular dystrophy (17% [82/490]) and then Limb-girdle muscular dystrophy (11% [54/490]).

Half of the participants reported having at least one co-morbid condition, most commonly asthma, diabetes, cardiovascular conditions, and mental health difficulties. A third of the participants were in either full- or part-time employment at the time of the study. Fourteen percent (n = 66) of the participants required either invasive or non-invasive ventilatory support. Satisfaction with health care was reasonably high with a mean rating of 7 out of 10 (± 2.1).

Table 1. Overall sample characteristics

	Current sample n = 490
Age, y	45.6 ± 16.3 (16-90)
Sex, n (%)	
Male	255 (52%)
Ethnicity, n (%)	
NZ European	439 (87%)
Diagnosis, n (%)	
Myotonic dystrophy	202 (41.2%)
Facioscapulohumeral muscular dystrophy	82 (16.7%)
Limb-girdle muscular dystrophy	54 (11.0%)
Ion channel muscle disease	33 (6.7%)
Dystrophinopathies	
Becker muscular dystrophy	28 (5.7%)
Duchenne muscular dystrophy	23 (4.7%)
Congenital myopathy	22 (4.5%)
Other	46 (9.4%)
At least one co-morbid condition, n *(%)*	242(49%)
Employed, n (%)	159 (32%)
Need for ventilation support, n (%)	66 (14%)
Satisfaction with health care, 0-10	7 (2.1)

4.2 Average annual per person cost of GMDs in NZ

A detailed breakdown of the resources used and average per person costs for 12 months is presented in Table 2. The total direct costs (which includes direct health care and direct non-healthcare costs) per person was estimated to be on average NZ$62,853 (95% CI $54,865 - $71,904). The total direct healthcare costs per patient amounted to NZ$29,762 (95% CI $24,354 - $35,224). Of the 490 cases, approximately 49% were not hospitalised in that year for their GMD. Among those cases who were hospitalised, patients spent on average 8.64 days (min one day, max 108 days) in hospital. Hospitalisation costs were on average approximately NZ$14,938 per admission (minimum $530, maximum $124,984). For visits to health professionals over the 12 months, 54 percent of the participants saw a medical specialist, 53 percent saw allied health professionals, and 92 percent visited a general practitioner. The mean number of specialist medical and allied health visits over 12 months was 3.41 and 15.84 visits respectively. For the 450 cases (92%) who saw a general practitioner within the year, the mean number of visits was 6.08. A third of the participants [172/490] required formal paid home and personal care within the year, which was estimated to be on average NZ$57,209 (95% CI $46,226 - $67,779) per patient for the year. Formal care was the largest cost component of direct healthcare costs (67%), followed by hospital admissions (26%). Prescribed medications cost on average NZ$16 (min $0, max $80) per person and approximately 62 percent

[304/490] of the cohort required prescribed medication from a general practitioner or clinician. Complementary therapies such as aromatherapy or homeopathic remedies were used by 13% [63/490] of the participants.

Total direct non-healthcare costs were estimated at NZ$33,090 (95% CI $28,207 - $38,517) per patient. The largest cost component of direct non-healthcare costs was unpaid informal care (74%), followed by medical aids (14%) and then automobile adaptations (6.6%). Approximately 44% [216/490] of the cohort received unpaid informal care, totalling 38 hours per week per person. This unmet need was translated to an average of NZ$55,283 per person over one year (min $10,220, max $245,280). Automobile adaptations were the second largest contributor for this group of costs and were estimated at NZ$12,165 per person. More than half the cohort (57% [279/490]) required medical aids, where bathroom equipment (37% [179/490]), walking sticks (28% [135/490]), and manual wheelchairs (26% [126/490]) were the top three aids utilised. The medical aids needed most were access to an electric wheelchair (9% [43/490]), rollover equipment (5.9% [29/490]) and an adapted chair (5.7% [28/490]). Nearly half the cohort (44% [216/490]) indicated that they had modified their home to accommodate their GMD and the top three home modifications were rails in the toilet (31% [151/490]), permanent ramps (25% [123/490]), and portable ramps (12% [61/490]). Based on need, 8.2% (40/490) of the cohort needed permanent ramps and 8.0% (39/490) needed portable ramps.

Non-funded medication, including nutritional and herbal or vitamin supplements, cost on average NZ$698 (min $20, max $10,400) per person. When looking at disaggregated proportions of non-funded medication requirements, 11% of the cohort [52/490] needed medications that were prescribed or recommended but were not funded or subsidised. Four percent [19/490] of the cohort were not taking medication prescribed to them as they were not funded or subsidised by the government. For supplements, herbal or vitamin supplements were used by 35% [279/490] of the cohort and nutritional supplements were required by 11% [52/490] of the cohort.

Indirect costs were firstly estimated as temporary productivity losses due to missed workdays or reduced work hours, using the friction cost method. Approximately, 11% [54/490] reported productivity losses which were valued at NZ$11,466 (95% CI $7,695 - $16,141). Interestingly, we found no temporary productivity loss due to absentee of work for participants with DMD as no participants indicated a reduction in workhours or missed workdays. When using the human capital cost approach to estimate the long-term productivity loss, 13% [64/490] of the participants were over the retirement age of 65 (New Zealand Government, 2020). Therefore, 87% [426/490] were included into the calculations and the estimated long-term productivity loss for people with GMDs per case was approximately NZ$591,911 (95% CI $516,010 - $624,790). The results show that with the inclusion of temporary productivity losses, the total one-year cost per person equated to NZ$64,114 (95% CI $57,045 - $73,777). With the exclusion of informal care, the total one-year cost per person reduces to NZ$39,789 (95% CI $34,717 - $46,983).

Table 2. Annual proportion and cost per case for the categories of resource use for genetic muscle disorders in New Zealand

	Utilisation % (n= 490)	Resources per patient*	Cost per category	
			Mean ($)	95%CI ($)
Direct healthcare costs				
Emergency department	28	2.74	1,012	903 - 1,132
Hospital admission	51	8.64	14,938	12,616 - 17,543
Surgery	4	-	2,195	1,631 - 2,780
Respite care	3	18.07	3,451	1758 - 5,399
Specialised medical care	54	3.41	383	347 - 427
Allied healthcare	53	15.84	1,163	937 - 1414
General Practice	92	6.08	487	452 - 526
Nursing	35	9.88	395	284 - 537
Formal care costs	35	5.6 hrs/day	57,209	46,226 - 67,779
Prescribed medications	62	-	16	15 - 18
Complementary therapies	13	-	1,745	1,243 - 2,321
Total direct healthcare cost per person	100	-	29,762	24,354 - 35,224
Direct non-healthcare costs				
Cost of medical aids	57	-	8,345	7,284 - 9,485
Cost of home modification	44	-	664	579 - 751
Cost of respiratory management	16	-	4,010	3,195 - 4,956
Cost of automobile adaptions	18	-	12,165	-
Travel expenses	51	-	1,175	888 - 1,613
Non-funded medications	4	-	698	556 - 885
Unpaid informal care	44	5.41 hrs/day	55,283	46,110 - 65,028
Total direct non-healthcare costs per person	100	-	33,090	28,207 - 38,517
Total direct costs per person	100	-	62,853	54,865 - 71,904
Indirect costs				
Temporary loss due to missed workdays	11	-	11,466	7,695 - 16,141
Long term productivity^	87	-	591,911	516,010 - 624,790

Table 2. Continued

Total one-year per person costs *including informal care*	44	-	64,114	57,045 - 73,777
Total one-year per person costs *excluding informal care*	100	-	39,789	34,554 - 46,235

** Mean visits per patient, length of stay, or hours per day*
^ 3.5% discount rate
Note: Bootstrap results are based on 1,000 bootstrap samples

4.3 Annual cost per person for different GMDs

Tables 3-10 below detail the annual resources used and average per person costs for six of the most common GMDs in New Zealand. Only the following six GMDs were analysed, as they met the inclusion criterion of having a sample size larger than 30, with the additional inclusion of Duchenne and Becker muscular dystrophy, in order to be consistent with previous research. Therefore, this analysis excluded other GMDs such as Pompe disease, Emery-Dreifuss muscular dystrophy and distal muscular dystrophy as they did not meet the criterion.

4.3.1 Duchenne muscular dystrophy

As shown in Table 3, the total number of dystrophinopathies was 51, and 23 of those participants were diagnosed with DMD. The total direct healthcare cost per annum per patient was estimated to be NZ$113,151 (95% CI $71,908 - $154,229). Of the 23 participants, 70% of these cases were hospitalised, and although patients spent on average 4.10 days in hospital, the mean cost was NZ $10,427 (min $1,303, max $30,216). At least half of the cases visited various health care professionals. Ninety-six percent (22) visited an allied health professional, with an average of 35 allied health visits. The annual mean cost of allied health care was approximately NZ $2,509 (min $138, max $15,645). Participants with DMD had an average stay of 41 nights at a respite care centre, costing an average of NZ$7,896.

Notably among the direct healthcare costs, formal care was the largest cost component (89%) by a significant amount, as the next largest cost was hospital admission costs (6.5%). Formal care was a significant cost, for 91% (21) of participants, where the mean cost was estimated at NZ$110,960 per year (min $10,220, max $245,280). However, the annual unpaid informal care cost was estimated to be larger, with a mean cost of NZ$142,479 (min $10,220, max $245,280) for the approximately 75% (17) requiring informal care. On average, these participants received 10.86 hours of formal care per day, compared with 13.94 hours of informal care per day on average.

Of the direct non-healthcare costs, informal care was the largest cost component (73%) and was followed by the cost of medical aids (15%). High proportions of cases used medical aids (96%), home modifications (91%), and automobile adaptations (87%). The mean cost of medical aids was valued at NZ $22,481 and were the largest out of pocket expenses for participants with DMD. The long-term productivity loss was high and on average, this was NZ$1,077,475 (95% CI $1,017,571 - $1,131,453). This finding could reflect the early age of onset and thus younger age of participants at the time of the study, which results in larger long-term productivity losses.

On average, the total direct healthcare cost per patient was NZ$113,151 (95% CI $71,908 - $154,229). The estimated total one-year cost per patient, excluding informal care, was NZ$151,728 (95% CI $115,459-$191,072). This cost increased significantly to NZ$257,163 (95% CI $202,985-$302,824) when unpaid informal care was included in the total first-year cost for participants with DMD. Overall, patients with DMD had the highest total direct healthcare, direct non-healthcare, long-term productivity and total one-year costs in comparison to the other GMDs.

4.3.2 Becker muscular dystrophy

Shown in Table 3, there were 28 participants diagnosed with BMD. The estimated total direct healthcare cost per annum per person was NZ$36,827 (95% CI $11,623 - $64,723). Around 20% of patients with BMD visited a nurse. Although this was a lower proportion of resource use compared to patients with DMD, patients with BMD on average saw a nurse 21 times per annum (min 2 visits, max 104 visits). Similarly, formal care was the largest component at 87% and then hospital admissions (8.6%). Of the total direct non-healthcare costs, informal care contributed to 57% of costs and medical aids contributed 23%. While this group of participants with BMD saw higher use of unpaid informal care (52%) compared to paid formal care (38%), the average cost of unpaid informal care was NZ$32,023 (min $10,220 max $245,280) and formal care was nearly triple that, approximated at NZ$84,547 (min $10,220 max $245,280). Additionally, the average hours per day of formal care was 8.27 compared to the average hours per day of informal care, which were 3.13.

Patients with BMD experienced some temporary productivity loss which was estimated at NZ$3,080 (95% CI $2,761 - $3,240). Long-term productivity loss was valued at NZ$614,253 per person, which was lower compared to that of patients with DMD. The total one-year cost per patient with BMD was estimated at NZ $49,679 (95% CI $22,693-$89,839). With unpaid informal care included, this total one-year cost increased to NZ $66,331 (95% CI $39,119-$108,589).

Table 3. Annual proportion and cost per case for the categories of resource use for Duchenne and Becker muscular dystrophy

	Duchenne muscular dystrophy				Becker muscular dystrophy			
	Utilisation % (n= 23)	Resources per patient*	Cost per category		Utilisation % (n= 28)	Resources per patient*	Cost per category	
			Mean ($)	95%CI ($)			Mean ($)	95%CI ($)
Direct healthcare costs								
Emergency department	35	2.75	1,018	740 - 1,434	14	2.00	740	-
Hospital admission	70	4.40	10,427	6,205 - 15,198	34	4.33	9,345	5,012 - 13,636
Surgery	-	-	-	-	-	-	-	-
Respite care	13	41.33	7,896	764 - 11,462	-	-	-	-
Specialised medical care	83	3.74	420	286 - 578	45	3.46	392	258 - 573
Allied healthcare	96	34.59	2,509	1,051 - 4,261	59	13.88	983	333 - 1,909
General Practice	91	4.76	381	263 - 504	79	5.17	414	288 - 555
Nursing	48	13.45	538	110 - 1,366	21	21.00	840	80 - 2,364
Formal care	91	10.86 hr/day	110,960	72,144 - 149,080	38	8.27 hr/day	84,547	4,319 - 150,957
Prescribed medications	83	-	15	10 - 20	55	-	12	8 - 17
Complementary therapies	9	-	1,345	90 - 2,600	7	-	2,170	180 - 4,160
Total direct healthcare cost per person	100	-	113,151	71,908 - 154,229	100	-	36,827	11,623 - 64,723
Direct non-healthcare costs								
Medical aids	96	-	22,481	20,296 - 23,780	69	-	9,684	5,602 - 13,645
Home modification	91	-	1,363	1,107 - 1,582	55	-	659	406 - 954
Respiratory management	61	-	6,414	3,814 - 8,773	14	-	6,350	1,800 - 11,200
Automobile adaptions	87	-	12,165	-	34	-	12,165	-
Travel expenses	78	-	881	449 - 1,459	59	-	696	403 - 1,132
Non-funded medications	52	-	1,100	378 - 2,483	21	-	303	117 - 611
Informal care	74	13.94 hr/day	142,479	100,747 - 185,418	52	3.13 hr/day	32,023	18,759 - 47,012
Total direct non-healthcare costs per person	100	-	144,012	108,501 - 179,842	100	-	29,196	18,494 - 40,886
Total direct costs per person	100	-	257,163	204,992 - 307,188	100	-	66,023	37,939 - 111,041

Table 3. Continued

Indirect costs								
Temporary loss due to missed workdays	-	-	-	-	10	-	3,080	2,761 - 3,240
Long term productivity^	100	-	1,077,475	1,017,571 - 1,131,453	90	-	614,253	476,639 - 761,017
Total one-year per person costs *including informal care*	74	-	257,163	204,496 - 303,511	52	-	66,331	37,012 - 111,203
Total one-year per person costs *excluding informal care*	100	-	151,728	113,125 - 192,048	100	-	49,679	22,415 - 89,161

** Mean visits per patient, length of stay, or hours per day*
^ 3.5% discount rate
Note: Bootstrap results are based on 1,000 bootstrap samples

4.3.3 Facioscapulohumeral muscular dystrophy

Table 4 shows that there were 82 cases diagnosed with FSHD. The total direct healthcare cost per patient with FSHD was NZ$30,185 (95% CI $17,683 - $43,213). The highest proportion of resource use over 12 months were visits to a general practitioner, at 99%, then visits to allied healthcare at 52%. The mean number of visits to allied healthcare was 17.12 (min 1 visit, max 104 visits). However, the largest cost contributors to direct healthcare costs were formal care (74%) followed by hospital admissions (20%) and then allied healthcare (2.1%). Half of the participants were admitted to hospital and, on average, patients stayed for 7.67 days (min 1 day, max 52 days).

Around a third of the cases required formal care and the estimated mean cost was NZ$69,575 (95% CI $38,543 - $100,550) and on average, 6.81 hours of formal care per day were recorded. Similar to people with BMD, 52% of the cases with FSHD required unpaid informal care; on average, that care cost NZ$50,625 (95% CI $30,667 - $73,522) and 4.95 hours per day of informal care on average were recorded. Informal care made up 74% of direct non-healthcare costs and this was the largest cost component for this category. The total direct non-healthcare costs were estimated to be NZ$35,461 (95% CI $22,789 - $50,001). More than 20% of the group reported that they experienced temporary productivity loss, and this was the highest proportion across the six GMDs. This indirect cost was estimated as NZ$9,243 and the long-term productivity loss was lower than for either DMD or BMD. The total one-year cost per person with FSHD was NZ$41,354 (95% CI $24,756-$56,738), and when unpaid informal care was included, this increased to NZ$67,679 (95% CI $45,399-$86,914).

4.3.4 Myotonic dystrophy

A total of 202 cases diagnosed with DM were included in the study (Table 4). This was the largest sample size of the six GMDs analysed. The total direct healthcare cost per person was NZ$22,776 (95% CI $15,801 - $30,557) and this was the second lowest cost of the GMDs. Half of the cases were admitted to hospital and spent on average 9.45 days (min one day, max 103 days) in hospital. The mean cost for hospital admissions was relatively high at NZ $16,842 (95% CI 12,412-$21,298) and contributed to 37% of direct healthcare costs. The largest contributor was formal care costs at 54%, which was lower when compared to other GMDs. Similar to previously discussed GMDs, unpaid informal care was the largest cost component (79%) for direct non-healthcare costs. When comparing formal and informal care received for people with MD, fewer people required formal care. Nearly a third (63) of this group indicated they received formal care, whereas 40% (81) indicated they received informal care. The average cost per patient for formal care was NZ$39,582 (min $10,220 max $245,280), and the average cost per patient for informal care was NZ$39,986 (min $10,220 max $245,280).

There were high proportions of resource use for travel expenses (49%), medical aids (45%), non-funded medication (40%), and informal care (40%). Although only 12% of participants indicated a temporary loss of productivity, it was valued at NZ$11,264 (95% CI $2,761 - $3,240), which was higher than the temporary productivity loss of FSHD and BMD. Total one-year costs per person with MD were estimated at approximately NZ$28,499 (95% CI $20,733-$35,779), and with unpaid informal care included, the total one-year cost per person nearly doubled to NZ $44,494 (95% CI $34,264-$53,658).

Table 4. Annual proportion and cost per case for the categories of resource use for Facioscapulohumeral and Myotonic muscular dystrophy

	Facioscapulohumeral muscular dystrophy				Myotonic dystrophy			
	Utilisation % (n= 82)	Resources per patient*	Cost per category		Utilisation % (n= 202)	Resources per patient*	Cost per category	
			Mean ($)	95%CI ($)			Mean ($)	95%CI ($)
Direct healthcare costs								
Emergency department	22	2.50	925	740 - 1,144	29	2.78	1,028	857 - 1,254
Hospital admission	49	7.67	12,067	8,161 - 16,796	50	9.45	16,842	12,412 - 21,298
Surgery	4	-	1,998	778 - 4,023	16	-	2,066	1,469 - 2,749
Respite care	-	-	-	-	2	13.00	2,484	1,299 - 3,343
Specialised medical care	50	3.44	389	304 - 483	57	3.37	378	321 - 434
Allied healthcare	52	17.12	1,231	771 - 1,762	46	13.29	993	660 - 1,463
General Practice	99	6.06	485	418 - 549	95	6.29	503	439 - 575
Nursing	35	14.31	572	230 - 963	37	10.45	418	233 - 650
Formal care	32	6.81 hr/day	69,575	38,543 -100,550	31	3.87 hr/day	39,582	25,944 - 55,370
Prescribed medications	61	-	15	12 - 18	57	-	16	13 - 18
Complementary therapies	10	-	2,005	1,019 - 3,447	7	-	1,318	644 - 2,218
Total direct healthcare cost per person	100	-	30,185	17,683 - 43,213	100	-	22,776	15,801 - 30,557
Direct non-healthcare costs								
Medical aids	63	-	8,402	5,866 - 10,933	45	-	4,659	3,337 - 6,121
Home modification	45	-	716	498 - 929	33	-	376	285 - 486
Respiratory management	10	-	3,850	1,800 - 6,720	14	-	3,329	2,185 - 4,689
Automobile adaptions	18	-	12,165	-	6	-	12,165	-
Travel expenses	55	-	991	633 - 1,613	49	-	1,484	901 - 2,406
Non-funded medications	48	-	834	427 - 1,490	40	-	570	404 - 773
Informal care	52	4.95 hr/day	50,625	30,667 - 73,522	40	3.91 hr/day	39,986	28,557 - 54,012
Total direct non-healthcare costs per person	100	-	35,461	22,789 - 50,001	100	-	20,366	14,657 - 27,394
Total direct costs per person	100	-	65,645	44,228 - 88,050	100	-	43,142	33,488 - 53,094

Table 4. Continued

Indirect costs								
Temporary loss due to missed workdays	22	-	9,243	4,851 - 17,425	12	-	11,264	6,453 - 18,572
Long term productivity^	84	-	511,264	448,664 - 581,455	89	-	550,709	503,178 - 593,944
Total one-year per person costs *including informal care*	52	-	67,679	49,265 - 87,986	40	-	44,494	35,595 - 54,501
Total one-year per person costs *excluding informal care*	100	-	41,354	28,575 - 58,743	100	-	28,499	21,772 - 35,413

** Mean visits per patient, length of stay, or hours per day*
^ 3.5% discount rate
Note: Bootstrap results are based on 1,000 bootstrap samples

4.3.5 Limb-girdle muscular dystrophy

Table 5 shows there were 54 cases diagnosed with LGMD. The total direct healthcare cost per person was NZ$41,103 (95% CI 26,657 - $59,627) which was the second highest cost among the GMDs. A third of these participants visited the emergency department and over half were admitted to hospital. Of those admitted to hospital, the mean number of days stayed was 14.11 days (min one, max 61), with a high mean cost of NZ$22,221 (min $1,130, max $92,392). Nearly 60% (32) of this group with LGMD required formal care and the mean cost was estimated to be NZ$44,074 (95% CI $28,745-$65,150) with around 4.31 hours of formal care indicated per day. This cost accounted for 63% of the direct healthcare costs and was the largest component. In comparison, unpaid informal care was required by 43% (23) and the mean cost of this informal care was NZ$50,211 (min $10,220 max $204,400), with 4.91 hours of informal care indicated per day. Similar to many of the other GMDs, unpaid informal care contributed the most to direct non-healthcare costs (61%), followed by medical aids (23%).

Only seven percent of the cases indicated a temporary productivity loss due to missed work days or reduction of work hours, which was the lowest proportion among the six GMDs. However, this cost was estimated to be NZ$29,922 (95% CI 5,842 - $61,065), which was the highest indirect cost per person reported among the GMDs. Similarly, this group had the lowest proportion of long-term productivity loss at 69%, but had a high productivity cost estimated at NZ$1,037,316 (95% CI $815,332 - $1,274,671). The total one-year costs per person with LGMD were estimated at NZ$56,931 (95% CI $38,853-$72,220), and with the inclusion of informal care costs, the total one-year cost per person increased to NZ$78,522 (95% CI $57,372-$99,780). Overall, the total costs excluding informal care for patients with LGMD were the second highest, second only to patients with DMD.

4.3.6 Ion channel muscle disease

As shown in Table 5, 33 cases diagnosed with ION were included in the study. Results indicated that costs were relatively lower for this GMD compared to others. The total direct healthcare cost was estimated to be NZ$3,646 (95% CI $ 2,295 - $5,352) and, unlike the other GMDs, the largest cost component was hospital admissions (73%). Notably, there was no record of formal care required by patients with ION, which would explain the lower direct healthcare cost. Half of the cases were admitted to hospital and the average cost was NZ$5,919 (min $1,003, max $16,161). The second highest cost contributor to this category were visits to a general practitioner, was valued at NZ$406 (95% CI $301 - $504).

In the absence of formal care, the estimated unpaid informal care was relatively large. Informal care accounted for 92% of direct non-healthcare costs when only eight out of the 33 patients (24%) needed the care. This cost equated to a significant amount of NZ$75,373 (95% CI $13,615 - $154,347). However, when compared to other GMDs, it was at the lower end of costs with BMD and MD. This group had relatively high temporary productivity loss costs, which were estimated at NZ$19,488 (95% CI $8,762 - $24,851) for a proportion of only nine percent [3/33]. Interestingly, the long-term productivity was significant and could reflect the early age of onset for most ION conditions, similar to that of DMD.

There were no costs associated with respiratory management or automobile adaptions. This could be explained by the lack of respiratory complications or need for maintenance of ambulation among ION diseases (Maggi et al., 2021). The total one-year cost per person with ION was estimated at NZ$7,062 (95% CI $3,615-$9,197), and with unpaid informal care included this tripled to NZ $25,152 (95% CI $6,099-$50,321).

Table 5. Annual proportion and cost per case for the categories of resource use for Limb-girdle muscular dystrophy and Ion channel muscle disease

	Limb-girdle muscular dystrophy				Ion channel muscle disease			
	Utilisation % (n= 54)	Resources per patient*	Cost per category		Utilisation % (n= 33)	Resources per patient*	Cost per category	
			Mean ($)	95%CI ($)			Mean ($)	95%CI ($)
Direct healthcare costs								
Emergency department	33	2.33	863	740 - 1,036	33	2.27	841	740 - 1,073
Hospital admission	59	14.11	22,221	14,266 - 30,908	45	2.29	5,919	3,473 - 8,992
Surgery	-	-	-	-	-	-	-	-
Respite care	6	9.67	1,847	382 - 4,585	-	-	-	-
Specialised medical care	57	3.23	364	295 - 444	42	3.07	345	225 - 513
Allied healthcare	61	12.36	884	464 - 1,522	45	4.13	308	181 - 461
General Practice	96	7.00	560	432 - 745	82	5.07	406	301 - 504
Nursing	41	5.14	205	140 - 270	24	2.63	105	69 - 152
Formal care	59	4.31 hr/day	44,074	28,745 - 65,150	-	-	-	-
Prescribed medications	80	-	18	14 - 22	64	-	19	13 - 25
Complementary therapies	7	-	3,003	1,127 - 4,446	6	-	858	676 - 1,040
Total direct healthcare cost per person	100	-	41,103	26,657 - 59,627	100	-	3,646	2,295 - 5,352
Direct non-healthcare costs								
Medical aids	87	-	9,493	6,992 - 12,247	18	-	4,293	905 - 9,037
Home modification	72	-	679	486 - 887	12	-	341	207 - 455
Respiratory management	20	-	2,709	1,800 - 4,527	-	-	-	-
Automobile adaptions	28	-	12,165	-	-	-	-	-
Travel expenses	61	-	1,147	645 - 1,829	45	-	1,201	353 - 2,193
Non-funded medications	44	-	770	487 - 1,113	39	-	789	454 - 1,204
Informal care	43	4.91 hr/day	50,211	29,732 - 73,979	24	7.38 hr/day	75,373	13,615 - 154,347
Total direct non-healthcare costs per person	100	-	35,325	23,773 - 49,022	100	-	19,751	4,173 - 40,181
Total direct costs per person	100	-	76,428	55,545 - 96,762	100	-	23,398	5,993 - 53,165

Table 5. Continued

Indirect costs								
Temporary loss due to missed workdays	7	-	29,922	5,842 - 61,065	9	-	19,488	8,762 - 24,851
Long term productivity^	69	-	1,037,316	815,332 - 1,274,671	88	-	1,207,260	1,154,600 - 1,677,750
Total one-year per person costs *including informal care*	43	-	78,522	57,637 - 99,021	24	-	25,152	7,766 - 49,793
Total one-year per person costs *excluding informal care*	100	-	56,931	42,183 - 74,181	100	-	7,062	4,129 - 11,683

** Mean visits per patient, length of stay, or hours per day*
^ 3.5% discount rate
Note: Bootstrap results are based on 1,000 bootstrap samples

4.4 Health System Cost Drivers for the Six Common GMDs and Comparisons

Details for the main annual cost drivers for the subcategorised GMDs are illustrated in the figures in Appendix G. There are consistent results indicating that costs for formal care and unpaid informal care are the largest drivers of costs for the GMDs, with the exception of ION, as there was no record of any formal care costs for these participants. However, informal care was the largest driver of cost for ION. When looking across all cost components, medical aids were also a consistent driver of overall costs; excluding unpaid informal care, the cost of medical aids was the highest contributor of direct non-healthcare costs for all six GMDs. If formal care is excluded from the direct healthcare costs, the cost of hospital admissions was the highest cost contributor for this cost category across the six GMDs analysed in this study.

Overall, the results showed that DMD had the highest per person direct healthcare, direct non-healthcare, long-term productivity loss, and total one-year costs across the six GMDs. Five of the six GMDs recorded a formal care cost and DMD had the highest per person cost for formal care, at NZ$100,974, followed by BMD with an estimated cost of NZ$32,128, and then LGMD with a cost of NZ$26,004. DMD and BMD had the highest mean number of formal care hours per day, which were 10.86 and 8.27 hours respectively. Patients diagnosed with DMD had the highest mean number of nights spent at a respite care centre and visits to allied health professionals. Patients with BMD had on average 21 nurse visits within a year, which was followed by patients with FSHD (14.31 visits) and then patients with DMD (13.45 visits). Patients with LGMD had an average of 14.11 days admitted to hospital, which was the highest incidence among the GMDs.

Informal care was estimated to be a significant cost for all six GMDs, where DMD had the largest per person cost (NZ$105,434), followed by FSHD (NZ$26,325), and then LGMD (NZ$21,591). Interestingly, patients with LGMD recorded the highest per person temporary productivity loss costs due to missed work days or reduced work hours at NZ$2,095. This rate was closely followed by patients with FSHD who had a productivity loss cost of NZ$2,033 and then patients with ION who had an estimated cost of NZ$1,754. The per person long-term productivity loss costs were highest among DMD and ION, which are the disorders that have early age of onset.

4.5 Current and Future Burden of GMD in New Zealand

Future forecasting was based on current prevalence and NZ Age and Structure population projections from Census 2018 (Statistics New Zealand, 2020b; Theadom et al., 2019) As shown in Table 6, the current burden for annual costs per person with GMD was estimated at approximately NZ $31.9 million. In 27 years' time, this cost was estimated to increase by 1.5 times and in 52 years' time, this

burden would increase by 1.7 times to NZ $90.2 million. The current total one-year costs per person with unpaid informal care were significantly higher at NZ $52.0 million. Similarly, the future burden inclusive of unpaid informal care increased by 1.6 in 27 years' time and increased by 1.7 in 52 years' time.

Table 6. Current and future cost estimates of genetic muscle disorders in New Zealand

Cost estimates for New Zealand	Current burden 2021 ($)	Future burden 2048 ($)	Future burden 2073 ($)
Direct health care cost	31,713,644	49,465,642	55,023,294
Total 1-year costs per person	31,891,844	49,743,591	55,332,472
Total 1-year costs per person incl. informal care	51,959,573	81,044,412	90,150,059

Note: These projections are based on population growth and are not adjusted for impacts over time including adverse events

4.6 Sensitivity Analysis

Results from the sensitivity analyses can be seen in Table 7 below. The discount rate of 3.5% was the base case as recommended by PHARMAC (PHARMAC, 2020b). The analysis also considered a 0% discount rate and a 6% discount rate. With the varying rates, the long-term productivity costs of GMD in NZ ranges between NZ $342,000 and NZ $1.3 million.

As shown below, patients with DMD had a significantly high average long-term productivity cost of NZ $1.1 million. The sensitivity analysis for this group suggested that these long-term costs range between NZ $622,000 to NZ $2.4 million, which nearly doubles the productivity loss costs of the other subtypes of GMDs in NZ. This further indicates the large burden individuals with DMD experience.

Table 7. Sensitivity analysis of varying discount rates for long-term productivity

	0% Mean ($)	3.50%* Mean ($)	6% Mean ($)
Genetic muscle disorders	1,305,823	591,911	341,861
Duchenne muscular dystrophy	2,377,033	1,077,475	622,301
Becker muscular dystrophy	1,355,112	614,253	354,765
Facioscapulohumeral muscular dystrophy	1,127,908	511,264	295,283
Myotonic dystrophy	1,214,928	550,709	318,065
Limb-girdle muscular dystrophy	1,037,316	470,200	271,566
Ion channel muscle disease	1,207,260	547,234	316,057

**3.5% discount rate is the base case*

4.7 Regression Analysis

Results from the three generalised linear regression models can be seen below in Tables 8-10. The results indicate that the predictors of high direct costs, total one-year costs and total one-year costs including unpaid informal care were consistent across the three models. When the log of direct costs was predicted, it was found that higher direct costs were significantly associated with owning an electric wheelchair (beta=1.668, p<0.001) and a manual wheelchair (beta= 0.867, p<0.001), full-time or part-time employment (beta=-0.812, p<0.001), need for ventilatory support (beta=0.529, p=0.009), and having at least one co-morbid condition (beta=0.266, p=0.042). The overall model fit is R2=0.424.

Table 8. Predictors of high direct costs

Independent variables	**B**	**SE**	**Sig.**
Constant	8.712	0.119	<0.001
Electric wheelchair	1.668	0.196	<0.001
Employed	-0.812	0.144	<0.001
Manual wheelchair	0.867	0.185	<0.001
Need for ventilatory support	0.529	0.201	0.009
At least one co-morbid condition	0.266	0.130	0.042
R2	0.424		
n	485		

Similarly, the second model shown in Table 9 found that direct costs were significantly associated with owning an electric wheelchair (beta=1.665, p<0.001) and a manual wheelchair (beta= 0.863, p<0.001), full-time or part-time employment (beta=-0.734, p<0.001), need for ventilatory support (beta=0.521, p=0.010), and having at least one co-morbid condition (beta=0.260, p=0.047). The overall model fit is R2=0.414.

Table 9. Predictors of high total one-year costs excluding informal care

Independent variables	**B**	**SE**	**Sig.**
Constant	8.719	0.119	<0.001
Electric wheelchair	1.665	0.197	<0.001
Employed	-0.734	0.144	<0.001
Manual wheelchair	0.863	0.185	<0.001
Need for ventilatory support	0.521	0.201	0.010
At least one co-morbid condition	0.260	0.131	0.047
R2	0.414		
n	485		

Lastly, the third model shown in Table 10 also found that direct costs were significantly associated with owning an electric wheelchair (beta=1.507, p<0.001) and a manual wheelchair (beta= 1.0433, p<0.001), full-time or part-time employment (beta=-0.903, p<0.001), need for ventilatory support (beta=0.637, p=0.003), and having at least one co-morbid condition (beta=0.409, p=0.003). The overall model fit is R2=0.417. These consistent results indicate the strength of these variables as predictors for direct costs and total one-year costs of GMDs in New Zealand.

Table 10. Predictors of high total one-year costs including informal care

Independent variables	**B**	**SE**	**Sig.**
Constant	9.151	0.126	<0.001
Electric wheelchair	1.507	0.209	<0.001
Employed	-0.903	0.153	<0.001
Manual wheelchair	1.043	0.196	<0.001
Need for ventilatory support	0.637	0.213	0.003
At least one co-morbid condition	0.409	0.139	0.003
R2	0.417		
n	485		

4.8 Summary

In summary, the economic burden of GMDs in New Zealand is high compared to other countries. The total one-year per person cost excluding informal care for adults living with GMDs in New Zealand was estimated at NZ$39,789. When unpaid informal care is included into the total one-year per person cost, it increases significantly up to NZ$64,114. These results reflect the multidisciplinary management of care, where patients across the GMDs seemed to frequently utilise specialised medical care, allied healthcare, and general practice care. Unpaid informal care was a cost reported consistently among the six most common GMDs. Informal care was also the highest cost component of direct non-healthcare costs, which clearly indicates the magnitude of informal care across GMDs and overall. Temporary productivity loss per person for all GMDs was approximately NZ$1,261 and long-term productivity loss costs was estimated at NZ$514,963 per person. Importantly, the results discovered a range of predictors for high direct costs and total one-year costs. This study has identified areas of high cost, large cost components for different types of costs, and predictors of costs, which can be targeted for significant cost savings and improvements in outcomes for people with GMDs.

Chapter 5. Discussion

5.1 Key Findings

The main objective of this study was to estimate the annual societal costs per person and total costs for adults living with GMD in NZ. This research drew upon data from a population-based study linked with self-reported health service usage and electronic hospital records to calculate the societal costs of GMDs (Theadom et al., 2019). Conservatively estimated, the annual national burden of GMDs was NZ$52.8 million, which equates to an annual per patient cost of NZ$64,114 (95%CI $57,045 - $73,777). When excluding informal care costs, the burden of GMDs in NZ was NZ$32.8 million, which equates to an annual per patient cost of NZ$39,789 (95% CI $34,554 - $46,235). This is approximately seven times higher than the mean per-capita health expenditure in New Zealand (Organisation for Economic Co-operation and Development, n.d.).

Notably, the results illustrated a nearly two-fold increase in annual per person costs when unpaid informal care was included into this total cost. A relatively high average yearly cost for formal care was estimated at NZ$57,209 (95% CI $46,226-$67,779), yet a similar average informal care cost was estimated at NZ$55,283(95% CI $46,110-$65,028). In addition, informal care was the highest cost driver for GMDs in NZ, at NZ $20.1 million, and formal care was second highest at NZ $16.5 million. This finding was reflected as a consistent trend seen across the analysed GMDs which showed that informal and formal care were the two most significant cost components of annual costs (Blokhuis et al., 2021; Schepelmann et al., 2010). Informal care contributed to 38% of total societal costs, followed by formal care (31%) and then hospital admissions (12%). These findings clearly support the fact that adults with GMDs experience various impairments in their daily life, therefore requiring significant amounts of ongoing support in order to function optimally.

Informal caregiving was a major cost component overall and for the six subtypes of GMDs. Informal care was categorised as a direct non-healthcare cost, with the rationale that if care was not provided by an informal caregiver, it would be provided by a formal health care professional. The high level of informal care was seen among previous economic studies on various GMDs (Blokhuis et al., 2021; Kanters et al., 2011; Larkindale et al., 2014; Schepelmann et al., 2010; Schreiber-Katz et al., 2014). The high level of informal care also indicates that this is a substantial area of unmet need and suggests the government is not remunerating the care covered by non-professional caregivers such as friends and family (Hatton, 2021; Radio New Zealand, 2021). Nearly half of the patients with GMDs reported that they required informal care while only a third reported formal care costs. If the care needs of these individuals and their caregivers were being formally met or compensated, we would see a more distinct difference between the two cost categories. Despite the public need for the remuneration of caregivers of people with disabilities, there is a lack of financial support from the Ministry of Health (Hatton, 2021; Radio New Zealand, 2021). Ideally, with sufficient formal care or

compensation provided, informal care costs would remain lower. Notably, all six subtypes of GMDs reported informal care costs while only five GMDs reported formal care costs further indicating the significance of informal care.

Quantifying the high informal care cost stresses the importance of and need for providing adequate support for informal caregivers. The high informal care cost in this present study corresponds with findings in literature about the burden on informal caregivers for patients with GMDs or other genetic neuromuscular diseases. A study by Flores et al. (2020) emphasised that caregivers of children with DMD reported significant financial burdens, predominantly due to monthly expenditure for drugs and formal care not covered by the Spanish National Health System and suffering from work changes (Flores et al. (2020). Research has also shown that informal care is associated with social deprivation, coronary heart disease, anxiety and depression, and impaired immune system (Adelman et al., 2014; Gouin et al., 2008; Lee et al., 2003), which can result in reduced quality of life and health status of caregivers of patients with chronic diseases such as GMDs (Canam & Acorn, 1999). Landfeldt et al. (2016) noted that caregivers of children with DMD experienced a substantial burden with impaired health-related quality of life. They found that anxiety and depression were significantly associated with annual household cost burden (>$5000 vs. <$1000, odds ratio 1.76, 95 % CI 1.18–2.63) and hours per week of leisure time devoted to informal care (25–50 vs. <25 h 2.01, 1.37–2.94; >50 vs. <25 h 3.35, 2.32–4.83) ($p<0.007$) (Landfeldt et al., 2016). Additionally, anxiety and depression were recorded for up to 70% of the caregivers, therefore this burden was both a significant economic and mental burden for informal caregivers of children with DMD (Landfeldt et al., 2016). The estimate of informal care for patients with GMDs in the present study notably reflects the significant financial burden and adverse effects that informal caregivers experience.

Another key finding was the high utilisation of outpatient care provided by general practitioners, nurses, and allied health professionals. Most patients with GMDs in the present study visited their general practitioner around an average of six times per annum. Over half the patients visited an allied health professional for an average of 16 visits and over a third visited a nurse for 10 visits. Notably, annual allied health care costs were on average NZ$1,163 per patient (95% CI $937-$1,414) and were the third highest cost driver within the direct health care cost category. These results demonstrate the need for outpatient care, emphasising the need for allied health professionals to manage the various physical, cardiac, respiratory, and cognitive complications associated with GMDs.

Furthermore, the high utilisation of primary and community care services highlights the value of multidisciplinary care management to restore or maintain optimal function for patients with GMDs. This key finding supports the objectives and outcomes of the Allied Health Business Plan 2021-2023 proposed by the Ministry of Health (Ministry of Health, 2021a). Often, community care services are not prioritised for funding support (Ministry of Health, 2016). So the present findings align with the need for more funding for allied health professionals to provide sufficient support. It is also known that healthcare professionals support the patient and informal caregivers throughout different caregiving

stages, including end-of-life care for certain GMDs (de Visser & Oliver, 2017; Hilton et al., 1993). This support is important as some GMDs reduce life expectancies, such as Duchenne muscular dystrophy, and require planning and support for end-of-life care (de Visser & Oliver, 2017). Poppe et al. (2021) noted that healthcare professionals often want to provide support for informal caregivers of patients with amyotrophic lateral sclerosis, particularly at the bereavement stage, but cost, resources and time were an issue. These informal caregivers also noted that proactive support from healthcare professionals before the bereavement stage could help decrease their mental and psychosocial burden after a loss (Poppe et al., 2021). Therefore, these findings from the present study support the need to create stronger community care, so that with sufficient funding and innovative freedom, professionals can provide the appropriate care for both the patients with GMD and their informal caregivers.

The cost of medical aids was a consistent annual driver of overall costs and for the costs of the six GMDs. This finding corresponds with a study on Duchenne and Becker muscular dystrophy highlighting that medical aids were among the top three cost drivers of direct costs (Schreiber-Katz et al., 2014). The average annual cost of medical aids in the present study was NZ$8,345 (95% CI $7,284 - $9,485). This study also identified bathroom equipment, walking sticks and manual wheelchairs to be the most frequently used aids, as also seen in studies that identified wheelchairs and other aids that support mobility as major costs (Blokhuis et al., 2021; Kanters et al., 2011; Schreiber-Katz et al., 2014). The present findings differed from previous literature by identifying specific areas of unmet need regarding medical devices and home modifications. The results indicated that participants needed electric wheelchairs, rollover equipment and an adapted chair, which could be due to the higher cost of electric wheelchairs or the limited access to equipment. More people may need or want an electric wheelchair in order to increase competence, accessibility, and adaptability compared to a manual wheelchair (Pellegrini et al., 2004; Pousada García et al., 2015).

The annual cost per person for prescribed medication was NZ$16, and if patients were on medication, this was on average three different medications (range 1 – 16). This cost was relatively low, as expected due to the subsidised nature of medicines that are funded by the government. This finding corresponded with previous studies which indicated a low medication cost (Blokhuis et al., 2021; Kanters et al., 2011; Schreiber-Katz et al., 2014; Teoh et al., 2016). It was noted that prescribed medication costs increased with age in boys with Duchenne muscular dystrophy (Teoh et al., 2016). It may be worth further investigating the association between age groups and prescribed medications to determine if similar patterns in medication consumption seen in the Teoh et al. (2016) study occur in NZ.

In comparison, non-funded medication costs were higher at NZ$698 per person, with 11% of the cohort accessing this resource. The low proportion of patients taking non-funded medications may highlight that people are a bit apprehensive to access these treatments as these high costs are borne by the individual. Flores et al. (2020) highlighted there were high financial burdens in Spain due to

monthly expenditures on non-funded drugs. Families incurred a regular cost for drugs higher than €50 per month which converts to approximately NZ$124 per month and NZ$1,485 a year (Flores et al., 2020). Teoh et al. (2016) similarly found that in Australia, when including the cost of therapy from clinical trials, the mean cost of medications jumped from AUD$567 to AUD$2,669 (NZ$663 to NZ$3,121), resulting in a significant skew to the left when compared to the medication cost excluding clinical trial therapies. This area of non-funded medications should be further investigated to identify medications that would ideally be funded in order to improve the wellbeing of patients with GMDs. The need for more research was also highlighted by Azer (2019), where non-funded medications with an evidence base for effectiveness were not being funded by the NZ government. For example, deflazacort as a corticosteroid alternative for patients with Duchenne muscular dystrophy has been shown to improve quality of life and prolong life (McAdam et al., 2012). Deflazacort slows the decline in muscle strength and function which subsequently delays the onset of cardiomyopathy, stabilising pulmonary function and prolonging ambulation (Barber et al., 2013; McAdam et al., 2012; Ricotti et al., 2013). Despite this evidence base and continued lobbying from NZ community groups, it is not listed on the pharmaceutical schedule and thus not funded by PHARMAC.

Many studies that reported medication or pharmaceutical costs did not include non-funded medications, so it is difficult to compare the results of this study with others (Blokhuis et al., 2021; Kanters et al., 2011; Schepelmann et al., 2010; Teoh et al., 2016). Research has also indicated variable access to the same therapies across insurers (Margaretos et al., 2022). This variance emphasises the need for further international research surrounding non-funded medication and therapies for patients with GMDs.

When looking at employment rates of people with GMDs, 22% [109/490] were working full-time and 10% [50/490] were working part-time at that point in the study, so nearly a third (32% [159/490]) of the cohort were participating in work. This employment rate was lower than the national employment rate for disabled people in 2021 (42.5%) and significantly lower compared to the national rate of non-disabled people (78.9%) (Statistics New Zealand, 2021). This study estimated productivity loss in two ways. Firstly it used the human capital approach to estimate the long-term productivity loss due to premature death or disability. The human capital approach is approximated by the value of an average individual's future earnings over the entire absence from work due to illness (Pike & Grosse, 2018). The estimated long-term productivity loss was NZ$591,911 (95% CI $516,010-$624,790) per person with GMDs, and although this is a high cost, research criticises that the human capital approach often calculates potential costs which overestimate the losses (Koopmanschap, 1998; Koopmanschap et al., 1995; van den Hout, 2010).

It has been argued that the friction cost method is the most realistic approach in terms of capturing societal costs because an individual who is unable to work for more than three months would most likely be replaced (Koopmanschap et al., 1995). For comparisons, this study also estimated temporary productivity loss using the friction cost method for individuals in paid employment at the

time of the MD-Prev study. The friction cost method allows an account for people who may be absent from work due to the complications or comorbidities associated with their GMDs (Koopmanschap et al., 1995). Productivity loss in terms of missed work days was recorded for 11% [54/490] of the employed cohort, which illustrates that a third missed days at work due to their GMDs. This average cost of productivity loss due to missed work days was NZ$11,466 (95% CI $7,695-$16,141) per patient.

Notably, the low employment rates of people with GMDs and the proportion of people recording missed work days could be due to physical and cognitive impacts of their disorders among other factors or illnesses (Mulroy, 2019). Mulroy (2019) looked at employment for adults with myotonic dystrophy (MD) in NZ, and found that the main reasons for reducing work hours were due to fatigue and daytime sleepiness. Mulroy (2019) also stated that the lack of awareness of MD and resources to support people with MD in employment contributed to the lower employment rates compared to other disability groups. Interestingly, being in full- or part-time employment, having a manual or electric wheelchair, having at least one co-morbidity, and requiring ventilatory support were associated with higher direct and total one-year costs. Although, these variables could suggest that poor illness and mobility functioning leads to increased costs, it may also indicate that when people are supported with the correct equipment, it enhances the potential to obtain and maintain employment to contribute as productive members of society (Frank, 2016; Lindsay et al., 2019; Padkapayeva et al., 2017).

It is known that people with GMDs, particularly people with child-onset disabilities such as Duchenne muscular dystrophy (DMD), experience significant disadvantages in pursuing employment (Lindsay et al., 2019; Lindsay et al., 2015). Lindsay et al. (2019) noted that some barriers to meaningful occupations were inaccessible workplace environments, lack of support and resources in the workplace, medical challenges, and fatigue. These barriers to employment can have consequences for social isolation, poor psychological wellbeing, and poorer general health (Abbott & Carpenter, 2014; Frank, 2016; Lindsay et al., 2019). Research has identified that physical and technological modifications can significantly support a person with physical disabilities to remain in employment or enhance work performance (Padkapayeva et al., 2017). For instance, assistive devices and workplace modifications to increase the accessibility of the built environment can overcome barriers experienced by people with disabilities (Padkapayeva et al., 2017).

The low employment rate of people with GMDs compared to both people with disabilities and non-disabled people could also suggest system-level barriers. Although employers may employ people with disabilities, they often cannot accommodate to them at the workplace due to a lack of disability awareness, education, and strategies (Lindsay et al., 2015; Padkapayeva et al., 2017). These limitations in the workplace suggests there is a lack of funding and policies for employers to accommodate to people with disabilities (Lindsay et al., 2015; Padkapayeva et al., 2017). Therefore, this finding suggests that a sufficient initial investment into medical aids, environmental modifications, and system-level policies can lead to crucial personal employment and health gains for people with

GMDs, as well as societal benefits as they contribute effectively to the workforce (Frank, 2016; Lindsay et al., 2019; Lindsay et al., 2015; Mulroy, 2019; Padkapayeva et al., 2017).

5.2 In Context with Previous Research

5.2.1 The Known Economic Burden of Genetic Muscle Disorders

As mentioned in Chapter 1, a general understanding was established that, in comparison to other brain disorders, neuromuscular diseases had the highest total per person cost and the highest indirect costs (Gustavsson et al. 2011). The literature review in Chapter 2 found that the global economic burden of GMDs ranged from NZ$41,651 to NZ$117,654 (Blokhuis et al., 2021; Kanters et al., 2011; Ouyang et al., 2008; Ouyang et al., 2019; Schepelmann et al., 2010; Teoh et al., 2016). Formal and informal care comprised a consistent cost component that contributed to societal costs. Formal care costs ranged from NZ$1,076 to NZ$17,356 while informal care costs ranged from NZ$12,473 to NZ$16,975 (Blokhuis et al., 2021; Kanters et al., 2011; Schepelmann et al., 2010). However, it is essential to note that these were estimates for one type of GMD rather than a range of GMDs. Productivity loss as an indirect cost ranged from NZ$1,565 to NZ$22,727 (Blokhuis et al., 2021; Kanters et al., 2011; Schepelmann et al., 2010; Teoh et al., 2016). Considering the known economic burden of GMDs, some findings of the present study were consistent with previous literature as detailed in the following section 5.2.2.

5.2.2 Putting the Results in Context with Other Genetic Muscle Disorders

Any direct comparison of costs should be interpreted with caution as there are differences across studies in health care systems, cost-sharing systems, and methods used for cost estimation. However, generally speaking, the total one-year cost per person in NZ, including informal care, was NZ$64,114 and this was within the range of the costs reported in other studies (NZ$41,651 - $117,654) (Blokhuis et al., 2021; Kanters et al., 2011; Ouyang et al., 2008; Ouyang et al., 2019; Schepelmann et al., 2010; Teoh et al., 2016). The estimated total direct healthcare cost per person for GMDs in NZ was NZ$29,762, close to that of Kanters et al. (2011) which was NZ$29,719. The temporary productivity loss due to missed work days or reduced work hours in this study was NZ$11,466, which was higher than the range of NZ$1,565 to NZ$10,091 for the temporary productivity loss reported in previous studies.

The patterns in literature about the dystrophinopathies was consistent with what was found in this study. Schreiber-Katz et al. (2014) found that the mean annual cost of DMD (NZ$175,408) was double that of BMD (NZ$86,823). This study similarly found that the total cost of DMD (NZ$151,728)

was higher than the total cost of BMD (NZ$49,679), that is, this difference was threefold. The average one-year cost of DMD (NZ$151,728) was relatively similar to the average one-year cost of equivalent NZ$117,654 for patients with DMD aged 25 to 34 in the study by Teoh et al. (2016). There was limited information on the disaggregated cost estimates from the Teoh et al. (2016) study as only one age group could be compared to our study. Teoh et al. (2016) included formal care as a nonmedical cost which limited comparisons between those costs. However, when looking at the total direct cost of DMD, the reported cost of this present study was NZ$113,151, while the cost reported by Teoh et al. (2016) was NZ$116,089. These similar costs can be explained by the similar age groups that were studied. The mean age of participants in this study was 22, ranging from 16 to 37 years, which is close to that of Teoh et al. (2010)'s study. The younger age range is due to the nature of DMD which results in early mortality around the third decade, so most participants with DMD would be younger or at this stage of the disorder (Bushby et al., 2010a; Cardamone et al., 2008; Emery, 2002). There was no report of temporary productivity loss for this group in this study by Teoh et al (2010), which may be why they chose to calculate the productivity loss of the parent caregiver. Similar to Teoh et al. (2020), this present study found that informal, formal and medical aids were the most significant contributors to total costs.

The reported average annual cost of FHSD in previous literature was NZ$57,187 (Blokhuis et al., 2021) and NZ$61,355 (Schepelmann et al., 2010). In comparison, this study reported a higher but relatively similar average annual cost per person of NZ$67,679. Interestingly, the biggest difference was with the study by Blokhuis et al. (2021), as the methods for cost estimation were the same and the resources identified were very similar. This difference may simply reflect the differences between the health systems of The Netherlands and NZ. The slightly lower costs seen in the other studies may also be due to limitations with case ascertainment which may have missed cases and underestimated the total costs for patients with FSHD (Blokhuis et al., 2021; Schepelmann et al., 2010). The most significant cost components were informal care (39%), formal care (33%) and hospital admissions (9%) for this study. Blokhuis et al. (2020) found that formal care (32%), informal care (26%) and productivity losses (19%) were the highest cost components of total costs.

For myotonic dystrophy, which included both type 1 and type 2, this research reported an average total annual cost per patient of NZ$28,499, while Ouyang et al. (2019) reported a cost of NZ$61,355 in the United States. The difference here may be attributed to methodological differences in ascertaining cases. Ouyang et al. (2019) used a broad ICD-9 code which likely would have included more cases than myotonic dystrophy alone. In addition, not all patients with muscular dystrophies undergo genetic analyses to confirm their diagnosis (Theadom et al., 2019). Therefore, basing inclusion on clinical diagnoses and ICD-codes alone presents a potential for including more participants than the actual number of people with myotonic dystrophies, which could explain the higher reported costs. The data from the MD-Prev study received diagnostic confirmations to address methodological issues like these and likely estimated the costs for people with myotonic dystrophy accurately.

This study identified variables that were associated with higher direct and total costs for GMDs and suggested that poorer illness functioning led to increased costs. If having a wheelchair that was either manual or electric were used as a proxy for mobility, it would suggest that decreased mobility was associated with higher direct and total costs. Blokhuis et al. (2021) found that there was an inverse relationship between mobility and the cost of productivity losses, where there were higher losses in more mobile groups. They explained that this might be because more severely affected patients with less mobility would be less likely to participate in work. Therefore, this group would report lower productivity losses than those who are more mobile, work more, and report more temporary productivity losses (Blokhuis et al., 2021). This study did not look at predictors for productivity loss which could be an area for further research. Particularly, participation in the work force allows people with GMDs to contribute meaningfully to society and improve the quality of life and health outcomes of this group (Frank, 2016; Lindsay et al., 2019; Padkapayeva et al., 2017).

5.3 Strengths and Limitations

5.3.1 Strengths

A key strength of this research is that it utilised a dataset from a nationwide prevalence-based study that obtained cases using the capture-recapture method (Theadom et al., 2019). This dataset addressed the limitations of selection bias that was noted in previous literature. The capture-recapture method involved ascertaining cases using overlapping sources including neurologists' patient lists, hospital records, the national Ministry of Health database, the NZ Muscular Dystrophy Association membership database, and the NZ Neuromuscular Disease Registry (Theadom et al., 2019). Compared to previous studies that obtained cases from one registry or hospital admission data alone, this method was more comprehensive, so the number of missed diagnosed cases were estimated to be very low (<1%) (Theadom et al., 2019). The strength here is that the likelihood for selection bias is low, providing a much more accurate participant population that better captures the health expenditures of adults with GMDs in NZ (Theadom et al., 2019).

Furthermore, using a prevalence-based dataset provided a large and representative population which allowed for increased generalisability and comparability with other studies. This present study was the first to estimate the costs for GMDs in NZ and the first study that distinguished and analysed costs for the six most common subtypes of GMDs in NZ. Previous literature, such as the study by Kanters et al. (2011), only used data from adults with Pompe disease who received supportive care. This sample population from the Kanter et al. (2011) study limits the generalisability of their results, which could not be applied to the wider group of adults with Pompe disease who do not receive supportive care. Ouyang et al. (2008) and Ouyang et al. (2019) used of broad ICD-9 codes (335 and 359.21) to identify patients with muscular dystrophies and myotonic dystrophy from administrative claims data.

This was another limitation, as those studies were unable to investigate or even distinguish the different types of muscular dystrophies or myotonic dystrophies, which significantly reduced the comparability of their results with other studies (Ouyang et al., 2008 & Ouyang et al., 2019). The benefit of using a larger representative population is that a detailed breakdown of health resource use can be determined for different subtypes of GMDs in NZ, which is significant for decision makers when allocating funding or locating areas of unmet and met need (Rice, 2000).

Additionally, the sample size of this study was relatively large. Among the previous literature that similarly analysed the societal costs of GMDs, this study had the largest sample size of 492 participants. This sample size indicates that the uncertainty surrounding the estimates is likely to be smaller than these other studies. Using the large prevalence-based dataset allowed for a more accurate illustration of resource utilisation for adults with GMDs and gives more confidence when making statements about the costs of GMDs in NZ.

As this current study took a societal perspective of analysis, it used both self-reported health resource utilisation information and hospital records over the past year to determine the costs associated with GMDs. GMDs and their effects are not limited to just the individual patient and therefore the costs to the individual, families, and wider society had to be included. This approach was a strength of this study as it utilised longitudinal data which included information about resource use inside and outside the hospital environment, encompassing a significant range of costs for people with GMDs. Some previous studies only looked at hospital admissions data, limiting the costs to the individual and health system despite GMDs having a broader impact on society (Ouyang et al., 2008 & Ouyang et al., 2019). Notably, using this data and perspective for the analysis found that allied health professionals, general practitioners and nurses played a significant role in the management of care for patients with GMDs. It highlighted the need for multidisciplinary care and supported the ‘whole-of-system’ model of services proposed in the Allied Health Business Plan. Ultimately, collecting longitudinal data about outpatient and inpatient care for people with GMDs is also key for informing allocations and identifying areas in which interventions or management models of care might improve outcomes (Rice, 2000).

Lastly, being the first study in NZ to analyse the overall societal costs of GMDs in adults and the six subtypes of GMDs filled a gap in the published literature. This study illustrated the costs and patterns of health resource utilisation for this population. Before this study, the economic burden of GMDs was consistent in discourse among the individuals living with GMDs and their families and understood qualitatively but never quantitatively. The findings demonstrated that, although GMDs are rare, the costs associated with living with GMDs are large, thus validating the struggles of this group that the government has overlooked for many years. In particular, this study was able to quantify the significant issue surrounding informal unpaid care and highlighted a substantial area of unmet need. It was revealed that people with GMDs require on going caregiver support yet face barriers in accessing formal care services and receive minimal remuneration from the government for the informal care provided.

Given the current health and disability system reforms and the subsequent establishment of the Ministry for Disabled People and the Accessibility Governance Board, these findings have been presented at a suitable time (Ministry of Social Development, n.d.-a, n.d.-b). They provide key economic evidence as the new Ministry for Disabled People begins to manage relevant legislation, implement the Enabling Good Lives approach and provide people with long-term home-based and community support, equipment, and modification services (Ministry of Social Development, n.d.-b). These findings equip groups such as the NZ Muscular Dystrophy Association with evidence-based recommendations during this reform when advocating for people with muscular dystrophies. Lastly, this study provides people living with GMDs with a voice. As mentioned above, this economic burden is a prominent topic among this group yet has remained largely hidden. Quantifying this burden demonstrates the struggles of this group and further helps to understand how to improve the health and wellbeing of adults living with GMDs in NZ.

5.3.2 Limitations

This study utilised data that asked participants to report their health resource use in the past year. This retrospective nature of the data may have resulted in recall bias and suggested a lower estimation of costs. However, patients were asked how many visits they made to a professional in the past month in some instances, which required assuming the patients had an equal number of visits each month over the past year, which likely overestimated costs for these categories.

Secondly, accurate information on funded health services (e.g., primary care, home and vehicle modifications, medication, and rehabilitation) were challenging to obtain. Although electronic records contain this information, there are no central, accessible, and reliable data sources with complete health service usage. This gap highlighted a significant need for a centralised data source/database that provides accurate and regularly updated information on funded health services. Having such a database would increase the transparency and generalisability of cost-of-illness studies for all illnesses or disorders in NZ as research could utilise one accurate source.

Additionally, this study used the proxy good method to calculate informal care, which assumes that informal care provision is priced equally with formal care provision (Hodgson & Meiners, 1982; Koopmanschap et al., 2008). Informal care should reflect the time contributed by caregivers in the form of forgone income or forgone leisure; however the methodology used in this study may not have captured accurate estimates of the total caregiver time and effort dedicated to supporting people with GMDs (Hodgson & Meiners, 1982; Koopmanschap et al., 2008). The MD-Prev study only asked how many hours unpaid informal care was provided to participants and lacked further detail to estimate informal care costs accurately. Exploring informal care for people with GMDs in NZ is a significant

area for further research, where an alternative methodology such as the contingent valuation method should be used to capture accurate estimates. This is further described in Section 5.4.

The human capital cost approach was used in this study to estimate the long-term productivity loss of people with GMDs. This approach valued the future economic production of people up to the age of 65 as this was the retirement age in NZ (New Zealand Government, 2020). The present study reported that 13% of the cohort were over the retirement age of 65. However, the Te Ara Ahunga Ora Retirement Commission found that 44% of New Zealanders aged 65 to 69 were still in the workforce (Te Ara Ahunga Ora Retirement Commission, n.d.). It was also noted that the proportion of employed people aged 65 and above would increase as the population ages (Te Ara Ahunga Ora Retirement Commission, n.d.). This information suggests that the long-term productivity loss reported in this current study was underestimated as it is likely that some of those participants aged above 65 were still in the workforce.

Lastly, residual confounding may be present from any unmeasured variables in the predictor analyses (Fewell et al., 2007). Given that this study was not a randomised controlled trial and utilised a population-based sample, there is the possibility of some unmeasured confounders that contributed to the associations with high costs of GMDs. This limitation suggests that these associations between predictor variables and the direct and total one-year costs of GMDs should be regarded as statistical associations as they may not be causal relationships.

5.4 Recommendations for Future Research

The information above indicates that informal care had a significant impact on the economic burden of GMDs. However, these results may not reflect the true burden of informal care due to the methodology used. For future research, the alternative use of the contingent valuation method is recommended. That method estimates informal care by using the willingness to accept (WTA) and willingness to pay (WTP) approaches for the informal caregiver, which more likely reflect the true preferences of the caregiver (Hodgson & Meiners, 1982; Koopmanschap et al., 2008). This process asks the caregiver the minimum amount of money they would want to receive for providing an additional hour of informal care (WTA) or the maximum amount of money they would want to pay for reducing caregiving by an hour (WTP) (Hodgson & Meiners, 1982). Therefore, qualitatively exploring informal care provided by caregivers and adopting this method would likely present more accurate cost estimates of informal care for people with GMDs.

Given the findings noted in Section 5.1, the present study identified and quantified an area of unmet need regarding the substantial informal care costs. Further research should be undertaken to identify what types of formal care are effective and efficient for people with GMDs. This area of formal care

was largely understudied in previous literature and would provide more comprehensive evidence for decision makers if and when they address the unmet need of informal care.

As mentioned above, the lack of available cost data on funded health services and resources for people with GMDs and generally for people with disabilities was a limitation of the study. It indicated the need for a more accessible, consistent, and comprehensive data source that could be developed and updated annually by an advisory group. For instance, the National Health Service (NHS) in England annually publishes a National Cost Collection, which is a crucial source of information about the cost of NHS services (National Health Service, n.d.). Future research should develop a national standard data source for the cost of health services and resources. This would strengthen the transparency and consistency of economic evaluations of health within New Zealand, improving the comparability across studies and illnesses.

Predicting variables for high costs is significant for health resource allocation (Diehr et al., 1999). Future research could benefit from collecting data about disease progression, severity, and mobility to investigate the statistical association between these predictors and higher costs of GMDs. For instance, a Likert scale could be used to improve the measurement of wheelchair use and perform regression models to determine which level of mobility is associated with increased costs (Cavazza et al., 2016).

Finally, using data collected prospectively would reduce the recall bias noted in Section 5.3.2. Future research could provide participants with an electronic patient diary to record the utilisation of health services as they happen (Hodgson & Meiners, 1982). This method can potentially provide richer and more accurate information if kept diligently (Hodgson & Meiners, 1982).

5.5 Conclusion

With insufficient international and national knowledge about the costs of GMDs due to the lack of available data, this study addressed a gap in research by utilising the robustly collected national data from the MD-Prev study. This was the first study in New Zealand to quantify the economic burden of GMDs for adults in New Zealand. The results highlighted the substantial total cost per person and identified that the largest cost components of this cost were informal care, formal care, and hospital admissions. This study was able to quantify the burden of informal caregiving, which was qualitatively known to be significant from literature and public discourse. Consistent with previous research, informal care costs were large and a top driver of costs for GMDs and for each of the subtypes of GMDs analysed. Several variables were identified as predictors of increased costs suggesting that poorer illness and functioning led to higher costs. Notably, this study highlighted the large drivers and predictors of high costs which at a policy level can inform decision makers to provide cost-effective health care services and treatments to improve outcomes for people living with GMDs.

Appendices

Appendix A. Literature Review Search Strategy

The following search strategies were used in MEDLINE, EMBASE, and Scopus on 21 May 2021.

Medline Search Strategy

1. "Cost of Illness"/
2. exp Health Care Costs/
3. Health Expenditures/
4. (cost? adj2 (illness or disease or sickness)).tw.
5. (direct cost? or indirect cost?).tw.
6. 1 or 2 or 3 or 4 or 5
7. exp Muscular Dystrophies/
8. muscular dystroph*.tw.
9. myotonic dystroph*.tw.
10. neuromuscular disease?.tw.
11. Pompe* disease?.tw.
12. (myopath? adj2 (Nemaline or Myotubular or Inclusion body)).tw.
13. (congenita? adj2 (Myotonia or Paramyotonia)).tw.
14. Periodic paralysis.tw.
15. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
16. 6 and 15
17. limit 16 to English

EMBASE Search Strategy

1. "cost of illness"/
2. exp "health care cost"/
3. (cost? adj2 (illness or disease or sickness)).tw.
4. (direct cost? or indirect cost?).tw.
5. 1 or 2 or 3 or 4
6. exp muscular dystrophy/
7. muscular dystroph*.tw.
8. myotonic dystroph*.tw.
9. neuromuscular disease?.tw.
10. Pompe* disease.tw.
11. (myopath? adj2 (Nemaline or Myotubular or "Inclusion body")).tw.
12. (congenita? adj2 (myotonia or paramyotonia)).tw.

13. Periodic paralysis.tw.
14. 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
15. 5 and 14
16. limit 15 to english

Scopus Search Strategy

((TITLE-ABS-KEY ({cost of illness}) OR TITLE-ABS-KEY ({health care cost?}) OR TITLE-ABS-KEY (cost? W/2 (illness OR disease OR sickness)) OR TITLE-ABS-KEY ({direct cost?}) OR TITLE-ABS-KEY ({indirect cost?})) AND (TITLE-ABS-KEY ("muscular dystroph*") OR TITLE-ABS-KEY ("myotonic dystroph*") OR TITLE-ABS-KEY ("neuromuscular disease?") OR TITLE-ABS-KEY ("Pompe* disease?") OR TITLE-ABS-KEY (congenita? W/2 (myotonia OR paramyotonia)) OR TITLE-ABS-KEY (myopath? W/2 (nemaline OR myotubular OR “inclusion body”)))

Appendix B. Tables of Studies Included in the Literature Review

Table B.1 Study Design

Reference	Aim/Hypothesis	Genetic muscle disorder	Country	Year of valuation	Currency	Participants	Age range
Blokhuis et al., 2021	To determine the socioeconomic burden of facioscapulohumeral muscular dystrophy (FSHD).	Facioscapulohumeral muscular dystrophy	Netherlands	2018	Euro (€)	172	18-80
Kanters et al., 2011	To estimate all relevant aspects of burden of illness including societal costs, use of home care and informal care, productivity losses and losses in health-related quality of life for adult Pompe patients only receiving supportive care.	Pompe disease	Netherlands	2009	Euro (€)	80	25-76
Ouyang et al., 2008	To estimate medical care utilization and expenditures for patients younger than age 30 with muscular dystrophies in the United States.	Muscular dystrophies	United States	2004	Dollars ($)	1002	0-29
Ouyang et al., 2019	To examine the gender differences in adult hospitalisations with myotonic dystrophy	Myotonic dystrophy	United States	2014	Dollars ($)	1891	18-61+
Schepelmann et al., 2010	To evaluate the socioeconomic impact and resource utilisation of three neuromuscular disorders in Germany.	Facioscapulohumeral muscular dystrophy	Germany	2009	Euro (€)	107	15-83
Teoh et al., 2016	To evaluate the socioeconomic impact and resource utilisation of three neuromuscular disorders in Germany.	Duchenne muscular dystrophy	Australia	2014	Dollars ($)	104	1-33

Table B.2 Case and Diagnosis Identification

Reference	Perspective	Case identification	Diagnosis identification/verification	Data collection
Ouyang et al., 2008	Health care payer	Patients younger than 30 years of age, complete coverage for 12 months during calendar year 2004 from the MarketScan Commercial Claims and Encounters Database	Identified by ICD-9 codes 359.0 for congenital hereditary muscular dystrophy and 359.1 for hereditary progressive muscular dystrophy	Database from paid medical and prescription drug claims of people covered by employer-sponsored health insurance
Schepelmann et al., 2010	Societal	Patients diagnosed with ALS, FSHD or MG and 18 years or older, from specialised centres randomized through the German Network of Muscle Disorders	Fulfilled diagnostic criteria for ALS, FSHD or MG according to international guidelines	Questionnaire measuring disease-related expenditures for 12 months retrospective and patient diaries for four months prospective
Kanters et al., 2011	Societal	Patients with Pompe disease seen through The Center for Lysosomal and Metabolic Diseases, a referring centre for patients with Pompe disease	Not stated	Questionnaire measuring medical consumption, informal and home care, productivity loss, and health-related quality of life. Data collection started in 2005 and is ongoing.
Teoh et al., 2016	Societal	Families with at least 1 child diagnosed with DMD living in Australia invited by national and state-specific muscular dystrophy charities, advocacy groups, disability providers and muscular dystrophy patient support organisations	Not stated	Survey measuring the associated costs for DMD in the previous 12 months. Also measured health-related quality of life
Ouyang et al., 2019	Not stated	Hospital discharge records from 2010 through 2014 in the Nationwide Inpatient Sample database	Identified by ICD-9 code 359.21 for myotonic muscular dystrophy – includes both Type 1 and Type 2 myotonic dystrophy	Nationwide Inpatient Sample database containing clinical and nonclinical data for each hospital stay

Table B.2 Continued

Reference	Perspective	Case identification	Diagnosis identification/verification	Data collection
Blokhuis et al., 2021	Societal	Patients with FSHD within the Dutch FSHD registry, 18 years or older and residing in the Netherlands	Not stated	Questionnaire consisting of four parts: patient and disease characteristics; health care utilization; productivity loss; and patient health-related quality of life. Collected between August and November 2018.

Note: Studies are listed in order of publication

Table B.3 Summary of Results in NZD, 2021

Cost component	Ouyang et al., 2008	Schepelmann et al., 2010	Kanters et al., 2011	Teoh et al., 2016	Ouyang et al., 2019	Blokhuis et al., 2021
Direct medical costs		$21,675	$29,719	$4,305		$25,187
Hospitalisations	$7,760	$3,554	$680		$22,383	$1,093
Intensive care			$1,755			
Rehabilitation		$1,590				
Outpatient care	$29,996	$1,216	$5,586			$1,260
Medication	$3,897	$5,612	$430			$569
Tests and assessments			$1,629			$48
Medical specialist						$1,168
Other healthcare professionals			$1,380			$2,841
Ventilatory support			$1,247			$776
Home care		$1,076	$15,232			$17,356
Direct non-medical costs				$111,574		$19,143
Adaptations, medical aids, and devices		$2,268	$893			$4,599
Travel costs		$23	$343			$29
Informal care		$16,975	$12,473			$14,515
Total direct costs				$116,089		$44,331
Total indirect costs		$39,702				
Productivity loss		$22,727	$5,245	$1,565		$10,091
Total annual cost per patient	$41,651	$61,355	$48,829	$117,654		$57,187

Appendix C. Full List of Included Genetic Muscle Disorders

Table C.1 Full list of included Genetic Muscle Disorders

Muscular dystrophies	**Myopathies**
Dystrophinopathies	Ion channel muscle disease
Duchenne	Myotonia congenita
Becker	Periodic paralysis
Manifesting carrier	Paramyotonia congenita
Myotonic dystrophy	Congenital myopathy
Type 1	Central core disease
Type 2	Multi minicore
Limb-girdle muscular dystrophy	Congenital fibre type proportion
Facioscapulohumeral muscular dystrophy	Pompe disease
Congenital muscular dystrophy	Myofibrillar myopathy
Emery-Dreifuss muscular dystrophy	Inclusion body myopathy
Distal muscular dystrophy	
Oculopharyngeal dystrophy	

Appendix D. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Checklist

Topic	No.	Item	Location where item is reported
Title			
	1	Identify the study as an economic evaluation and specify the interventions being compared.	Title, Page I
Abstract			
	2	Provide a structured summary that highlights context, key methods, results, and alternative analyses.	Abstract, Page III
Introduction			
Background and objectives	3	Give the context for the study, the study question, and its practical relevance for decision making in policy or practice.	Chapter 1, Page 1-11
Methods			
Health economic analysis plan	4	Indicate whether a health economic analysis plan was developed and where available.	Chapter 3, Page 19-22
Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).	Chapter 4, Page 29-30
Setting and location	6	Provide relevant contextual information that may influence findings.	Chapter 3, Page 19-20
Comparators	7	Describe the interventions or strategies being compared and why chosen.	Not applicable
Perspective	8	State the perspective(s) adopted by the study and why chosen.	Chapter 3, Page 21
Time horizon	9	State the time horizon for the study and why appropriate.	Not applicable
Discount rate	10	Report the discount rate(s) and reason chosen.	Chapter 3, Page 26
Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).	Not applicable

Topic	No.	Item	Location where item is reported
Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.	Not applicable
Valuation of outcomes	13	Describe the population and methods used to measure and value outcomes.	Chapter 3, Page 20-27
Measurement and valuation of resources and costs	14	Describe how costs were valued.	Chapter 3, Page 22
Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.	Chapter 3, Page 20-27
Rationale and description of model	16	If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed.	Chapter 3, Page 20-22
Analytics and assumptions	17	Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.	Chapter 3, Page 20-27
Characterising heterogeneity	18	Describe any methods used for estimating how the results of the study vary for subgroups.	Not applicable
Characterising distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.	Not applicable
Characterising uncertainty	20	Describe methods to characterise any sources of uncertainty in the analysis.	Chapter 3, Page 28
Approach to engagement with patients and others affected by the study	21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (such as clinicians or payers) in the design of the study.	Not applicable
Results			
Study parameters	22	Report all analytic inputs (such as values, ranges, references) including uncertainty or distributional assumptions.	Chapter 4, Page 29-30
Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarise them in the most appropriate overall measure.	Chapter 4, Page 29-31

Topic	No.	Item	Location where item is reported
Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable.	Not applicable
Effect of engagement with patients and others affected by the study	25	Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study	Not applicable
Discussion			
Study findings, limitations, generalisability, and current knowledge	26	Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice.	Chapter 5
Other relevant information			
Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis	Not applicable
Conflicts of interest	28	Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.	Not applicable

Appendix E. Unit cost tables

Table E.1 Unit costs for cost calculations of medical aids (NZD, 2021)

Item	Unit	Price or cost per unit (NZD)	Range	Source
Communication aids *Amplified Dect Cordless Phone with Answering Machine* *Bellman MAXI Amplifier Kit – Head & Earphones*	Per item	$330	$69.95-$820.00	Mobility Centre (2021) https://www.mobilitycentre.co.nz/shop/daily-living-kitchen-aids/telephones-hearing-assistance/amplified-dect-cordless-phone-w-answering-machine/ https://www.mobilitycentre.co.nz/shop/daily-living-kitchen-aids/telephones-hearing-assistance/bellman-audio-maxi-with-headphones/
Commode chair *Bedside Commode Height Adjustable*	Per item	$288	$251.00-$359.00	Mobility Centre (2021) https://www.mobilitycentre.co.nz/shop/toilet-bathroom/toilet/commodes/standard-bedside-commode-chair/
Rails in toilet *Roma Stainless Steel Grab Rail – Various Lengths*	Per item	$164.75	$86.25-$310.00	Mobility Centre (2021) https://www.mobilitycentre.co.nz/shop/grab-rails-ramps/grab-rails-bars/stainless-steel-grab-bars-rails/stainless-steel-grab-bar-rail-300mm/
Rails in bedroom *Viking Bed Cradle Non-Adjustable*	Per item	$106	$39.00-$435.00	Mobility Centre (2021) https://www.mobilitycentre.co.nz/shop/bedroom-seating/bedroom/bed-rails-handles-canes-poles/viking-bed-cradle/
Mechanically assisted cough equipment	Per item	$10,000	-	Personal communication with Muscular Dystrophy Association (2021)

Table E.1 Continued

Item	Unit	Price or cost per unit (NZD)	Range	Source
Mechanically assisted cough equipment	Per item	$10,000	-	Personal communication with Muscular Dystrophy Association (2021)
Walking stick *Contour Handle Walking Sticks – Various colours*	Per item	$56.50	$35.00-$435.00	Mobility Centre (2021) https://www.mobilitycentre.co.nz/shop/crutches-walking-sticks/walking-sticks-canes/non-folding-walking-sticks/contour-handle-cane-metallic-blue/
Walking frame *Invacare Bariatric Indoor Walker*	Per item	$395	$229.00-$895.00	Mobility Centre (2021) https://www.mobilitycentre.co.nz/shop/walkers-walking-frames/indoor-walking-frames/invacare-heavy-duty-bariatric-walking-frame/
Manual wheelchair *Self Propel Wheelchair – Xlite All Terrain*	Per item	$720.50	$320.00-$1,650.00	Mobility Centre (2021) https://www.mobilitycentre.co.nz/shop/wheelchairs/manual-wheelchairs/self-propel-wheelchair-xlite-all-terrain/
Electric wheelchair *JAZZY Select 6 Power Chair Red*	Per item	$5,047	$1,600.00-$9,500.00	Mobility Centre (2021) https://www.mobilitycentre.co.nz/shop/mobility-scooters-power-chairs/power-chairs/jazzy-select-6/
Computer with special software *Dragon Professional Individual, v 15*	Per item	$721	-	Nuance (2021) https://www.nuance.com/dragon/business-solutions/dragon-professional-individual.html
Adapted chair *Memory FOAM Seat Wedge Deluxe*	Per item	$128	-	Mobility Centre (2021) https://www.mobilitycentre.co.nz/page/6/?s=chair&post_type=product&dgwt_wcas=1

Table E.1 Continued

Item	Unit	Price or cost per unit (NZD)	Range	Source
Bathroom equipment *Slipper Pan*	Per item	$49.50	$30.00-$230.00	Mobility Centre (2021) https://www.mobilitycentre.co.nz/product-category/toilet-bathroom/toilet/?orderby=price
Height adjustable bed *Icare IC333 Long Single Adjustable Bed inc Mattress & Headboard*	Per item	$6,310	$4,759.00-$9,860.00	Mobility Centre (2021) https://www.mobilitycentre.co.nz/shop/bedroom-seating/bedroom/adjustable-beds-mattresses-overlays/adjustable-beds-i-care-ic333-ultra-lo-bed-with-tilt-long-single/
Special mattress *Foam and air mattress 1070mm x 2020mm x 125mm*	Per item	$6,865	-	PHARMAC (2021) https://pharmac.govt.nz/assets/schedule-addendum-devices-2021-10.pdf
Equipment to help roll over at night	Per item	$304	-	Mobility Centre (2021)
Transfer device *Softech Slide Transfer Sheet*	Per item	$84.50	$69.00-$319.50	Mobility Centre (2021) https://www.mobilitycentre.co.nz/shop/daily-living-kitchen-aids/transferring-aids/slide-transfer-sheet/
Hoist *Ceiling hoist, Maximum patient weight 200kg*	Per item	$3,800	-	PHARMAC (2021) https://pharmac.govt.nz/assets/schedule-addendum-devices-2021-10.pdf
Feeding tube	Per item	$30	-	PHARMAC (2021) https://pharmac.govt.nz/assets/schedule-addendum-devices-2021-10.pdf

Table E.1 Continued

Item	Unit	Price or cost per unit (NZD)	Range	Source
Devices to facilitate access to the home/workplace *Bellman Maxi Pro with Bluetooth*	Per item	$820	-	Mobility Centre 2021 https://www.mobilitycentre.co.nz/shop/daily-living-kitchen-aids/telephones-hearing-assistance/assistive-listening-device-with-bluetooth/
Ramps installed *Threshold Ramp 50mm High*	Per item	$290	$167.00-$875.00	Mobility Centre (2021) https://www.mobilitycentre.co.nz/shop/grab-rails-ramps/ramps/threshold-ramp-50mm-high/
Ramps portable *Decpac Senior Portable Folding Ramp – 120cm Long*	Per item	$1,290	$345.00-$4,570.00	Mobility Centre (2021) https://www.mobilitycentre.co.nz/shop/mobility-scooters-power-chairs/scooter-wheelchair-accessories/portable-ramps/decpac-senior-portable-folding-ramp-120-cm-long/
Disability adjusted car	Per item	$12,165	-	Enable New Zealand (2021) https://www.disabilityfunding.co.nz/vehicle-and-driving
Respite care home based	Per day	$191.04	-	Ministry of Health, New Zealand (2015)
Respite care facility based	Per day	$191.04	-	Ministry of Health, New Zealand (2015)
Ventilation support *F&P SleepStyle CPAP (with modem)*	Per item	$1,800	-	NZ Respiratory and Sleep Institute https://www.nzrsi.co.nz/shop/CPAP+Machines/F%26P+SleepStyle+CPAP+%28with+modem%29/x_sku/01501.html

Table E.1 Continued

Item	Unit	Price or cost per unit (NZD)	Range	Source
Handy Reacher *LONG 820mm Easireach Stick*	Per item	$55.50	$38.00-$90.00	Mobility Centre (2021) https://www.mobilitycentre.co.nz/shop/daily-living-kitchen-aids/reachers-pick-up-tools/helping-hand-easireach-stick-long/
Overbed Table *Roma U-Base Non-Tilting Overbed Table*	Per item	$596	$251.00-$405.00	Mobility Centre (2021) https://www.mobilitycentre.co.nz/shop/bedroom-seating/tables-trolleys/deluxe-non-tilting-chair-bed-table/
Jar Opener *Good Grips Jar Opener*	Per item	$21.50	$11.00-$49.50	Mobility Centre (2021) https://www.mobilitycentre.co.nz/shop/daily-living-kitchen-aids/kitchen/good-grips-kitchen-tools-utensils/good-grips-jar-opener/
Can opener *EZ Squeeze One Handed Can Opener*	Per item	$40.00	$11.00-$46.00	Mobility Centre (2021) https://www.mobilitycentre.co.nz/shop/daily-living-kitchen-aids/kitchen/jar-bottle-tin-can-openers/ez-squeeze-one-handed-can-opener/
Mobility scooter *Pegasus Pro Mobility Scooter*	Per item	$5,795.00	$2,895-$11,995	Mobility Centre (2021) https://www.mobilitycentre.co.nz/shop/mobility-scooters-power-chairs/mobility-scooters/urban-and-light-terrain-mobility-scooters/mobility-scooter-invacare-pegasus-pro/

Table E.2 Unit costs for cost calculations of health professionals and transport (NZD, 2021)

Item	Unit	Price or cost per unit (NZD)	Source
Personal Care			
Informal care	Per hour	$28.00	Te Ao et al. (2021)
Formal care	Per hour	$28.00	Te Ao et al. (2021)
Allied Health Professionals			
Medical specialist	Per session	$112.31	ACC (2021) https://www.acc.co.nz/for-providers/invoicing-us/paying-patient-treatment/
Occupational therapist	Per session	$69.16	ACC (2021) https://www.acc.co.nz/for-providers/invoicing-us/paying-patient-treatment/
Physiotherapist	Per session	$69.16	ACC (2021) https://www.acc.co.nz/for-providers/invoicing-us/paying-patient-treatment/
Speech and language therapist	Per session	$69.16	ACC (2021) https://www.acc.co.nz/for-providers/invoicing-us/paying-patient-treatment/
Accident and emergency department	Per session	$370.00	PHARMAC (2020) https://pharmac.govt.nz/medicine-funding-and-supply/the-funding-process/policies-manuals-and-processes/economic-analysis/cost-resource-manual/

Table E.2 Continued

Item	Unit	Price or cost per unit (NZD)	Source
General Practitioner	Per session	$80.00	PHARMAC (2020) https://pharmac.govt.nz/medicine-funding-and-supply/the-funding-process/policies-manuals-and-processes/economic-analysis/cost-resource-manual/
Nurse	Per session	$40.00	PHARMAC (2020) https://pharmac.govt.nz/medicine-funding-and-supply/the-funding-process/policies-manuals-and-processes/economic-analysis/cost-resource-manual/
Dietician	Per session	$69.16	ACC (2021) https://www.acc.co.nz/for-providers/invoicing-us/paying-patient-treatment/
Psychologist/Counsellor	Per session	$90.00	Te Ao et al. (2021)
Other Allied Health Professional	Per session	$69.16	ACC (2021) https://www.acc.co.nz/for-providers/invoicing-us/paying-patient-treatment/
Dentist	Per session	$150.97	ACC (2021) https://www.acc.co.nz/for-providers/invoicing-us/paying-patient-treatment/
Hospitalisation			
Weighted Inlier Equivalent Separations (WIES) National price 2020/2021	Cost weight	$5,545.26	Ministry of Health (2021) https://www.health.govt.nz/nz-health-statistics/data-references/weighted-inlier-equivalent-separations/wiesnz20-cost-weights

Table E.2 Continued

Item	Unit	Price or cost per unit (NZD)	Source
Same day stay (nzdrg70 B06C)	Cost weight	$4040.28	Ministry of Health (2019) https://www.health.govt.nz/nz-health-statistics/data-references/weighted-inlier-equivalent-separations/wiesnz20-cost-weights
One day stay (nzdrg70 B06C)	Cost weight	$4040.28	Ministry of Health (2019) https://www.health.govt.nz/nz-health-statistics/data-references/weighted-inlier-equivalent-separations/wiesnz20-cost-weights
Transport			
Public transport	Per km	$0.79	Inland Revenue (2021) https://www.ird.govt.nz/income-tax/income-tax-for-businesses-and-organisations/types-of-business-expenses/claiming-vehicle-expenses/kilometre-rates-2020-2021
Own car/disability adjusted car	Per km	$0.79	Inland Revenue (2021) https://www.ird.govt.nz/income-tax/income-tax-for-businesses-and-organisations/types-of-business-expenses/claiming-vehicle-expenses/kilometre-rates-2020-2021
Privately paid transport	Per km	$0.79	Inland Revenue (2021) https://www.ird.govt.nz/income-tax/income-tax-for-businesses-and-organisations/types-of-business-expenses/claiming-vehicle-expenses/kilometre-rates-2020-2021

Table E.2 Continued

Item	Unit	Price or cost per unit (NZD)	Source
Funded transport	Per km	$0.79	Inland Revenue (2021) https://www.ird.govt.nz/income-tax/income-tax-for-businesses-and-organisations/types-of-business-expenses/claiming-vehicle-expenses/kilometre-rates-2020-2021
Transport by friends/family	Per km	$0.79	Inland Revenue (2021) https://www.ird.govt.nz/income-tax/income-tax-for-businesses-and-organisations/types-of-business-expenses/claiming-vehicle-expenses/kilometre-rates-2020-2021

Table E.3 Unit costs for surgeries

Surgery Type	Nzdrg70 code	Description	Cost weight	Cost (NZD 2021)
Botox twice	-	Retrieved from Caci Clinic NZ	-	$389
Cataract removal	C15Z	Glaucoma and Complex Cataract Procedures	0.6797	$3769.11
Colonoscopy	G48C	"Colonoscopy, Sameday"	0.3439	$1907.01
Cyst removal	J11W	Same day Skin Lesion Procedures	0.2316	$1284.28
Eye operation	C14Z	Other Eye Procedures	0.4573	$2535.85
Hand surgery – trigger thumb release	I30Z	Hand Procedures	0.7255	$4023.09
Mole removed	J11W	Same day Skin Lesion Procedures	0.2316	$1284.28
Murina implant	-	Retrieved from Women Clinic	-	$160
Rehydration drip after gastro illness	G67B	Oesophagitis and Gastroenteritis W/O Catastrophic or Severe CC	0.1640	$909.42
Removal of basal cell carcinoma	J69C	“Skin Malignancy, Sameday”	0.2153	$1193.89
Skin cancer removal	J69C	“Skin Malignancy, Sameday”	0.2153	$1193.89
Surgeries for nose/breathing	D10Z	Nasal Procedures	0.8258	$4579.28
Tooth extracted	D40Z	Dental Extractions and Restorations	0.5554	$3079.84
Wisdom tooth taken out	D40Z	Dental Extractions and Restorations	0.5554	$3079.84

Note: WIESNZ20 cost weights were retrieved from the Ministry of Health and the cost was calculated by multiplying the cost weight with the Weighted Inlier Equivalent Separations (WIES) National price 2020/2021 (NZ$5,545.26)

Appendix F. Publication of preliminary results in the Muscular Dystrophy Associations In Touch Magazine

RESEARCH

The financial cost of genetic muscle disorders

Hannah Park from Auckland University on the long-term costs and consequences of muscle disorders.

Genetic muscle disorders (including the muscular dystrophies, ion channel muscle disease and congenital myopathies) can have long term consequences for the individual and whānau/family. However, there have been few studies internationally that have tried to quantify the financial costs of these conditions for those affected. It is important to understand health care costs as this information can help with decision making in funding of services and treatments.

A New Zealand study used information collected as part of the nationwide MD-Prev study conducted with people with genetic muscle disorders (GMD) and their whānau in 2016. Information on direct healthcare costs (e.g., medical equipment, hospitalisations, outpatient care, and paid formal home care support), direct non-healthcare costs (e.g., unpaid, informal care provided by a non-professional), and indirect costs (e.g., missed workdays or productivity loss) was collected. Based on this information, we were able to estimate costs of these services/resources using cost data from administrative databases (e.g. Pharmac). This enable us to calculate the average cost per person and costs to New Zealand per year.

Our study estimated that the direct healthcare costs per year for all genetic muscle disorders was $38,441 per person, with indirect costs (for those people currently in paid employment) averaging around $4,320 per person per year. Taken together the total one-year cost per person was $38,657. Importantly the study highlighted a significant unmet need relating to unpaid care (i.e., care from a family member or friend that is not funded by the state), this was estimated to be $55,283 per person. At a national level, the total costs of GMD in NZ is $31.8 million. Unpaid care contributed the most to this national cost ($20 million), followed by paid formal care ($16.5 million) and then hospital admissions ($3.9 million). These findings illustrate that even with relatively high formal care utilisation, informal care is still a significant area of unmet need and suggests that people with GMDs struggle with accessing formal care support services. As would be expected, increased severity was associated with higher costs.

In summary, our study illustrates and quantifies the unmet health service needs and difficulties with accessing health care resources/services for people with genetic muscle disorders in New Zealand. With our health and disability system undergoing a reform and the subsequent establishment of the Ministry of Disabled People and Accessibility Governance Board, we hope that these findings will bring awareness and help provide evidence-based recommendations to improve the health and wellbeing of people and their whānau living with these conditions.

Genetic muscle disorders (including the muscular dystrophies, ion channel muscle disease and congenital myopathies) can have long term consequences for the individual and whānau/family.

The research was supervised by Professor Alice Theadom (above left) and Dr Braden Te Ao from Auckland University of Technology. The health economics analysis was conducted by Hannah Park from Auckland University as part of her Masters in Public Health.

Figure F.1. Publication in the In Touch Magazine, February 2022 Issue

Appendix G. Figures of Cost Drivers for the Six Common Subtypes of Genetic Muscle Disorders

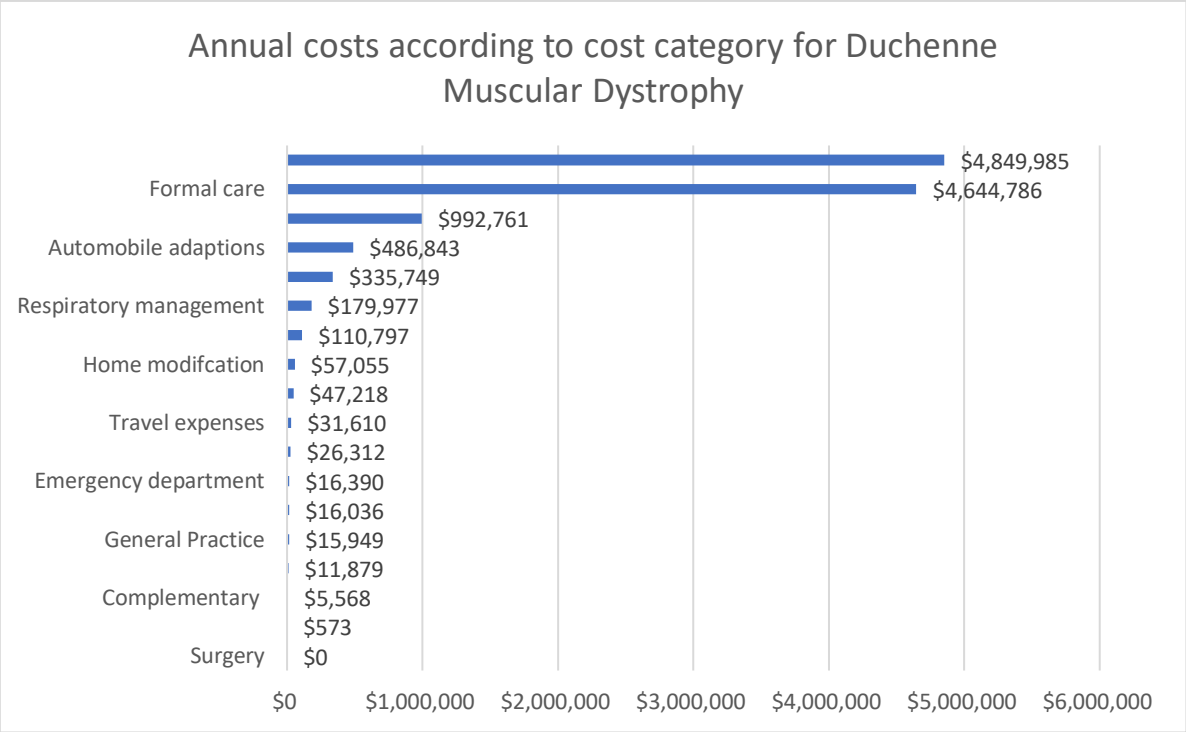

Figure G.1 Bar Chart of Cost Drivers for Duchenne Muscular Dystrophy

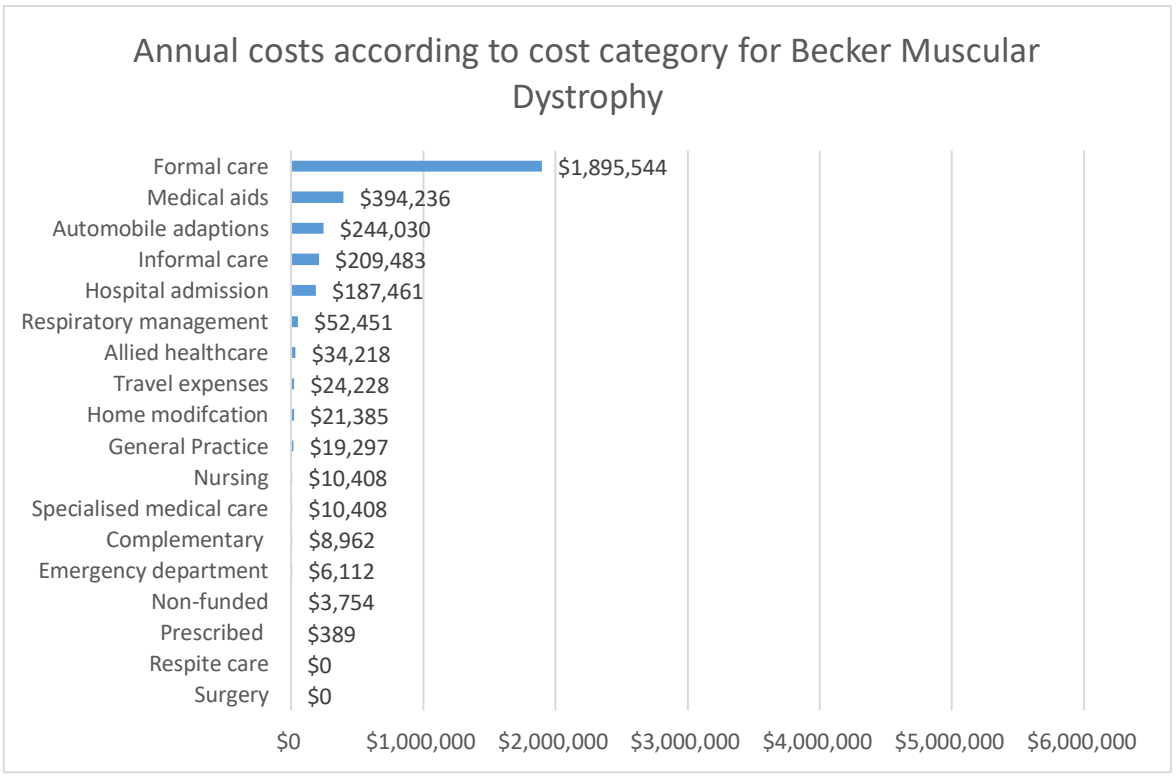

Figure G.2 Bar Chart of Cost Drivers for Becker Muscular Dystrophy

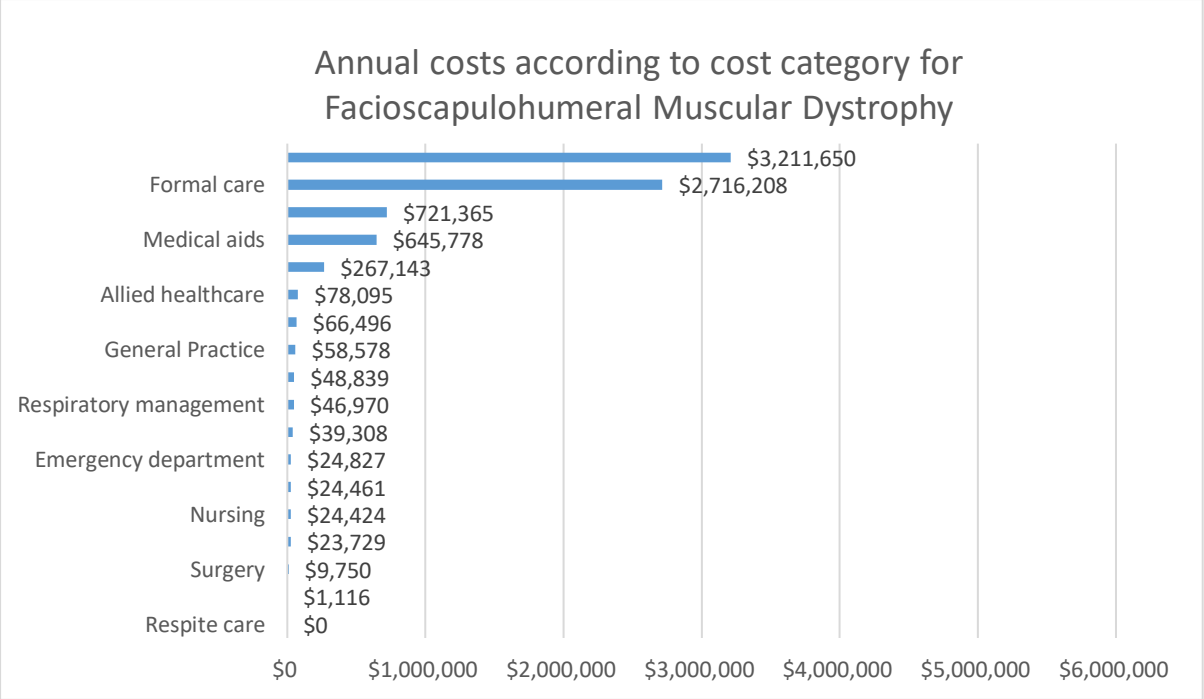

Figure G.3 Bar Chart of Cost Drivers for Facioscapulohumeral Muscular Dystrophy

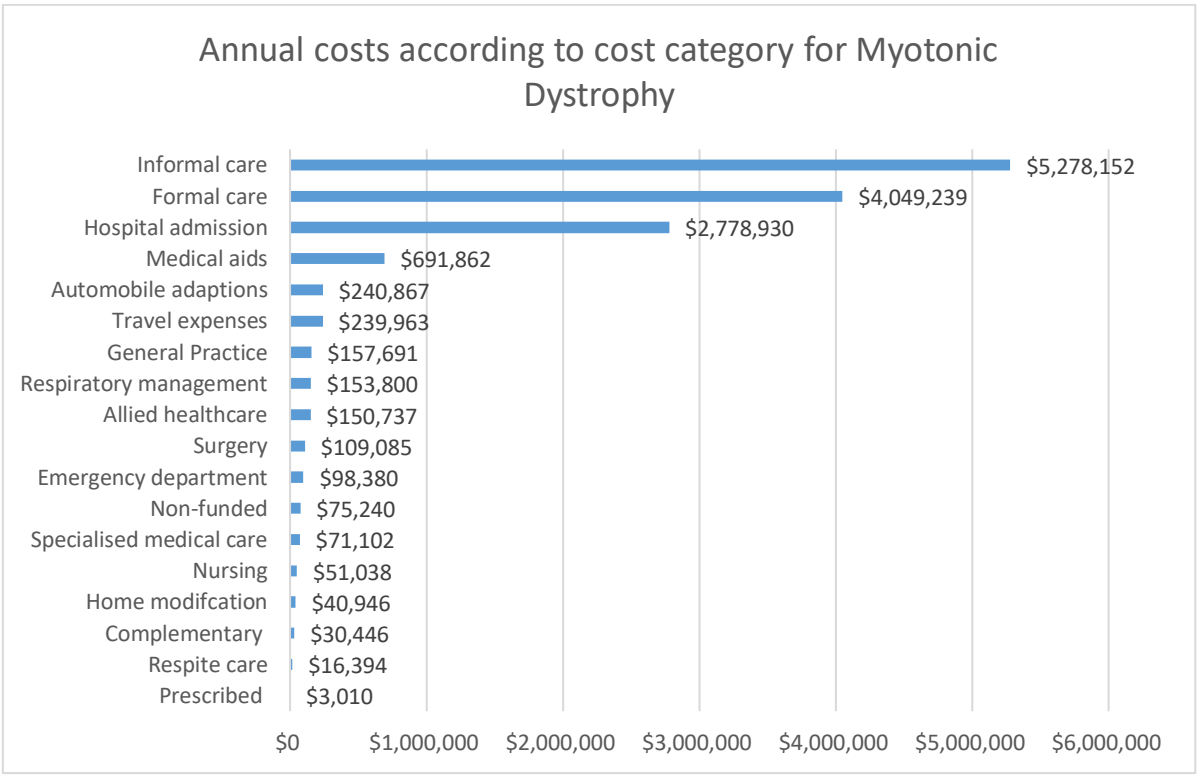

Figure G.4 Bar Chart of Cost Drivers for Myotonic Dystrophy

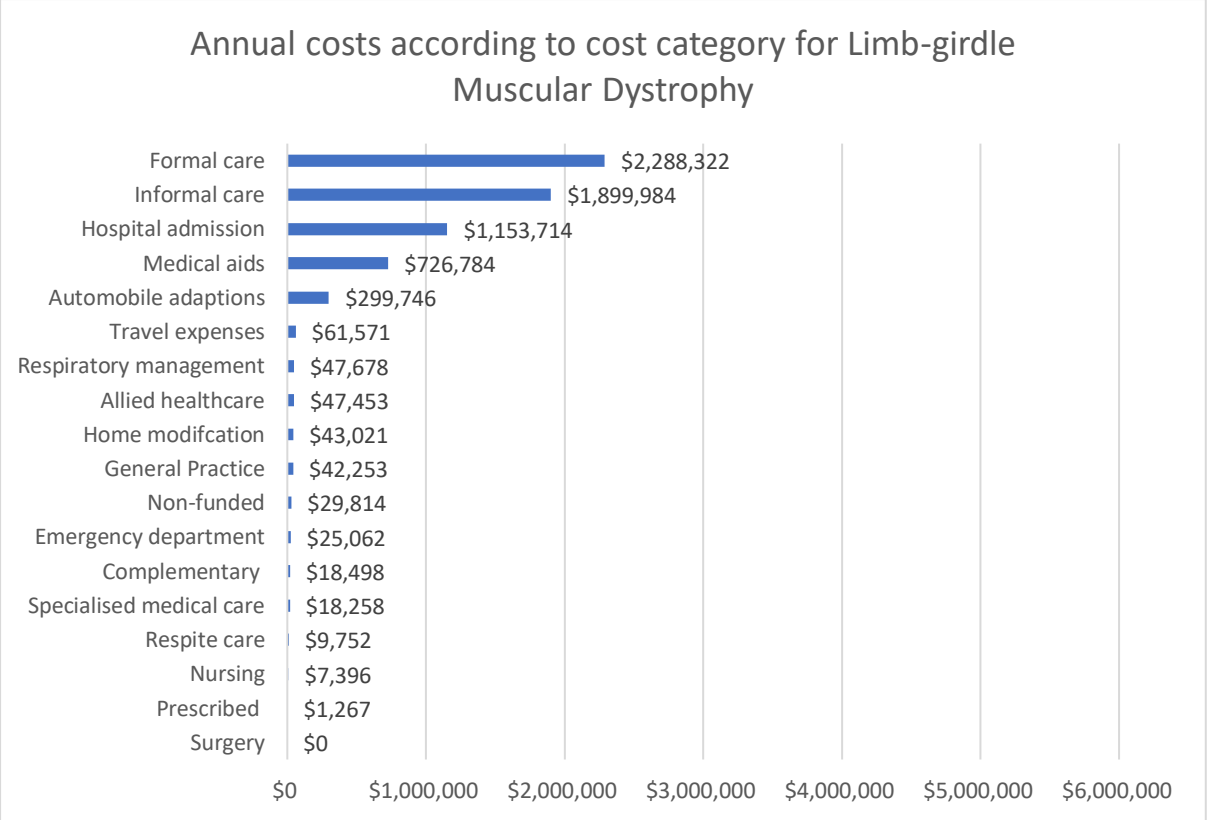

Figure G.5 Bar Chart of Cost Drivers for Limb-girdle Muscular Dystrophy

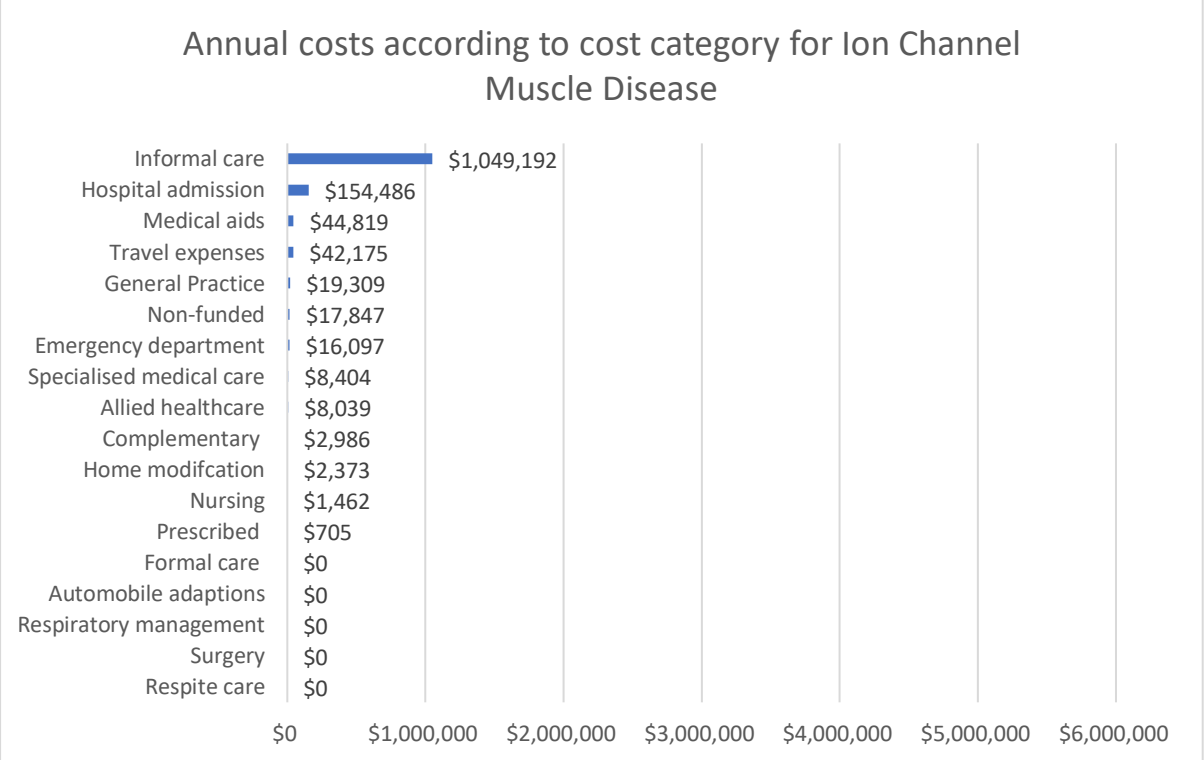

Figure G.6 Bar Chart of Cost Drivers for Ion Channel Muscle Disease

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