Pharmacological and non-pharmacological treatment in people living with Myotonic Dystrophy (DM) in NZ

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Attestation of Authorship

I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person (except where explicitly defined in the acknowledgements), nor material which to a substantial extent has been submitted for the award of any other degree or diploma of a university of other institution of higher learning

Signed

Miriam Hanna

28 February 2019

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Abstract

This study aimed to investigate the type and funding of pharmacological and non-pharmacological medications taken by people diagnosed with myotonic dystrophy (DM) in NZ, and to explore the factors associated with medication use.

Data on 213 individuals with a confirmed diagnosis of myotonic dystrophy identified through a nationwide population-based prevalence study, MDPrev, were extracted. Socio-demographic information, details of funded, non-funded prescription medications they were taking or not taking as well as use of herbal or vitamin supplements, nutritional supplements and complementary therapies were analysed. Chi square and t-tests were used to determine any differences between those who were taking medication and those who weren't to identify any associations between demographic characteristics and medication use. Correlation analysis was then performed and a regression model to determine predictors of medication use.

The findings revealed that medication use amongst individuals with myotonic dystrophy was high, with a number of associated comorbidities and symptoms being treated simultaneously. There were 120 different prescription medicines identified and grouped according to the WHO ATC/DDD classification. Some participants reported taking up to 13 medications with the majority taking up to four different medications. Use of some medications, for example modafinil, was low in NZ, potentially due to this being an unfunded medication in NZ. Modafinil is recommended for managing symptoms common in myotonic dystrophy, such as excessive daytime sleepiness. The study suggests therefore that funding of medicines that have strong evidence for in

international literature, could make a difference in management of the symptoms associated with this condition more effectively in NZ. Use of herbal, nutritional and complementary therapies was diverse and low.

The study highlighted that access to neurology services was a major predictor of medication use. There are only 8 centres in NZ with neurology clinics, access to neurology services needs to be considered for individuals with myotonic dystrophy who are not within easy reach of one of these centres, or by funding and making available more clinics throughout the country. Given the high use and frequency of medications used by people with myotonic dystrophy, increased access medication-review services through community pharmacies could assist in the effective medication use and management of symptoms. In alignment with current literature, this study also suggests that a multidisciplinary approach to management of a complex and multi-systemic chronic progressive condition like myotonic dystrophy may be more effective, and perhaps setting up of neuromuscular clinics that involve a wide range of specialists such as cardiology and gastroenterology, is likely to make significant difference to prescribing and use of appropriate medication.

Chapter 1 Introduction

Myotonic Dystrophy (DM) is a progressive, genetically inherited muscle wasting disorder that is associated with several multi-systemic features or comorbidities. There are two main distinct forms that have been identified, myotonic dystrophy type 1 (DM1), also known as Steinert's Disease, and myotonic dystrophy type 2 (DM2) which is a milder later onset form, also known as proximal myotonic dystrophy (Turner and Hilton-Jones, 2010). Myotonic dystrophy type 1 is the most common of the two forms. Prevalence studies have revealed large variations in frequency depending on regions, from 1 in 100,000 to 1 in 500,000 (Harper, 2001). Myotonic dystrophy type 2 is characterised mainly by myotonia and muscle weakness particularly proximally, along with pain, stiffness and fatigue, and has a better prognosis than myotonic dystrophy type 1 (Klein, 2015). Both conditions are associated with multisystem clinical features but myotonic dystrophy type 2 to a lesser extent. These include cardiac conditions (conduction disturbances and tachyarrhythmias), ocular (posterior subcapsular cataracts), central nervous system conditions (cognitive impairment, peripheral neuropathy, behavioural, emotional and socialization difficulties, excessive daytime sleepiness), gastrointestinal tract conditions (cholecystitis, gallstones, dysphagia), skin conditions (balding and epitheliomas), respiratory difficulties, psychiatric conditions (anxiety, depression, apathy) and complications with pregnancy such as spontaneous abortion, prolonged labour, retained placenta and post-partum haemorrhage (Sarnat, O'Connor, Byrne, 1976; Webb, Muir, Faulkner, 1978). General anaesthetics should be used with caution in myotonic dystrophy and there are several medications contraindicated such as barbiturates and morphine. The most common causes of

death amongst individuals with myotonic dystrophy type 1 are respiratory (40%) and cardiac complications (30%) (Mathieu, Allard, Potvin, Prevost, & Begin, 1999). Pharmaceutical and non-pharmaceutical treatments have a role in managing these complications.

Active management has been shown to improve outcomes in myotonic dystrophy type 1 and myotonic dystrophy type 2 (Mathieu et al, 1999; Kurihara 2005; Schara & Schuser, 2006). There is some evidence to support use of sodium channel blockers such as mexilitine, phenytoin and procainamide to manage myotonia (Trip, Drost, Faber, 2007). Other drug classes that could be used include tricyclic antidepressants, benzodiazepines, calcium antagonists, taurine, clomipramine, imipramine and prednisolone.

Other medication that has been trialled for myotonic dystrophy in the literature include DHEA for muscle weakness (Penisson-Besnier, Devillers, Porcher, Orlikowski, Doppler, Desnuelle, Ferrer, Bes, Bouhour, Tranchant, Lagrange, 2008) and Insulin-like growth factor 1 for muscle mass increase (Furling, Marette, Puymirat, 1999). There is strong evidence for the use of creatine/phosphocreatine based on a Cochrane review (Kley, Vorgerd, Tarnopolsky, 2007). CNS stimulants such as modafinil (Talbot et al, 2003; MacDonald et al, 2002; Damian & Schmidt 2001), dexamphetamine and methylphenidate are often prescribed to combat excessive daytime sleepiness with good evidence for modafinil (Van De Meché, Boogaard, Van Den Berg, 1986). Cholestyramine has been prescribed for patients with gastrointestinal symptoms such as diarrhoea, incontinence and pain, with norfloxacin and erythromycin have been used as a second line (Rönnblom, Forsberg, Danielsson, 1996).

Non-pharmacological management of the condition includes physiotherapy, occupational therapy, exercise and strength training, speech and language therapy, non-invasive ventilation, as well as surgeries such as for cataracts, epiretinal membranes or insertion of pacemakers. Vitamins and mineral such as selenium and Vitamin E have also been studied for myotonic dystrophy (Örndahl et al, 1994). The literature suggests there was a positive effect on myotonia, namely improved muscle relaxation time, however, effects of treatment on motor functions were minimal, and overall motor performance was not improved. Further larger scale studies would be needed to support the use of selenium and Vitamin E. Given the increased risk of medication interactions and contraindications in myotonic dystrophy type 1 and myotonic dystrophy type 2, it is important to find out what medication people are being prescribed, what they are taking off prescription, and the alignment with recommended treatment guidelines currently available internationally.

1.1 The New Zealand Health Care System

New Zealand has a unique and complex network of organisations and people delivering health and disability services which has to be understood in order to evaluate the effective treatment of a chronic genetic multi-system condition as myotonic dystrophy. The health system is New Zealand is mainly funded through general taxation. The Ministry of Health is NZ allocates more than three quarters of the funds received to District Health Boards, of which there are currently twenty in New Zealand, to plan, purchase and provide health services in their local geographic areas.

The remaining public funding, less than 25%, is used to fund national services such as disability support services and medical education and training.

The New Zealand health and disability system has a statutory framework made up of multiple legislature. Of particular importance are the New Zealand Public Health and Disability Act 2000 and the Health Act 1956.

The New Zealand Public Health and Disability outlines the structure and organisation of health and disability services. It defines the District Health Boards (DHBs) and sets out the duties and roles of key organizations, committees and individuals. It also identifies the strategic direction and goals for health and disability services which include improving health and disability outcomes for all New Zealanders, to reduce disparities by improving the health of Maori and other population groups, to provide a community voice in individual health, public health, and disability support services. It also aims to facilitate access to health and disability services in New Zealand and facilitate the dissemination of information relevant to these services. There are also four key strategies currently in place that provide a framework for the system; The New Zealand Health Strategy 2016, New Zealand Disability Strategy, The Maori Health Strategy and The Primary Health Care Strategy.

Key organizations within the Health and Disability System include Crown entities and agencies. These include the Health Quality and Safety Commission, The Health and Disability Commissioner, The Health Promotion Agency, the Health Research Council and PHARMAC. PHARMAC -or the Pharmaceutical Management Agency- is the New Zealand government agency that elects which medicines in community and hospital settings, and other products such as vaccines and devices, to become publicly funded in New Zealand and to what level, which is all set out in the Pharmaceutical Schedule.

Within District Health Boards also lie other important organizations- primary health organizations. Primary health organizations (PHOs) are not for profit organizations, that are funded by the district health boards to support the provision of essential primary health care services through general practices to those people who are enrolled within the PHO. A patient's first point of contact therefore, would be their local general practitioner, who would be able to refer the patient to other primary health care services (such as allied health services as physiotherapy, occupational

therapy.etc.) to ensure a seamless continuum of care, in particular to better manage long-term conditions such as myotonic dystrophy.

This all becomes important to consider and analyze the effectiveness of this model in relation to myotonic dystrophy patients in New Zealand, and although this is not the main aim of this research, it is important to recognize the impact this system may have in terms of access to services, and prescribing of medication, which may differ to other countries.

Chapter 2 Literature Review

2.1 Pharmacological management of myotonic dystrophy

A comprehensive search of literature on myotonic dystrophy treatment and management pharmacologically and non-pharmacologically was conducted until 2018 through a wide range of medical databases. Complete comprehensive evidence-based guidelines were not found to be available, however, as of September 2018, consensus-based care recommendations for adults with myotonic dystrophy type 1 was published to help standardize and improve care for individuals with this condition. With regards to pharmacological treatment, the consensus paper states mexiletine could be considered for treatment of myotonia unless contraindicated due to cardiac condition of the individual. For management of gastrointestinal symptoms such as reflux, bloating, abdominal pain, diarrhoea, constipation and incontinence to name a few, the consensus recommended a number of pharmacological and non-pharmacological treatment. Non-pharmacological treatment included fibre for diarrhoea or constipation and increased water intake. The consensus also recommended nutritional supplements for management of weight loss or gain, or dysphagia. There was a recommendation for the use of loperamide for diarrhoea and laxatives for constipation such as senna, docusate, polyethylene glycol or linaclotide as first- line treatment and bisacodyl and lubiprostone as second line treatment. Metoclopramide was recommended for management of gastroparesis, pseudo-obstruction and reflux. Antibiotics were recommended for bacterial overgrowth-induced diarrhoea and the recommendations also mention that mexiletine can be considered to treat diarrhoea or constipation unless contraindicated for cardiac complications. Modafinil was

recommended for excessive day time sleepiness, and main-stream standards treatments of hyperlipidaemia, diabetes and erectile dysfunction as long as, once again, there are no cardiac side effects (Ashizawa T, et al, 2018).

Another recent review of management and therapeutics in myotonic dystrophy type 1 was published in the Neuromuscular Disorders Journal in November 2016 in the USA (Smith, Gutmann, 2016). The report provided an overview of the underlying causes of the condition, and symptoms that patients present with, as well as recommendations for diagnosis. Due to the lack of current guidelines, the authors have suggested care guidelines by providing recommendations or considerations for each of the conditions associated with myotonic dystrophy type 1. The paper also included a review of current clinical trials, with a focus on antisense oligonucleotides, DHEA, lamotrigine, erythromycin. The authors stress the importance of a multidisciplinary team approach, to undertake vigilant monitoring and pre-emptive measures.

With regards to medication use, Smith and Gutmann (2016) discussed mexilitine as having class 1 evidence for myotonia at doses of 150 to 200mg three times daily, with other sodium channel blockers as phenytoin, procainamide, propafenone, flecainide, carbamazepine and quinine as alternatives that have been reported to improve myotonia. The authors recommend methylphenidate or modafinil for excessive daytime sleepiness and the use of anti-hyperglycemic medication for insulin resistance associated with myotonic dystrophy type 1 and anti-hypercholesterolemia medication for dyslipidemia.

The authors also recommended non-steroidal anti-inflammatory drugs, gabapentin and/or tricyclic antidepressants for pain management. With respect to endocrinopathies associated with myotonic dystrophy type 1, thyroid dysfunction, low testosterone and erectile dysfunction in males can also be treated with medication. To manage gastrointestinal symptoms, mainly intestinal dysmotility, prokinetic medication is recommended by the authors including metoclopramide and erythromycin. Laxatives are recommended for constipation and cholestyramine for diarrhoea, incontinence and pain, followed by norfloxacin to treat bacterial overgrowth if cholestyramine therapy fails. The authors discussed clinical trials of antisense oligonucleotides, DHEA, lamotrigine, and erythromycin in mouse models to potentially reduce myotonia.

The limitation of this review was that it only focused on myotonic dystrophy type 1, there was no in-depth analysis of the data available for the medications recommended. However, the article serves as a reference for clinicians treating myotonic dystrophy and encompasses a holistic view of the management required, referrals to other specialties needed, and tests and monitoring recommended initially and with disease progression.

Turner and Hilton-Jones (Turner & Hilton-Jones, 2014) discussed treatment options available for the conditions associated with myotonic dystrophy type 1 and myotonic dystrophy type 2 and the evidence available for them. This includes DHEA for muscle weakness and insulin-like growth fact 1 (IGF1) to potentially improve insulin sensitivity, gastro intestinal function, lipid profile and increase muscle mass. Turner and Hilton-Jones (2014) noted that most myotonic dystrophy type 1 patients do not have a major

problem with myotonia and would decline treatment with drugs that are potentially arrhythmogenic. This provides a helpful reference guide for clinicians.

For myotonia, a large number of medications have been reviewed, the main class being sodium channel blockers- mexilitine, phenytoin and procainamide. Other classes include tricyclic antidepressants, benzodiazepines and calcium antagonists. A Cochrane review identified only positive effects for small three cross over trials using imipramine, taurine and clomipramine (Trip, 2007).

For daytime sleepiness, CNS stimulant drugs are recommended for trialling including modafinil which has the most evidence and was subject of a number of trials to date, dexamphetamine and methylphenidate. A Cochrane review found overall the evidence was inconclusive and suggested more trials are needed (Annane, 2006).

For gastro-intestinal symptom management of myotonic dystrophy, Turner and Hilton-Jones (2014) make mention of food thickeners as used by some patients to manage aspiration, cholestyramine improves diarrhoea, incontinence and pain, the authors suggest the possible mechanism of action being prevention of large bowel osmotic diarrhoea due to failure of absorption of bile salts in the terminal ileum. Norfloxacin can be used if this fails, to reduce bacterial overgrowth, as per Ronnbloms papers on the possible effect of erythromycin on slowing gastric emptying by compensating for reduced motilin levels in myotonic dystrophy type 1 (Ronnblom, Forsberg, Danielson, 1996; Ronnblom, Andersson, Hellstrom, 2002). There is little evidence of the effectiveness of medical treatment for muscle pain and referral to a pain specialist is recommended (Udd and Krahe, 2012).

Hormone replacement therapy and erectile dysfunction medication are recommended for hypothyroidism and gonadal failure respectively. Turner and Hilton Jones (2014) discuss the potential severity of fatigue and daytime sleepiness in myotonic dystrophy type 1, and state that the effects of treatment have been found to be modest. Udd and Krahe (2012)discuss the potential risk of using statins and have noted the increased risk of some cancers. They finally discuss experimental treatments with a focus on antisense oligonucleotides and molecular approaches.

Heatwole et al (2013) found that there are benefits of treating patients for myotonia, where benefits may even extend beyond improved muscle function to include of relief of gastrointestinal symptoms and in some cases also pain. They present evidence to support the use of antiarrhythmic medications mexiletine, tocainamide, flecainide and procainamide. Mexilitine was found to be the most effective, but also safe and well tolerated, in doses of 150-200mg three times daily. The authors do not recommend tocainamide due to the risk of life-threatening side effects, and there is limited data supporting flecainide as an anti-myotonic agent in general. Procainamide has also shown concerning side effects.

Heatwole, Statland and Logigian (2013) also looked at the evidence for antiepileptic drug use, such as phenytoin and carbamazepine, both of which were shown in studies reviewed by the authors to reduce electrical myotonia, however, phenytoin's potential neurotoxicity and other side effects may limit its use. The authors reviewed evidence for amino acids such as taurine, which in a small study of nine patients reduced subjective clinical myotonia and myotonic after-discharges, however, was also seen to have side effects as amino aciduria and increases in LDL levels triglycerides in the

blood. They look at evidence for antidepressant use, namely imipramine, clomipramine, amitriptyline and calcium channel blocker nifedipine which have different modes of actions, have shown varying response and side effect profile.

Diuretics such as acetazolamide were reviewed, where the authors deemed the evidence was not very clear in myotonic dystrophy type 1 and myotonic dystrophy type 2, and response in patients greatly varied. Quinine was not recommended for use with its life-threatening side effect profile, evidence for danroltene was minimal and on the other hand it seems there is promising emerging data for the use of DHEAS (Dehydroepiandrosterone Sulfate), a naturally occurring adrenal androgen (Heatwole et al, 2013).

Experimental treatments currently include antisense oligonucleotides as a new class of medication, and several animal models and trials have been completed and published to date, however, there are yet to be large scale human trials and readily available options to be prescribed (Udd and Krahe, 2012). Overall there still lacks strong, high standard evidence to support clinical guidelines on medication use in myotonic dystrophy. The consensus recommendations bring this one step closer for myotonic dystrophy type 1, however, this has not yet been published for myotonic dystrophy type 2 or for children with myotonic dystrophy.

Gagnon et al (2007) recommend development of a comprehensive health and community management framework for myotonic dystrophy type 1 and present a conceptual model. They list risk factors for myotonic dystrophy type 1 and organic system involvement and discuss spectrum of symptoms and disabilities associated with

the condition. They highlight that the environmental factors such as social and physical factors that have an impact on myotonic dystrophy type 1 outcomes. It is observed that poverty and social exclusion are common amongst patients with myotonic dystrophy type 1 and education standards as well as employment are lower than the average population. They also look at life habits such as nutrition, fitness, personal care, communication, housing, mobility, relationships and recreation. The limitation of this review is that it did not take into account medication and medication costs, as well as examine access to alternative or complementary therapies. They do acknowledge the need for a holistic approach to management and a focus on patient-oriented outcomes in a community setting rather than clinical settings.

A 12 week prospective, randomized, double blinded, placebo controlled multicenter trial of placebo versus 400mg DHEA was conducted in 75 patients with myotonic dystrophy type 1. The trial showed no significant difference in the primary objective, the relative change in the manual muscle testing score from baseline. There was also no significant difference in the secondary outcome measures, which were change in quantitative muscle testing and timed functional testing, respiratory and cardiac function, and quality of life. It therefore could not be concluded that treatment with DHEAs improves muscle strength in ambulatory myotonic dystrophy type 1 patients. (Penisson-Besnier, I. et al., 2008)

A review of ACE inhibition in muscular dystrophy by Russo et al. (2017) discussed ACE-I or ARB therapy in myotonic dystrophy type 1, where dilated cardiomyopathy is present, to delay or prevent heart failure. They also suggested early initiation of ACE-I therapy which could possibly delay or prevent cardiac dysfunction, rather than

introduction of therapy when ventricular dilation or systolic dysfunction occurs. They recommend more studies to establish evidence for this approach. (Russo et al., 2017).

A double blinded crossover trial of selegiline, an effective treatment in narcolepsy, was conducted in ten patients with myotonic dystrophy related hypersomnolence, at a dose of 20mg daily. Selegeline is a rapidly acting potent mono-amine oxidase inhibitor that enhances dopaminergic tone in the brain. Although this was found to be well tolerated in patients with myotonic dystrophy, no effect on hypersomnolence was seen, and it was recommended that further studies at higher doses of selegiline could be conducted to examine whether there is any efficacy. (Antonini, et al., 1996)

A recently published phase II randomized control trial investigated the effect of metformin on mobility in myotonic dystrophy type 1. This was based on improvements seen in mouse models. Forty patients were enrolled and randomized to receive placebo or metformin three times daily with a dose escalation period over four weeks up to 3g per day, maintained for 48 weeks. Results showed that the treated group had a significantly increased distance in the six minute walk test, and an increased mechanical power suggesting the treatment has an effect on gait. There were no other positive effects noted, however there were increased side effects as would be expected in the treatment group which included gastrointestinal disturbances and weight loss. The authors call for a wider well-powered multi-centre phase III trial to further establish the positive effect on mobility and gait. (Bassez, et al. 2018).

Constipation is one of the many gastrointestinal symptoms associated with myotonic dystrophy. A paper was published looking at the role of prucalopride in treatment of

chronic constipation and recurrent functional intestinal pseudoobstruction in a 37 year old female with type 1 myotonic dystrophy. Prucalopride, a new serotonin receptor agonist that acts as a prokinetic agent, was selected as second line after failure of conventional first line treatments as enemas, polyethylene glycol and trimebutine. Following a two week period of prucalopride use, the woman reported normal stool frequency and consistency. She continued on the medication and at a six month follow-up, this was maintained with no new episodes of intestinal pseudo-obstruction. Large scale randomized placebo controlled trials are needed before it is recommended for use in patients with chronic constipation as a result of myotonic dystrophy. (Giglio et al., 2015).

A review of chemical and herbal remedies for constipated patients by Kumar and Kishore makes mention of myotonic dystrophy as a myopathic condition resulting in constipation due to muscular disability. They list chemicals with laxative effects of natural or synthetic origin that could be used to treat constipation. These include bentonite, bisacodyl, bisoxatin, carboxy methylcellulose, cellulose, dantron, ethyl hydroxyl ethyl cellulose, glycerin, lactulose, lactitol, liquid parrafin, magnesium citrate, magnesium sulfate, maltitol, mannitol, methylcellulose, olestra, oxyphenisatin, pentaerythritol, polycarbophil, polyethylene glycol, sodium picosulfate and sorbitol. These either act by being bulk-forming, contact, stimulant or osmotic mechanisms. (Kumar & Kishore, 2013)

2.2 Non-pharmacological management of myotonic dystrophy

There is very little literature on non-pharmacological therapy in myotonic dystrophy. A Cochrane review of creatinine in dystrophies showed a potentially increased maximum voluntary contraction, however, it was identified that larger double blinded trials are needed in order to routinely recommend creatine in myotonic dystrophy. Vitamins and mineral such as selenium and Vitamin E have also been studied for myotonic dystrophy (Örndahl et al, 1994). The literature suggests there was a positive effect on myotonia, namely improved muscle relaxation time, however effects of treatment on motor functions were minimal, and overall motor performance was not improved.

In an observational open label study of two myotonic dystrophy type 1 patients, it was noted that high-dose thiamine (Vitamin B1) treatment was well tolerated and effective in improving the motor symptoms such as muscle strength and activities of daily living (Costantini, 2016).

Terracciano et al (2013) also recommend oral supplementation of Vitamin D in myotonic dystrophy type 1 since they found that myotonic dystrophy type 1 patients had a lower serum 25-hydroxyvitamin D (25(OH)D) which may influence the level of insulin-like-growth-factor 1 (IGF1) and respectively muscle strength (Terracciano, 2013).

As mentioned previously, Kumar and Kishore published a review of natural and synthetic treatments of constipation, a common comorbidity amongst myotonic dystrophy patients. Natural food laxatives rich in fibre make stool bulkier and encourage peristalsis and defecation. Examples of fruits with laxative effects are

bananas, apples, melons, berries, prunes, avocados and tomatoes. Seeds with laxative effects include flaxseed, pumpkin, almonds, walnuts, hemp, sunflower, sesame, chia, Siberian and cedar nuts, Examples of flowers include broccoli and cauliflower. Leaves with natural laxative effects include aloe vera, barley, bitter gourd, wheatgrass, kale, spinach, dandelion, spirulina, mustard, onions, chicory, senna, garlic and argula. There are some rhizomes also that can act as natural stimulants such as ginger and turmeric. Roots with a bulk laxative effect include carrots, and natural oils that can act as natural lubricants include hemp, flax seed, avocado seed oil, olive oil and coconut oil. A long list of plants or herbal remedies used as laxatives with evidence in literature is also included in the review by Kumar and Kishore. These are commonly known as baneberry, bael, giant taro, ghritakumari, amaranth, jangli mendi, kdamba, cabbage tree, agar wood, hingot, danti, orchid tree, petha, arhar, madar, balloon vine, caraway, cascara, badikanodi, crested celosia, mosambi, vasanvel, coffee, aravi, varuna chhal, mango ginger, laijabori, vidang, amla, white head, mandara, ain larneb, kapoorkachari, lady's fingers, subabul, luffa, plantain, night jasmine, olive, prickly pear, dudhialata, amla, rasbhari, paan, rasana, Indian beech, almond, burans, semi-plena, gaach-munga, nightshade, gorakhmundi, spinach, harra, serpent, damiana and cocklebur. Systematic reviews that were completed to evaluate efficacy of plants in constipation were also listed by Kumar and Kishore, these plants are commonly known as Magali, manakachu, red aloe, aloe, edlebur, pithraj, aavartaki, amaltas, kasuna, nilkanthi, watermelon, lechosa, dudhiya, homaira, linseed, oyia, girdlepod, drumstick, dudhialata, karanja, sudburg, cassia, makok, parwal, banafshah, nirgundi. In addition to this they recommend lifestyle changes increased fluid intake, exercise such as yoga, dietary

changes such as avoidance of constipating foods as alcohol, coffee, tea, spice, vinegar, tomatoes and fried foods can help reduce incidence of constipation. (Kumar & Kishore, 2013).

A systematic review looking at exercise therapy and other types of physical therapy concluded that there may be evidence for aerobic exercises, muscle-strengthening exercises and breathing exercises for patients with myotonic dystrophy. There was a call however for large multi-centred trials with standardised measures in order to build a more robust evidence base and produce comparable results (Cup, 2007).

A randomized, multi-centre, single blinded, randomized trial by Okkersen et al (2018) investigated whether cognitive behavioural therapy alongside graded exercise was more beneficial for individuals with myotonic dystrophy type 1 versus standard care. A total of 255 individuals over 18 years of age with severe fatigue took part in this study over a period of ten months. The researchers were particularly interested in looking at the effect of cognitive behavioural therapy on activity levels and social participation, which was measured using the myotonic dystrophy type 1-Activ-c outcome scores. It was shown that whereas the myotonic dystrophy type 1-Activ-c scores reduced in the standard care group, the myotonic dystrophy type 1-Activ-c scores increased amongst those in the intervention group receiving cognitive behavioural therapy and an individualized graded exercise programme, resulting in increased capacity for activity and social participation and reduced fatigue. The study design had limitations and has not been replicated outside the four centres where this study took place, so care should be taken when interpreting these results and before making widespread recommendations.

Myotonic dystrophy was amongst several neuromuscular conditions that were examined through a systematic review of literature for evidence pertaining to psychosocial interventions and impact on quality of life. The review included ten controlled trials and cohort studies looking at cognitive behavioural therapy, dignity therapy, hypnosis, expressive disclosure, gratitude lists, psychoeducation and psychologically informed rehabilitation. Whist seven of the ten trials reported short term benefit of Due to the variation in therapies, conditions included and outcome measures of these trials, there remains a lack of evidence to support psychosocial interventions in myotonic dystrophy. (Walklet et al., 2016).

A pilot study by Hammaren et al (2015) investigated a balance exercise programme in individuals with myotonic dystrophy type 1 who specifically have balance difficulties. The intervention was carried out over ten weeks, but was not compared to a non-intervention group for comparision. The study demonstrated however that compared to baseline, measures such as the Activities-Specific Balance Confidence (ABC Scale), Step Test and Timed Ten Metre Walk increased as reported by the participants directly after the intervention, and amongst some, also at follow up after twelve weeks. As this was only a pilot study involving a small number (eleven) participants, larger scale, randomized controlled trials are needed to validate these results and to make wider scale recommendations for balance exercise programmes in individuals with balance difficulties with myotonic dystrophy.

Lindeman et al. (1995) designed a randomized control trial to investigate a muscle strength training programme over 24 weeks in individuals with myotonic dystrophy, and the effect this has on strength, fatigue, functional abilities and performance as

well as well-being. These were measured using knee torque, time sustaining an isometric contraction in proximal lower extremity muscles, timed motor performance and questionnaires. Serum myoglobin also measured any change in membrane permeability of muscle fibres in these individuals. The study was not conclusive as there was no significant change seen across these outcome measures, however since no negative or harmful effects resulted, the authors still concluded that it would be worthwhile investigating a more intensive programme at an even earlier stage in the disease progression, hypothesizing that perhaps outcomes would be favourable and more conclusive.

Orngreen et al., (2005) studied the effect of aerobic training in 12 participants with myotonic dystrophy using cycle testing and muscle morphology before and after the training for comparison. With increases in maximal oxygen uptake, maximal workload and muscle fiber diameter, it was concluded that aerobic training is safe and can improve fitness in individuals with myotonic dystrophy. This study had limitations, and did not compare to a control group, therefore further larger scale, randomized placebo controlled trials are needed once again before recommendations are made for this type of therapy amongst myotonic dystrophy patients worldwide.

A systematic review of strength training and aerobic exercise training for muscle disease concluded that moderate intensity strength training and aerobic exercise training in myotonic dystrophy appear to have no harm but more evidence is needed in order to conclude that they would offer benefit. (Voet, et al., 2010).

A 12 week progressive high resistance training programme was also studied in six patients with myotonic dystrophy showing increased muscle strength but no significant difference in isokinetic values, histopathology of muscle fibre and magnetic resonance imagine of the trained muscle groups. Once again, although there was no harm observed and the programme was well tolerated, more evidence is needed to substantiate any claims of benefit amongst patients with myotonic dystrophy. (Tollback, et al., 1999)

A case report by Nogueria et al (2011) looked a kinesiotherapy in a 32 year old woman with myotonic dystrophy type 1. Twenty sessions were carried out, where a protocol was designed including stretching, strengthening of upper and lower limbs, lung expansion, functional exercises, postural transfer training, gait and stairs training. Physical examination and a quality of life questionnaire were used to assess the outcomes, and significant improvements were seen across functional ability, limitations due to physical aspects, pain, overall health including mental health, vitality, social functioning and muscle strength. Once again, larger scale randomized, blinded, controlled trials would be needed to investigate the effect on a larger number of individuals with myotonic dystrophy in order to draw conclusions and make wide scale recommendations.

A randomized controlled pilot study by Kierkegaard et al (2011) looked at a twice weekly, 14 week physical excercise programme in adults with myotonic dystrophy type 1 with no cardiac involvement, had distal or mild to moderate proximal muscle impairment and no severe cognitive impairment. The investigators chose the six-minute walk test as the primary outcome measure, and the timed-stands test, timed

up and go test, Epworth sleepiness scale and short Form-36 health survey as secondary measures. 35 participants were randomized to the intervention and control groups. Although no adverse events were reports and the programme was seen as well tolerated, no significant beneficial effects were reported.

Qigong was also investigated in myotonic dystrophy by Wennberg et al. (2004) both qualitatively and quantitively. In the quantitative study, 36 participants were randomized to an intervention or control group for three months. Quantitatively, balance and respiratory function was assessed using the Berg's Balance Scale and electronic spirometer. The Medical Outcome Study Short Form Health Survey (SF-36) was used to measure health-related quality of life. Coping levels was measured using the Ways of Coping Questionnaire, and depression was measured using the Montgomery Asberg Depression Rating Scale. The treatment group showed a maintained perceived general health, a decreased positive reappraisal coping and a tendency to maintain balance function whilst training. The authors concluded that qigong may be useful as an adjunct therapy in myotonic dystrophy, and could reduce the rate of deterioration of symptoms. Qualitatively, 26 participants were involved in semi-structured interviews which were analyzed by Grounded Theory, defining six broad categories: 1. experience of healthcare and alternative methods, 2. Expectations, acceptance and compliance, 3. Qigong as an adaptable form of exercise, 4. Stress reduction and mental effects, 5. Increased body awareness and physical effects, 6. Psychosocial effects of group training. There was a wide variation of experience reported amongst the participants, with some benefits perceived as reduction of stress and improved well-being amongst some. Once again, this was seen

as a well tolerated therapy with no harmful effects, however with insufficient evidence to promote it for management or treatment of myotonic dystrophy.

A controlled pilot study investigating the safety and efficacy of functional electrical stimulation in four eligible participants with myotonic dystrophy type 1 versus an equivalent control group. The training consisted of a daily half hour functional electrical stimulation cycling session for fifteen days, and the Medical Research Council Scale and functional assessments were performed to measure outcomes. Once again this was well tolerated, and resulted in an improved muscle strength and endurance than the control group.

Occupational therapy also has a role to play in the management of chronic conditions like myotonic dystrophy. A search of the literature did not result in extensive evidence or recommendations, however a myotonic dystrophy adapted version of the Stanford Chronic Disease Self-Management Program was used with five myotonic dystrophy patients in a pilot study, which was shown to be acceptable and feasible. It is recommended that occupational therapists incorporate, adapt and utilize self-management strategies with their patients. (Kateri et al., 2016).

There is a lot of evidence and literature around ventilation in patients with myotonic dystrophy, however for the purposes of this research question, ventilation has not been considered a complementary or alternative therapy.

Several studies have been published in recent years, and many more currently ongoing, to identify and design disease- modifying therapies for myotonic dystrophy. These are based on genome editing science and technology, small molecules and anti-

sense oligonucleotides. The majority of these trials are pre-clinical and in a lot of the promising work thus far has been conducted on mouse models and lab settings. (LoRusso, 2018) For the purpose of this research study, an extensive review of literature relating to molecular or pre-clinical therapies was deemed out of scope, as this study aims to investigate established and recommended therapies currently, and investigate the use of these amongst participants with myotonic dystrophy in NZ.

Chapter 3 Methods

3.1 MDPrev

MDPrev was a large population based epidemiological study funded by the Health Research Council of NZ to determine the prevalence, disease profile, impact and cost of all genetic muscle disorders in New Zealand (NZ) including myotonic dystrophy type 1 and myotonic dystrophy type 2.

Multiple case ascertainment sources were used, including hospital and community disability services. Diagnosis was confirmed through a review of medical and test results. Following confirmation, the individual was contacted and invited to complete a questionnaire to assess and the impact of the condition on functioning and quality of life. If interested in taking part in the study, participants were sent information sheets and had the opportunity to ask questions before a time to meet with a researcher was arranged or the participant was sent a link to the online questionnaire. Before completing the questionnaire, participants were asked to read and sign a consent form if they wished to participate. The broader questionnaire collected information on demographics, age of diagnosis and symptom onset, access to healthcare, symptoms, satisfaction with services, unmet needs, functioning, quality of life, employment or education, impact on relationships and involvement in the community, as well as direct and indirect costs. To facilitate participation, the questionnaire could be completed in person with a researcher, over the phone with a researcher or self-completed online. For those aged <16 years, the questionnaire was completed by a parent/guardian. The questionnaire took about 2 hours to complete in total. Ethics Committee approval was obtained from the Northern Y Regional Ethics Committee of

NZ (Reference: 14/NTB/118) and the Auckland University of Technology Ethics Committee (Reference: 14/296).

3.2 Study of pharmacological and non-pharmacological treatment of myotonic dystrophy in NZ

As part of the wider MDPrev data on medication use and non-pharmacological treatment was collected but was not analysed within the context of specific conditions such as in myotonic dystrophy. A research proposal was submitted, and permission was granted through the Steering Committee and principal investigators of MDPrev to extract data for individuals diagnosed with myotonic dystrophy in NZ and use this data to explore pharmacological and non-pharmacological treatment specifically for myotonic dystrophy patients in NZ.

3.2.1 Study Aims

(a) Investigate type, dosage and funding of pharmacological and non-pharmacological treatments of myotonic dystrophy in NZ.

(b) Explore the factors linked to medication use

3.2.2 Hypotheses

(a) It is hypothesized that a high proportion of myotonic dystrophy participants will be taking at least one medication to help them to manage their symptoms.

(b) It is hypothesized that participants taking medication will have greater levels of physical disability than those who do not.

(c) Lower levels of physical functioning and older age will be predictive of medication use.

3.2.3 Outcome Measures

As part of MDPrev, data was collected on the type of medications taken, frequency and how they were funded as well as the type of herbal and vitamin supplements, nutritional supplements and complementary therapies used by participants. Participants were asked the following questions:

"Do you currently require any prescription medication (given to you by your GP/clinician)? Yes or No.

"If yes, how many different medications are prescribed for you?"

"What medications do you currently take?"

"If yes, how many times a day do you need to take your medications?"

"Are you taking any medications recommended or prescribed for you that are not government funded/subsidised?" Yes or no

"If yes, please specify."

"If yes, how much in NZ dollars do you spend on personally funded medications each week?"

"Are there any medications recommended to you by your clinician that you are not taking because they are not funded by the government/subsidised?" Yes or no

“If yes, please specify.”

“Do you currently take any herbal or vitamin supplements?” Yes or no

“If yes, please specify.”

“How much in NZ dollars do you spend on herbal or vitamin supplements each week?”

“Are you currently taking any nutritional supplements (eg: energy drinks)?” Yes or no

“If yes, please specify.”

““How much in NZ dollars do you spend on nutritional supplements each week?”

“Are you currently using any complementary therapies e.g.: aromatherapy, acupuncture, homeopathic remedies?” Yes or no

“If yes, please specify.”

“How much in NZ dollars do you spend on complementary therapies each week?”

Responses to the above questions were extracted along with variables hypothesized to potentially have an influence or impact on medication use such as ethnicity, sub-type of myotonic dystrophy, household income, living situation, geographic location or District Health Board (DHB) that they belonged to, symptom burden and comorbidities. Symptom severity was assessed by asking whether each symptom was experienced none of the time or classified as being experienced mild, moderate or severe. There were fourteen different symptoms listed in the participant questionnaire, these were: headaches, muscle weakness, muscle spasms, limited

movement in a joint(s), joint(s) feeling stuck (contractures), Irregular heartbeat (e.g.: palpitations, faints/blackouts, pacemaker), muscle weakness of the heart (e.g.: shortness of breath, swollen ankles), respiratory difficulties (e.g. Needing oxygen, mucus in the lungs), ptosis (drooping of the eyelids), dysphagia (difficulty swallowing), poor balance, frequent falls, visual impairment and speech impairment. Levels of health care use such as hospitalisations, GP visits and access to a neurologist were also assessed using study-specific questions. Participants were also asked about their overall satisfaction with the standard of healthcare received on a scale of 1 to 10 (where 1 is least satisfied and 10 was most satisfied).

The ACTIVLIM measure was used to assess levels of physical functioning. This is a self-report questionnaire where participants are asked about the extent they perceived difficulty in performing daily activities (e.g. taking a bath, stepping up and down kerbs) on a three-point scale (ranging from easy to impossible). With lower scores representing greater difficulties. The complete questionnaires for adults and children are included appendices A and B.

3.2.4 Analysis

Demographic data were extracted, and tests of difference used to determine if there was any difference between those with myotonic dystrophy who completed the questionnaire versus those who chose not to participate. This was to ensure the population of participants is representative of the whole population of myotonic dystrophy patients in NZ. Medication reported by the participants was tabulated and classified according to the WHO/ATCDDD Classification System. Chi square and t-tests were used to determine if there were any differences between those participants on

medication and those were not. Spearman correlation coefficients were used to determine if there were any sociodemographic factors that were linked medication use, to inform a regression analysis to determine predictors of medication use as the data was not normally distributed.

Chapter 4 Results

4.1 Participant demographics

MDPrev identified 343 individuals in NZ living with myotonic dystrophy on the point prevalence date of the 1st April 2015. 213 (62.1%) agreed to participate in the study and completed the questionnaire. Demographics of the total population, those who participated and those who did not are included in Table 1. There was no statistical difference in the mean age, gender distribution or type of myotonic dystrophy between the two groups. However, there were a significantly higher proportion of non-European participants who declined to take part in the study. There were only 8 children under 16 years of age among the participants of the study. The majority of participants had myotonic dystrophy type 1. As shown in Table 1. participants taking part in the study were located across both the North and South islands of NZ, with the largest number of cases located within Canterbury DHB followed by Waitemata and Auckland DHBs.

Table 1. Participant Demographics

Characteristic	**All Myotonic (n=343)**	**Participants (n=213)**	**Non-participants (n=130)**	**Test of Difference**
Gender Male	149 (43%)	89 (42%)	60 (46%)	x^2=0.63, p=0.43
Female	194 (57%)	124 (58%)	70 (54%)	
Mean Age	44.79 years	44.50 years	45.25 years	t= , p=0.70
Ethnicity				
All European	309	206	103	X^2=15.31
Unknown/Other	34	3	31	<p=0.001
Type of Myotonic				
DM1	327 (95%)	201 (94%)	126 (97%)	X^2=1.19
DM2	16 (5%)	12 (6%)	4 (3%)	P=0.28
DHB				
Northland	10	8	2	
Auckland	39	30	9	
Waitemata	41	21	20	
Counties Manukau	14	5	9	
Bay of Plenty	23	15	8	
Waikato	24	13	11	
Tairawhiti	6	3	3	
Lakes	6	4	2	
Taranaki	9	7	2	
Hawkes Bay	14	11	3	
Whanganui	2	1	1	
Mid Central	13	9	4	
Hutt	8	4	4	
Capital and Coast	22	13	9	
Wairarapa	7	3	4	
Nelson Marlborough	7	3	4	
West Coast	4	4	0	
Canterbury	71	46	25	
South Canterbury	4	2	2	
Southern	19	11	8	

Amongst the study participants, overall satisfaction with the standard of healthcare received was high (Mean of 7.5 on a scale of 1 to 10). On average, participants reported 3-5 visits to their GP per year, and between zero and 2 visits to their specialists per year. Approximately 25% had been hospitalised and 9% had had surgeries in the past year. Only 54% reported having regular access to a neurologist specialising in neuromuscular conditions.

4.2 Medication Use

57% of respondents were taking prescription medications, with 120 different prescription medicines identified and grouped according to the WHO ATC/DDD classification. Table 2 includes a summary of medication reported and classification according to the WHO ATC/DDD index.

Some participants reported taking up to 13 medications with the majority (80%) taking between 1 and 4 different medications. 16% of participants were taking over six medications concurrently. The majority of prescription medicines taken were for the cardiovascular system, respiratory system and the gastrointestinal system. The most common prescription medicines taken were omeprazole, aspirin, salbutamol, atorvastatin, metoprolol. 9% of participants were paying for non- government subsidised medication, the rest were fully or partially subsidised according to the pharmaceutical schedule of NZ.

Table 2. Classification of medicines taken by participants

Medicine Classification	Reported Medicines
Alimentary Tract and Metabolism	Magnesium, Potassium, Calcium, metformin, insulin, gliclazide, omeprazole, pantoprazole, lansoprazole, hyoscine, ranitidine, loperamide, metoclopramide, domperidone, coloxyl, lactulose, laxsol.
Blood and Blood forming organs	Folic acid, aspirin, dabigatran, clopidogrel, warfarin
Musculoskeletal system	Allopurinol, Orphenadrine, glucosamine, diclofenac, Naprosyn, ibuprofen, etoricoxib, meloxicam
Genitourinary system and sex hormones	Progesterone, testosterone, oral contraceptives, Solifenacin, terazosin, tamulosin.
Nervous System	Methylphenidate, sumatriptan, modafinil, morphine, codeine, paracetamol, diazepam, temazepam, triazolam, clonazepam, midazolam, lorazepam, carbamazepine, gabapentin, levitracetam, sodium valproate, levomepromazine, fluoxetine, paroxetine, citalopram, venlafaxine, mirtazapine, zopiclone, nortriptyline, amitriptyline.
Respiratory System	Salbutmaol, salmeterol, atrovent, flixotide, symbicort, becotide, beclafort, loratadine, cetirizine, flixonase.
Cardiovasular System	Furosemide, spironolactone, duride, felodipine, amlodipine, cilazapril, enalapril, quinapril, atorvastatin, pravastatin, simvastatin, ezetimibe, metoprolol, sotalol, carvedilol, bisoprolol, doxazosin, losartan, diltiazem, digoxin, mexilitine, amiodarone
Systematic hormonal preparations	Prednisone, fluticasone, fludrocortisone, thyroxine
Antiinfectives for systematic use	Amoxicillin, penicillin, doxycycline

4.3 Comorbidities

46% of the participants reported having comorbidities. An analysis of the reported comorbidities showed that diabetes, asthma and sleep apnoea were common, followed by hypothyroidism/ thyroid problems/ thyroidectomy, atrial fibrillation or flutter, hyper-cholesterolaemia, heart diseases and hypertension. Other comorbidities

reported included cataracts, irritable bowel syndrome, depression, hearing impairment, epilepsy, reflux, arthritis, gout, osteoporosis and peripheral neuropathies. 58.5% of this population reported pain and 69.8% reported fatigue. with 57% of participants in our study with DM1 reporting pain and 69.7% reported fatigue

Table 3 compares the sociodemographic factors between participants on medication with those participants not on medication. There was a statistically significant difference in the age, with participants taking medication being of a significantly older age than those not on medication. There was also a statistically significant difference in physical functioning, household income, comorbidities, symptoms, access to neurology, hospitalization and use of complementary therapies.

Table 3.Differences in sociodemographic and illness characteristics between those taking medication and those who do not.

	All Participants	**Prescribed Medication**	**Not prescribed medication**	**Test of Difference**
	(n=213)	**(n=120)**	**(n=91)**	
Age (Mean)	44.5	48.21	40.26	t=3.65, *p*=0.00
ActivLim (Mean)	2.40	1.67	3.36	t= -5.01, *p*<0.01
Gender N (%)				
Male	89 (41.8)	55 (45.8)	36 (39.6)	X^2=0.45, *p*=0.50
Female	124 (58.2)	67 (55.8)	55 (60.4)	
Ethnicity N (%)				
All European	206 (96.7)	117 (97.5)	87 (96.5)	X^2=0.10, *p*=0.76
Maori	2 (0.9)	2 (1.7)	0 (0.0)	
Other	5 (2.4)	1 (0.8)	4 (4.4)	
Living Situation N (%)				
Living in own home		78 (65)	64 (70.3)	X^2=3.20, p=0.36
Renting		34 (28.3)	21 (23.1)	
Residential care		6 (5)	2 (2.2)	
Other		2 (1.7)	4 (4.4)	
DHB N (%)				
Larger DHB		103 (85.5)	78 (85.7)	X^2=0.00, *p*=0.98
Smaller DHB		17 (14.2)	13 (14.3)	
Household Income N (%)				
≤$60,000	90 (42.3)	57 (47.5)	33 (36.3)	X^2=4.89, *p*=0.03
>$60,000	54 (25.4)	24 (20.0)	30 (33.0)	
Comorbidities N (%)	99 (46.5)	75 (62.5)	24 (26.4)	X^2=27.78, *p*<0.01
Reported pain N (%)	117 (54.9)	71 (59.2)	46 (50.5)	X^2=2.01, *p*=0.16
Reported fatigue N (%)	141 (66.2)	86 (71.6)	55 (60.4)	X^2=3.14, *p*=0.76
Access to neurologist N (%)	116 (54.5)	78 (65)	38 (41.8)	X^2=9.48, *p*<0.01
Hospitalised in the past year N (%)	50 (23.5)	40 (33.3)	10 (11.0)	X^2=13.42, *p*<0.01
Herbal or vitamin supplement use N (%)	72 (33.8)	41 (34.2)	31 (34.1)	X^2=0.03, *p*=0.87
Nutritional Supplement Use N (%)	16 (7.5)	7 (5.8)	9 (9.9)	X^2=1.40, *p*=0.24
Complementary Therapies Use N (%)	23 (10.8)	8 (6.7)	15(16.5)	X^2=5.04, *p*=0.03

Variables for which there were found to be differences between those on medication and those who were not were entered into a correlation to explore which factors were related to medication use. Participants' geographical location was split according to the DHB they registered with and then due to the large number of DHBs, a larger DHB was classified as one with over 150,000 registrations, and a smaller DHB, classified as one with less than 150,000 registrations in accordance with NZ statistics (Stats NZ, 2018). As shown in Table 4 there were significant associations between age, comorbidities, access to neurology, ActivLim measure, hospitalization and complementary therapies and medication use.

Table 4. Correlations

Variables	1	2	3	4	5	6
1. Prescription Medicine Use						
2. ActivLim	0.36**					
3. Hospitalization	0.25**	0.26**				
4. Access to neurology	0.22**	0.12	0.13			
5. Comorbidities	0.36**	0.19**	0.10	0.02		
6. Age	-0.25**	-	-	-	-	

*= p<0.05 ** = p<0.01

A binary logistic regression using the stepwise forward conditional approach was conducted entering in the variables age, comorbidities, hospitalisations, ActivLim score and access to neurologist. The final model shown in Table 5 was able to correctly classify 72% of cases revealed that activity limitations and comorbidities were predictive of medication use in myotonic dystrophy.

Table 5. Logistic regression model

Variables in the Equation

								95% C.I.for EXP(B)	
		B	S.E.	Wald	df	Sig.	Exp(B)	Lower	Upper
Step 1[a]	Comorbidites	1.514	.306	24.558	1	.000	4.545	2.497	8.273
	Constant	-2.654	.508	27.255	1	.000	.070		
Step 2[b]	ActivLim	.249	.065	14.519	1	.000	1.283	1.129	1.458
	Comorbidities	1.429	.317	20.288	1	.000	4.175	2.242	7.775
	Constant	-3.129	.549	32.461	1	.000	.044		

4.4 Medication Use in Myotonic Dystrophy Type 2

A subgroup analysis was conducted to look at patterns within the myotonic dystrophy type 2 population separately, given the different disorder characteristics. There were 12 participants who were all of European ethnicity. Ages ranged from 32 to 76 with a mean of 59.33 years. There were 5 males and 7 females. 67% reported pain and similarly 67% reported fatigue. 67% reported access to neurology, 67% reported comorbidities. Muscle weakness was the single most reported symptom.

The mean ActivLim Measure was 2.18 (higher than the sample total). There appeared to be strong family history with multiple individuals located in the Christchurch area. 67% reported comorbidities which included: asthma, hypertension, high cholesterol, Sleep Apnoea, Epilepsy, Meniere's disease, ingrowing eyelashes and Osteoporosis. 75% reported taking prescription medication. This ranged from 1 medication up to 12, with a mean of 4.5meds, 50% reporting having to take their meds 1-2 times daily.

Reported Medication included: Metformin, Aspirin, Quinapril, Paracetamol & Codeine, Ployvinyl Drops, Simvastatin, Gliclazide, Frusemide, Fluticasone, Salmeterol, Salbutamol, Insulin, Vesicare, Cilazapril, Bisoprolol, Omeprazole, Amlodipine besylate,

Tamsulosin Hydrochloride, Amiodarone, Imigran, Enalapril, Ibuprofen , Beclafort, Diltiazem, Zopiclone and carbamazepine.

4.5 Medication Use in Children

A subset of child participants' data was extracted and analysed separately to examine patterns amongst children of medication use and other treatments. There were eight children under the age of 16 who participated in the study. Ages varied amongst child participants, the youngest at the time of completion of the questionnaire was seven years old and the oldest 15 years. The mean amongst child participants was 11.8 years old.

Looking at the characteristics of this small population, there were more females than males amongst child participants, five females to three males. Three participants had a family history, and all the children were diagnosed with myotonic dystrophy type 1. Similar to the adult population, the majority were of European descent, and one participant was from Māori descent.

Age at symptom onset varied with five out of eight being diagnosed at birth and one being diagnosed at the age of one year old. Comorbidities reported amongst this population included duplex kidney and a heart condition. Three (37.5%) children were on medication. The medication reported was ventolin syrup, antihistamine, Lactulose and Refresh Eye Ointment. There were two reports of hospital visits including one hospitalization. One mentioned having grommits. ActivLim Patient Measure ranged from -0.40 to 6.57 with a mean of 2.16. All the children have access to neurology. One

child required non-invasive ventilation. Two of the children reported experiencing pain and fatigue.

4.6 Non-pharmacological therapy use

In the total myotonic dystrophy sample about a third of participants were using vitamin and herbal supplements. Those listed by the participants were: Vitamin B, Calcium, Vitamin E, Vitamin C, Zinc, Magnesium, Menopause Support, Lesters Oil, Pez-Rez, Multivitamins, Vitamin D, Echinacea, Boost Revive, Berroca, Metamucil, Multiflora Digest, Omega 3 Fish Oil, Cranberry, Folic Acid, Iron, Enzyme Co Q10, St. John's Wort, Probitoics ,Garlic, Flax Seed Oil, L-carnatine, Molasses, Boron, Allergy support, Tumeric, Marijuana, Digestive Enzymes, Glutamin, Mintec, Chondroitin, Macu-vision, Sleep Ezy, Amino Acids, Sore no More Joint Relief, Boost Me Extreme Energy, Suma Root Powder and glutathione . The top five non-prescription medicines were magnesium, fish oils, multivitamins ± minerals, Vitamin C and Vitamin D. Parents reported giving their children herbal and vitamin supplements including three children were taking vitamins. These were Vitamin E, Calcium, Vitamin C, Zinc, magnesium, fish oil.

Only 11% of participants were using complementary therapies which included occupational therapy acupuncture, homeopathy, yoga, massage, osteopathy, aromatherapy, meditation, Health Kinesiology, Vibra-training, hydrotherapy pools and chiropractor visits. For those with myotonic dystrophy type 2 a quarter of participants

reported use of complementary therapies: Yoga, hydrotherapy and acupuncture. No nutritional supplements were reported.

Of the total participants, 8% were using nutritional supplements such as Protein shakes, Cacao supplements, Fortisip, BCAA Powder, Ensure, Complan and various sports and energy drinks as Red Bull and Power Aid.

Chapter 5 Discussion

5.1 Summary

This study was conducted to investigate pharmacological and non-pharmacological therapy use amongst individuals with myotonic dystrophy in NZ. The study revealed that as expected medication use was high with more than half of participants taking at least one medication, with many participants taking multiple different medications. Use of complementary, herbal and nutritional therapies was low. Predictors of medication use included presence of comorbidities and access to a neurologist. Compared to recommendations in the literature, there appeared to be gaps in medications prescribed in NZ, possibly due to availability and funding. This study therefore has the potential to inform practice, aid in lobbying for improved reach to neurology clinics and for medication funding.

5.2 Medication Use

Medication use amongst participants was high (57%), with the number of medications taken as high as 13 in some cases. The top five medications were omeprazole, aspirin, salbutamol, atorvastatin and metoprolol. When the general NZ population prescription data reported by PHARMAC was investigated, it was found that these were amongst the top ten medications prescribed in NZ (PHARMAC, 2018), suggesting that this may reflect general medication use not just specific to myotonic dystrophy. It is important therefore to further investigate the reason the medication was prescribed, and

whether the symptom is attributed to myotonic dystrophy or general ailments related to age for instance.

5.3 Predictors of medication use

The population of participants with myotonic dystrophy in NZ included more females (58%) than males. It is known that myotonic dystrophy affects both males and females equally, however, it may be that this reflects gender disparities in health care seeking (to get a diagnosis) and/or willingness to participate in the study. However, there was no statistical difference (p=0.63) by gender in those participating in the study and those that did not. This may also reflect an overall population trend, with a population estimated at 4.6 million in June 2015, there were 97 males for every 100 females in NZ (Stats NZ, 2018). Gender was not significantly associated with medication use in this study, however gender was seen in some studies to be associated with some symptoms (Heatwole et al). It is also known that females have higher rates of gastrointestinal problems, which in turn could lead to more medication use (Wilson et al, 2004).

As can be expected of patients living with a complex disorder such as myotonic dystrophy, report of comorbidities was high (46%). There was a very wide range of comorbidities reported with the most common being diabetes, asthma, sleep apnea, thyroid problems, atrial fibrillation, hypercholesterolemia, heart disease and hypertension. A study of medication adherence in patients with myotonic dystrophy was conducted by Fitzgerald et al (2016) that was completed by 110 individuals with myotonic dystrophy type 1 and 49 individuals with myotonic dystrophy type 2. This reported that the highest reported comorbidities were depression (29%), arrhythmias

(29%) and gastroesophageal reflux disease (24%) in myotonic dystrophy type 1 and hypertension (37%) and gastroesophageal reflux disease (30%) in myotonic dystrophy type 2. This was compared to the general population, rates in NZ, according to the New Zealand Health Survey (NZHS) for 2016 and 2017, where data available for depression rates in European males and females were 15.6 % and 23.7% respectively, and rates of hypertension being 16.2% and 16.9% respectively. (Ministry of Health, 2018). This highlights that rates are higher amongst those diagnosed with myotonic dystrophy and hence much higher awareness is needed around diagnosis and treatment of these comorbidities.

In a previous study in myotonic dystrophy type 1 patients, Fitzgerald et al (2016) also noted that of those patents with polypharmacy, myotonic dystrophy type 1 participants were younger (mean of 55 years) compared to myotonic dystrophy type 2 (mean of 59 years) and had shorter disease duration (mean of 26 years) compared to myotonic dystrophy type 2 (mean of 34.8 years).

Of interest is also the relationship between age and medication use. Whereas the average age across participants was 44.5 years, it was noted that the average age of participants on medication was significantly higher (48.2 years) than those not on medication (mean of 40.3 years) ($p=0.00$). This was also shown by Fitzgerald et al (2016) where the mean age of those with myotonic dystrophy type 1 on up to 5 medications was 48.7 years verses 55 years for those on 6 or more medications. Higher medication use with increasing age may be reflective of worsening health and progression of myotonic dystrophy or could reflect additional comorbidities as the

result of the aging process. To unpack this further details of the reason(s) for taking particular medications would be needed.

The symptom most reported in our study was muscle weakness, which was similarly seen in other studies as Fitzgerald et al, (2016). who also reported higher fatigue and lower pain in myotonic dystrophy type 1 (14% and 6.3%), compared to myotonic dystrophy type 2 (2% and 14.3% respectively). This was significantly different to what was reported in our study however, with 57% of participants in our study with myotonic dystrophy type 1 reporting pain and 69.7% reported fatigue. This is a striking difference and perhaps should alert to further investigations needed. The PRISM studies by Heatwole et al, (2013), yet again reported different fatigue and pain prevalence, 90.8% and 74% in DM1 respectively, and 89.2% and 79.7% in myotonic dystrophy type 2 respectively. The PRISM studies looked at wide range of symptoms for prevalence but also relative impact, which may be a better way to investigate symptoms across myotonic dystrophy in NZ in a further study, particularly as the symptom list included in the questionnaire was broad to encompass a number of genetic muscle disease and not tailored to myotonic dystrophy. (Heatwole et al. 2012; Heatwole et al. 2015) The PRISM studies interestingly demonstrated that the symptoms that were most prevalent, were not always the most important to the patients, for instance where muscle weakness is most prevalent, fatigue had the greatest impact on participants lives. This is important to note in further studies when identifying the most appropriate therapeutic objectives for patients.

Access to neurology was significantly correlated with medication use. It needs to be considered that medication use may not necessarily be a positive outcome as it is

important that medication is prescribed appropriately and those not taking it may not necessarily need it. However, it is important that those who need it are able to access it. In NZ, there are only eight centres with neurology clinics. These are located in Auckland, Hamilton, Bay of Plenty, Hawkes Bay, Capital and Coast, Nelson-Marlborough, Christchurch and Southern District Health Boards. A large number of participants therefore reside in locations where there is no access to neurology. Indeed, 97 (45.54%) of participants said they had no access to neurology. This could potentially mean that they also have no access to specialist knowledge to medication or treatment that could reduce their symptom scores and disease burden and may be reliant on GPs. Lack of access to neurology clinics could have been a result of not just the lack of availability of clinics in the area, but also a lack of awareness of the availability of clinics, distance needed to be travelled and lack of funding towards transport to clinics (Ranta et al. 2016). This current gap has been identified through a research study in NZ and is affecting all neurology patients not just myotonic dystrophy patients. A solution that potentially improve the current situation without putting large pressures on the health system is the provision of technology such as telehealth.

There was a significant difference in household incomes between those participants who were on medication verses those who were not ($p=0.03$). It is worth noting that the more than half the population in this study earnt a household income below that of the National average of $63,000 per annum. This could have an impact on the care accessed, including medication and non-funded therapies, therefore could impact on the quality of life. This also highlights that the government needs to look at funding of medication that is currently non-funded but has an evidence base, such as modafinil.

5.4 Non-pharmacological therapy use

The study showed a large variety of herbal and vitamin supplements used, nutritional supplements and complementary therapies, the vast majority of which has very little to no evidence in literature to support. It is important to note that these are non-funded treatments in NZ and may be difficult to access given the household income averages of this population, therefore health care professionals should discuss with their patients what they are taking, and whether there is any evidence for. On the other hand, it is also important not to dismiss any effect on improvement on symptoms, any of these therapies may have. Further studies should look at the effects on symptom scores and ActivLim Measures, whilst on these therapies for a sufficient period of time.

Particularly of interest is creatinine, which has a growing body of evidence and continuing trials across various muscular dystrophies, with positive evidence in Duchenne Muscular Dystrophy. This could potentially have a positive effect on myotonic dystrophy if studied on a wider scale although was not reported as being used by any participants within our sample.

5.5 Children with myotonic dystrophy

There were eight children amongst the participants (only 3.8%) whom all had myotonic dystrophy type 1 and were all of European ethnicity except for on who identified as Māori. Medication use amongst children was low. It is noted that one child was on non-invasive ventilation and the comorbidities reported amongst child participants were duplex kidney and aheart condition. Two participants reported pain and fatigue. The data was compared to the parent-reported multi-national study of the impact of

congenital and childhood onset myotonic dystrophy study by Johnson et al (2016) which reported that fatigue, gastrointestinal issues, urinary and bowel control, along with communication problems, had the greatest impact on children's lives and reported that 24.1% of children reported cardiac disorders and 15.8% had problems with anaesthesia, which was not particularly reported in our study. A higher rate of intellectual disability, ADHD and ASD was reported by Johnson et al (2016) compared to the general population, which again has not featured in our study results and perhaps should be studies in further detail to examine impact on children's lives. The difference between symptoms reported and impact on life experienced by adult-onset and child-onset myotonic dystrophy type 1 highlights the need to approach patients with child-onset DM differently and with a focus on issues that impact on their lives the most. The small number of children in this study group is a limitation and a wider population of children with myotonic dystrophy needs to be examined in order to have more conclusive outcomes.

It is of interest that all child participants reported access to neurology, which suggests paediatric services in NZ are more comprehensive and have a much greater reach and resources. It is recommended therefore that the health system in NZ examines a continuation of such services so that once a child with a chronic condition as myotonic dystrophy transitions into adult services, that they continue to have the same level of care and follow up.

5.6 Myotonic Dystrophy Type 2

There were 12 participants with myotonic dystrophy type 2, only 5.6% of the total participant population. Similar to Fiztgerald et al's (2016) findings, the majority of

those with myotonic dystrophy type 2 reported their onset of symptoms in their third to fifth decade. They had a mean age much higher than those with myotonic dystrophy type 1 (mean of 59.3 years). There seemed to be a prolonged delay between age of onset of symptoms as opposed to age of diagnosis. Previous studies have reported an average delay to diagnosis of 14.4 years (Hilbert et al, 2013), whereas there is an average of 50 years in the population of participants in our study. It is important to increase awareness so that patients seek clinical care in the first instance, but also the recognition by clinicians of early features of myotonic dystrophy type 2 can limit delay to diagnosis and lead to earlier treatment, monitoring and intervention to improve outcomes and disease progression. Diagnosis could be achieved sooner where there is family history and also with continued improvements in diagnostic technology and health services.

5.7 Limitations

There were several limitations to this study. This was a patient-reported study and apart from diagnosis, the symptoms and comorbidities reports has not been confirmed by review of medical records. Symptoms therefore were subjective, and no objective measures of physical constraints were carried out. Further research could investigate the actual prevalence of issues as pacemakers and occurrence of anaesthesia complications for example. Also, although the response rate was high, it is likely that the respondents do not perfectly represent the population in NZ with myotonic dystrophy. There could also be potential bias or inaccuracies where the questionnaire was completed by a carer of the individual with myotonic dystrophy or a parent of a child with myotonic dystrophy. Although this study helps understand disease burden,

further studies could evaluate which factors and treatments can best reduce disease burden, symptoms and comorbidities reported by this population. It is also important to investigate further whether comorbidities and associated medication are a result of age or are not associated with myotonic dystrophy. It may also be worthwhile categorizing myotonic dystrophy type 1 similar to other studies, into congenital, childhood onset or adult-onset for which have difference disease trajectories.

It is important to also highlight that Māori and Pacific Island populations seem to be under-represented. It is unclear whether there is a real difference in the prevalence of myotonic dystrophy, or whether other factors are to play such as lack of engagement with medical services, or cultural beliefs around chronic conditions may potentially influence approach to management and engagement with services. In this case, a more culturally appropriate study can focus just on Māori and Pacific Island populations to establish a true prevalence and impact of myotonic dystrophy as well as medication use.

The PRISM-2 study by Heatwole et al, (2015) revealed that difficulty with medication side effects was prevalent in 45.2% of patients with myotonic dystrophy type 2. A limitation of the current study was that there was no data on adherence to medication or experience of side effects only data on what was prescribed so it remains unclear as to the medications patients are actually taking, how often and whether they are taking them at the correct dose (as prescribed). Understanding actual medication use in participants would be useful to assist clinicians in their prescribing practices. Fitzgerald's et al (2016) found that regimen complexity, medication costs, health literacy, side effect profile and beliefs around treatment were all linked to what

medication was taken and how. For example, Fitzgerald et al (2016) reported that dysphagia in myotonic dystrophy type 1 was reported to significantly impact medication adherence. Interestingly, 35% of their study participants reported polypharmacy (six or more medications), which is much higher than in our population (16%). This could be attributed to the differences in the samples between the two studies.

Additionally a further limitation of the current research is that the emotional impact of myotonic dystrophy was not considered. Fizgerald et al (2016) highlighted that depression was amongst the top three reported comorbidities across myotonic dystrophy type 1 and myotonic dystrophy type 2. Emotional impact of myotonic dystrophy was outside of the scope of this study, however, it is important to investigate as it will give a clear picture of the condition, and better inform management. It is likely that anxiety and depression are more likely to be problematic given the uncertainty of the progression and prognosis of a complex condition such as DM. Few participants were taking medications such as anti-depressants, it is unclear is this is due to other treatments being used or participants not being screened for or assessed for emotional disorders.

5.8 Summary

The findings indicate that there is a diverse and broad range of medications prescribed for people living with myotonic dystrophy in NZ. Knowledge from this study will help increase understanding of the complexities of the disease from a patients perspective. Given such high use of multiple medications, the findings highlight the need for regular medication reviews and that access to neurology services may assist in helping

patients access medications that they may need. However, this study was unable to determine that whilst there was higher prescribing for patients seeing a neurologist it is unknown how appropriate the prescribing was. People with myotonic dystrophy may benefit from better utilization of already existing services in NZ such as medication reviews by pharmacists in community pharmacy that can reduce polypharmacy, avoid medication interactions and side effects, improve adherence and compliance and provide in depth information about the medication to the individuals. The findings highlight the importance of a multi-disciplinary approach to care and management of individuals with myotonic dystrophy in NZ due to wide symptoms reported and high use of medication. A multi-disciplinary approach may help to reduce reliance on medication by managing symptoms holistically such as reduction of pain by massage or hydrotherapy. A multi-disciplinary approach also means more collaboration and communication between healthcare professionals caring for the individual. Further research is also needed to look at current adherence, and perhaps the use of qualitative interviews to explore current beliefs with regards to medication and to explore adherence. A closer look at wider data collected from this group such as impact and cost on daily living, can help plan and deliver services that meet the needs of these individuals holistically, not just in terms of clinical outcomes in medical settings but also in a community setting.

Chapter 6 Conclusions

Medication use amongst the myotonic dystrophy population was high in NZ. It can also be seen in this population that polypharmacy and comorbidities is high. Medication use increases with age, with presence of mild to severe symptoms, disease progression and lower physical functioning (which was measured by the ActivLim Measure). Household income was found to be a significant factor in medication use, which indicates that this population may not be receiving optimum healthcare due to financial disparity. There was no difference in medication use across gender, location by DHB or ethnicity. We believe there is an underrepresentation of Māori and Pasifika in the study, and it could be an indication of lack of engagement with clinical services or lack of engagement with the research process.

There was a strong relationship between access to neurology and comorbidities on medication use. With limited neurology clinics and centres around NZ, and a widespread myotonic dystrophy population that does not seem to be centred around specialist centres, this indicates that those who do not have access to neurology are potentially not accessing specialist medication and may be potentially disadvantaged. Medication with strong evidence in literature for use in myotonic dystrophy such as mexilitine and modafinil was rarely prescribed in this population. There was no use of creatine at all in this population, indeed usage of nutritional and herbal supplements and vitamins was low. This suggests a potential lack of knowledge or awareness of supplements with evidence for use in myotonic dystrophy, or a lack of discussion with an appropriate healthcare professional before purchase of natural or nutritional supplements. There is therefore also an opportunity to advocate for funding of non-

funded medication or difficult to access medication that requires Special Authority or Specialist prescribing in NZ. Ensuring improved access to neurology could be a potential positive outcome of this study. Multidisciplinary team approach to management of myotonic dystrophy is highly recommended in the NZ setting as well given the wide variety of comorbidities and medication myotonic dystrophy patients are on. It has observed that paediatric services are a lot more comprehensive, where all children have access to specialist services and referrals through multidisciplinary clinics, however this was not observed in adult services. Lobbying for improved adult services, or a continuation of the same level of service provided in paediatrics when an individual is transitioning into adult services, is important, due to the noticeable drop in the level of care and service reported by individuals. The introduction or facilitation of mobile neurology clinics to address the lack of access to services for those outside of main centres is also recommended.

The promotion of already existing services and ensuring awareness and access to these services such as annual medication reviews through community pharmacy and pharmacist support is also of importance. Annual medication reviews could be a useful tool to assess suitability, adherence and compliance of medication and natural, herbal or nutritional supplements. Further studies to investigate adherence and compliance in myotonic dystrophy patients in NZ would also be recommended, as this has been identified as a limitation of this study. Qualitative interviews would also be useful in the future to delve in depth into individuals thoughts and feelings around seeking medical care, who they chose to see, the medication they request, or chose to have

dispensed, and behaviours related to taking medication and alternative therapies sought.

References

Annane, D., Moore, D.H., Barnes, P.R.J., et al. (2006). Psychostimulants for hypersomnia (excessive daytime sleepiness) in myotonic dystrophy. Cochrane Database of Systematic Reviews, 3, CD003218.

Antonini, G., Morinom S., Fiorelli, M., Fiorini, M., Giubilei, F. (1996). Selegiline in the treatment of hypersomnolence in myotonic dystrophy: a pilot study. Journal of neurological sciences. 147:167-169.

Ashizawa, T., Gagnon, C., Groh, W., et al. (2018). Consensus-based care recommendations for adults with myotonic dystrophy type 1. Neurology Clinical Practice. 8,507-520.

Bassez, G., Audureau, E., Hogrel, J., Arrouasse, R., Baghdoyan, S., Bhugaloo, H., et al. (2018). Improved mobility with metformin in patients with myotonic dystrophy type 1: a randomized controlled trial. Brain. 141, 10: 2855-2865.

Brook, J.D., McCurrach, M.E., Harley H.G., Buckler A.J., Church D., Aburatani H., et al. (1992). Molecular basis of myotonic dystrophy: expansion of a trinucleotide (CTG) repeat at the 3' end of a transcript encoding a protein kinase family member. *Cell,* 68(4), 799-808.

Caudia, P. Weis, L., Baba, A., Kiper, P., Marcante, A., Rossi, S., et al. (2016). Effects of Functional Electrical Stimulation Lower Extremity Training in Myotonic Dystrophy Type 1. A pilot controlled study. American Journal of Physical Medicine and Rehabilitation. 6, 95:809-817.

Costantini, A., Trevi, E., Pala, MI.,Fancellu, R. (2016). Can long-term thiamine treatment improve the clinical outcomes of myotonic dystrophy type 1?. Neurology Regeneration Research, 11(9), 1148-1401.

Cup, E., Pieterse, AJ., Munneke, M., Van Engelen, BG., Hendricks, HT., Van der Wilt, et al. (2007). Exercise therapy and other types of physical therapy for patients with neuromuscular diseases: A systematic review. Archives of Physical medicine and Rehabilitation. 88(11), 1452-1464.

Damian, M. S., Schmidt, F., & Reichmann, H. (2001). Modafinil for excessive daytime sleepiness in myotonic dystrophy. Neurology, 56(6), 794-796.

Fitzgerald, B.P., Conn, K.M., Smith, J., Walker, A., Parkhill, A.L., Hilbert, J.E., et al. (2016). Medication adherence in patients with myotonic dystrophy and facioscapulohumeral muscular dystrophy. Journal of Neurology, 263:2528-2537.

Furling D, Marette A, Puymirat J. (1999). Insulin-Like Growth Factor I Circumvents Defective Insulin Action in Human Myotonic Dystrophy Skeletal Muscle Cells 1. Endocrinology, 140(9), 4244-50.

Gagnon C, Noreau L, Moxley R, Laberge L, Jean S, Richer L, et al. (2007). Towards an integrative approach to management of myotonic dystrophy type 1. Journal of Neurology, Neurosurgery and Psychiatry, 78, 800-806.

Giglio, M., Luglio, G., Tarquini, R., (2015). The role of prucalopride in treatment of chronic constipation and recurrent functional obstruction in a patient with Steinert myotonic dystrophy. Journal of clinical gastroenterology. 49; 85-86

Hammaren, E., Lindberg, C., Kjellby-Wendt, G. (2015). Effects of a balance exercise programme in myotonic dystrophy type 1: A pilot study. Europeam Journal of Physiotherapy, 17: 123-131.

Harper, P. S., van Engelen, B. G. M., Eymard, B., Rogers, M., & Wilcox, D. (2002). 99th ENMC international workshop: myotonic dystrophy: present management, future therapy: 9–11 November 2001, Naarden, The Netherlands. Neuromuscular Disorders, *12*(6), 596-599.

Harper PS. (2001). Myotonic Dystrophy. 3rd Edition. London: Saunders.

Hilbert JE, Ashizawa T, Day JW, et al. (2013). Diagnostic odyssey of patients with myotonic dystrophy. Journal of Neurology, 260, 2497-2504.

Heatwole, C. R., Bode, R., Johnson, N., Quinn, C., Martens, W., McDermott, M. P., et al. (2012) Patient-reported impact of symptoms in myotonic dystrophy type 1 (PRISM-1). Journal of Neurology. 79, 348-357.

Heatwole, C. R., Johnson, N., Bode, R., Dekdebrun, J., Dilek, N., Hilbert, J. E., et al. (2015) Patient-reported impact of symptoms in myotonic dystrophy type 2 (PRISM-2). Journal of Neurology. 85, 2136-2146.

Heatwole, C. R., Statland, J. M., Logigian, E.R. (2013) The diagnosis and treatment of myotonic disorders. Muscle and Nerve. 47, 632-648.

Jatrana, S., Crampton, P., & Norris, P. (2011) Ethnic differences in access to prescription medication because of cost in New Zealand. Journal of Epidemiology & Community Health, 65(5), 454-460.

Johnson, N. E., Ekstrom, A., Campbell, C., Huang, M., Adams, H. R., Chen, W., et al. (2016). Parent-reported multinational study of the impact of congenital and childhood onset myotonic dystrophy. Developmental Medicine and Child Neurology, 58, 698-705.

Kateri, R., Levasseur, M., Chouinard, M., Mathieu, J., Gagnon, C. (2016). Stanford Chronic Disease Self-Assessment Program in myotonic dystrophy: new opportunities for occupational therapists. Canadian Journal of Occupational Therapy. 83, 3:166-167.

Klein, A. (2015). Therapeutic Approaches for Dominant Muscle Diseases: Highlight on Myotonic Dystrophy. Current Gene Therapy.

Kurihara T. (2005). New Classification and Treatment for Myotonic Disorders. *Internal Medicine.* 44, 1027-32.

Kley RA, Vorgerd M, Tarnopolsky MA. (2007). Creatine for treating muscle disorders. The Cochrane Library.

Kumar, N., & Kishore, K. (2013). Chemical and herbal remedies for constipated patients: a review. Indian Journal of drugs, 2:23-27.

Lindeman, E., Leffers, P., Spaans, F., Drukker, J., Reulen, J., Kerckhoffs, M. et al. (1995). Strength Training in patients with myotonic dystrophy and hereditary motor and sensory neuropathy: a randomized clinical trial. Arch Phys Med Rehabilitation, 76: 612-620.

LoRusso, S., Weiner, B. Arnold, D. (2018) Myotonic Dystrophies: targeting therapies for multisystem disease. Neurotherapeutics. 15, 4: 872-884.

MacDonald, J. R., Hill, J. D., & Tarnopolsky, M. A. (2002). Modafinil reduces excessive somnolence and enhances mood in patients with myotonic dystrophy. *Neurology,* 59(12), 1876-1880.

Mathieu J, Allard P, Potvin L, Prevost C, Begin P. (1999). A 10-year study of mortality in a cohort of patients with myotonic dystrophy. Neurology, 1;52(8):1658.

Nogueira, S. Machado, W., Goncalves, M., Pereira, C. (2011). Physiotherapy practice in the neuromuscular rehabilitation process of steinert's myotonic dystrophy- case report. Cuidado e Fundamental. 3, 3:2222-2232.

Okkersen, K., Jimenez-Moreno, C., Wenninger, S., Daidj, F., Glennon, J., Cumming, S., et al. (2018). Cognitive behavioural therapy with optional graded exercise therapy in patients with severe fatigue with myotonic dystrophy type 1: a multicentre, single-blind, randomised trial. Lancet Neurology. 17, 8, 671-680.

Orngreen, M., Olsen, D., Vissing, J. (2005). Aerobic training in patients with myotonic dystrophy type 1. Annals of Neurology. 57: 754-757.

Örndahl, G., Grimby, G., Grimby, A., Johansson, G., & Wilhelmsen, L. (1994). Functional deterioration and selenium-vitamin E treatment in myotonic dystrophy. A placebo-controlled study. Journal of internal medicine, 235(3), 205-210.

Peter S, Harper, Baziel V, Bruno E, Douglas E, Wilcox et al. (2004). Myotonic Dystrophy. Present management, future therapy. Oxford University Press.

Penisson-Besnier I, Devillers M, Porcher R, Orlikowski D, Doppler V, Desnuelle C, et al. (2008). Dehydroepiandrosterone for myotonic dystrophy type 1. Neurology, 5,71(6), 407-12.

PHARMAC. (2018). Accessed through www.pharmac.govt.nz.

Ranta, A., Tiwari, P., Mottershead, J., Abernethy, D., Simpson, M., Brickel, K., et al. (2015) New Zealand's neurologist workforce: a pragmatic analysis of demand, supply and future projections. The New Zealand Medical Journal, 128, 1419.

Rönnblom, A., Forsberg, H., Danielsson, Å. (1996) Gastrointestinal symptoms in myotonic dystrophy. Scandinavian journal of gastroenterology, 1;31(7), 654-7.

Rönnblom, A., Andersson, S., Hellstrom, P. M. (2002). Gastric emptying in myotonic dystrophy. European Journal of Clinical Investigations, 1, 31(7), 654-7.

Russo, V., Papa, A., Williams, E., Rago, A., Palladino, A., Politano, L., et al. (2018). ACE Inhibition to slow progression of myocardial fibrosis in muscular dystrophies. Trends in Cardiovascular Medicine. 28, 5:330-337.

Sarnat, H. B., O'Connor, T., Byrne, P.A. (1976). Clinical effects of myotonic dystrophy on pregnancy and the neonate. Archives of Neurology, 33: 459-465.

Schara, U., Schoser, B. G. (2006). Myotonic dystrophies type 1 and 2: a summary on current aspects. Paediatric Neurology, 13,71-9.

Smith, C., Gutmann, L. (2016). Myotonic Dystrophy 1 Management and Therapeutics. Neuromuscular Disorders. 18, 52.

Stats NZ (2018). Accessed through www.stats.govt.nz .

Talbot, K., Stradling, J., Crosby, J., & Hilton-Jones, D. (2003). Reduction in excess daytime sleepiness by modafinil in patients with myotonic dystrophy. Neuromuscular disorders, 13(5), 357-364.

Terracciano, C., Rastelli, E., Morello, M., Celi, M., Bucci, E., Antonini, G., et al. (2013). Vitamin D deficiency in myotonic dystrophy type 1. Journal of Neurology. 260, 9, 2330-2334.

Tollback, A., Eriksson, S., Wredenberg, A., et al. (1999). Effects of high resistance training in patients with myotonic dystrophy. Scandanavian Journal of Rehabilitative Medicine. 31: 9-16.

Tordoff, J. M., Bagge, M. L., Gray, A. R., Campbell, A. J., & Norris, P. T. (2010). Medicine-taking practices in community-dwelling people aged ≥75 years in New Zealand. Age& Ageing, 39(5), 574-580.

Turner, C., Hilton-Jones, D. (2010). The myotonic dystrophies: diagnosis and management. Journal of Neurology Neurosurgery and Psychiatry, 81, 358-367.

Trip, J., Drost, G., Faber, G. (2007). Drug treatment for myotonia. Cochrane Database of Systematic Reviews, 4, CD004762.

Udd, B., Karahe, R. (2012). The myotonic dystrophies: molecular, clinical, and therapeutic challenges. Lancet Neurology, 11, 891-905.

Udd B, Meola G, Krahe R, et.al. Myotonic dystrophy type 2 (DM2) and related disorders. (2011). Report of the 180th ENMC workshop including guidelines on diagnostics and management. Neuromuscular disorders, 21, 443-450.

Udd, B., Meola, G., Krahe, R., Thornton, C., Ranum, L. P. W., Bassez, G., Moxley, R. (2006). 140th ENMC International Workshop: Myotonic Dystrophy DM2/PROMM and other myotonic dystrophies with guidelines on management. Neuromuscular Disorders, *16*(6), 403-413.

Van De Meché, F. G., Boogaard, J. M., & van Den Berg, B. (1986). Treatment of hypersomnolence in myotonic dystrophy with a CNS stimulant. Muscle & nerve, 9(4), 341-344.

Voet, N., Van der Kooi, E., Ripgdahl, K., Edstrom, L., et al. (2010). Strength training and aerobic exercise training for muscle disease. Cochrane Database Systematic Reviews: CD003907.

Walklet, E., Muse, K., Meyrick, J., Moss, T. (2016). Do psychosocial interventions improve quality of life and wellbeing in adults with neuromuscular disorders? A systematic review and narrative synthesis. Journal of Neuromuscular Diseases, 3: 347-362.

Webb, D., Muir, I., Faulkner, J. (1978). Myotonia dystrophica: obstetric complications. American Journal of Obstetrics and Gynaecology, 132:265-270.

Wennberg, S., Gunnarsson, LG., Ahlstrom, G. (2004). Using a novel exercise programme for patients with muscular dystrophy. Part I; a qualitative study. Disability Rehabilitation. 26: 595-602.

Wennberg, S., Gunnarsson, LG., Ahlstrom, G. (2004). Using a novel exercise programme for patients with muscular dystrophy. Part II; a quantitive study. Disability Rehabilitation. 26: 595-602.

WHO Collaborating Centre for Drug Statistics Methodology. ATC Index, (2009). Available at www.whocc.no/atcddd/.

Wilson, S., Roberts, L., Roalfe, A., Bridge, P., Singh, S. (2004). Prevalence of irritable bowel syndrome; a community survey. British Journal of General Practice, 54, 495-502.

Appendices

Appendix A. Adult Information Sheet and Consent Form

Adult Participant Information Sheet

Study title:	**Prevalence and impact of genetic muscle disorders in New Zealand**		
Locality:	**New Zealand**	Ethics committee ref.:	**14NTB/118**
Lead investigator:	**Alice Theadom**	Contact phone number:	**0800 MDPREV**

You are invited to take part in a study that is looking at how many people are affected by genetic muscle disorders in New Zealand. We would also like to find out how people and their significant others are affected by these conditions.

If you don't want to take part, you don't have to give a reason, and it won't affect the care you receive. If you do want to take part now, but change your mind later, you can pull out of the study at any time.

This information sheet will help you decide if you'd like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide today whether or not you will participate in this study. Before you decide, you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this.

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

This document is 7 pages long, including the consent form. Please make sure you have read and understood all the pages.

WHAT IS THE PURPOSE OF THE STUDY?

We are a team of researchers who work in universities, hospitals and community organisations across New Zealand with an interest in supporting people with neuromuscular conditions. The purpose of this study is to find out how many people are affected by genetic muscle disorders in New Zealand. We would also like to find out how peoples' everyday lives are affected and to identify where there are unmet needs.

We hope that by finding out this information, will help us to improve the support and treatment people and their significant others receive. Even if you are not noticing any effects from your condition, this is just as important for us to know as if you do.

This study is being funded by the Health Research Council of New Zealand.

If you have any questions about the study please contact the Study Manager, Kerry Walker:

Telephone: 0800 MDPREV (637738)
Mobile: 021 2458597
E mail: kwalker@aut.ac.nz

This study has been approved by the Health and Disability Ethics Committee reference: 14/NTB/118

WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?

You have been identified as someone who may have a genetic muscle disorder. We are inviting everyone with a genetic muscle disorder in New Zealand to participate in this study (about 1200 people). This will enable us to explore the services and supports people receive across the country.

If you would like to take part in this study, we would like to arrange a time to come and talk to you. You will be asked questions about how you find completing everyday activities such as study/work, socializing, your quality of life and about any symptoms you experience. All researchers who will be asking these questions have been specially trained for this project. We can arrange for a member of the team to visit you at your home or other convenient location such as at your local GP surgery or a private room in a public library or you can complete the questionnaire over the phone or by yourself in your own time.

When a researcher comes to visit you or talks about the study with you, you will have the opportunity to ask any questions you may have. If you are happy to take

part, you will be invited to sign the consent form. The researcher will ask you some questions about how you have been doing and your ability to take part in everyday activities. The assessment should take about one and half hours. You will be able to have support people with you during the assessment and we can complete the assessment over several sessions if you prefer.

We aim to finish collecting data for this study by the end of March 2016.

WHAT ARE THE POSSIBLE BENEFITS AND RISKS OF THIS STUDY?

Taking part in this study will take some of your time and require you to answer a series of questions. There are no known risks caused by this study, however you may feel uncomfortable or embarrassed by some of the questions. You do not have to answer any questions you do not wish to do so. All our researchers have received training in administering these assessments and working with people who have a genetic muscle disorder.

Your usual medical care will not be affected in any way by participating in the study or withdrawing from the study at any stage. Your participation in this study will be stopped should you experience any harmful effects or if the doctor feels it is not in your best interests to continue. Similarly your doctor may at any time provide you with any other treatment he/she considers necessary.

As part of the study we will be working with health care and service providers about the findings of the study. We aim to identify areas of unmet need for people living with these conditions to improve service delivery. We will also be in contact with your GP or neurologist about your diagnosis and if any information that may be of benefit to you emerges during the study we will let them know.

WHO PAYS FOR THE STUDY?

There should be no direct costs to you in taking part in this study. A $20 food/fuel voucher will be provided to you after completion of the assessment to acknowledge your contribution to this research.

Assessments will be completed at your home or other accessible location. If for some reason you need to travel for the assessment, your mileage or costs (receipt/ticket required) will be reimbursed. Some questions can be asked over the phone.

WHAT IF SOMETHING GOES WRONG?

It is unlikely that you will be at risk of harm from taking part in this study. If something goes wrong, please contact the study manager as soon as possible 0800 MDPREV (637738)

WHAT ARE MY RIGHTS?

Your participation is entirely voluntary and you will be able to withdraw from the study at any time without experiencing any disadvantage.

The study files and all other information that you provide will remain strictly confidential, unless information is revealed that indicates you, your child or someone else is at risk. The answers to your questions will be stored separately to any document that has your name and contact details on.

No material that could personally identify you will be used in any reports or discussions about this study.

You will be able to access your information collected as part of the study if you wish to do so. If any information that may be of benefit to you emerges during the study we will contact you to let you know

WHAT HAPPENS AFTER THE STUDY OR IF I CHANGE MY MIND?

Upon completion of the study your records will be stored for 16 years in a locked cabinet. The cabinet will be based at AUT University in Auckland by the lead investigator (Dr Alice Theadom). All computer records will be password protected. Any identifying information will not be shared outside of the research team without seeking your permission.

As there will be a lot of valuable information collected as art of this study, we would like to make anonymized data collected as part of the study available to other international researchers on completion of the study. However, we will only share your anonymized data if you wish us to do so, otherwise your data will be deleted before being shared with other researchers.

After 16 years all electronic information will be deleted and paper forms will be shredded and destroyed with the university confidential waste.

After we have looked at all the data we will send you a summary of results if you would like to receive them. This will be in early 2016.

WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?

If you have any questions, concerns or complaints about the study at any stage, you can contact:

Kerry Walker, Study Manager

Telephone number: 0800 MDPREV (637738)

Email: kwalker@aut.ac.nz

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone: 0800 555 050
Fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@hdc.org.nz

For Māori health support please contact :

Te Puna Oranga (Waikato DHB Māori Health Unit),

Hockin Building, Level 1, Pembroke St, P.O.Box 934, Hamilton.

Ph: 07 834 3644. Fax: 07 834 3619.

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Phone: 0800 4 ETHICS

Email: hdecs@moh.govt.nz

Please keep this for your information.
Thank you for interest in this study

Registration Number:	Participant Initials:	Date of Birth:

Adult Consent Form

If you need an INTERPRETER, please tell us.

I have read, or have had read to me in my first language, and I understand the Participant Information Sheet dated 03/09/2014.

I have been given sufficient time to consider whether or not to participate in this study.

I have had the opportunity to use a legal representative, whānau/ family support or a friend to help me ask questions and understand the study.

I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet.

I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my medical care.

I consent to the research staff collecting and processing my information, including information about my health from medical records and health databases.

If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.

I consent to my GP or treating clinician being informed about my participation in the study and of any significant results obtained during the study.

I agree to an approved auditor appointed by the New Zealand Health and Disability Ethic Committees, or any relevant regulatory authority or their approved

representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.

I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.

I know who to contact if I have any questions about the study in general.

I understand my responsibilities as a study participant.

I wish to receive a summary of the results from the study.	Yes ☐	No ☐
I agree to my anonymised data being shared with researchers overseas for further research into neuromuscular conditions	Yes ☐	No ☐

Declaration by participant:

I hereby consent to take part in this study.

Participant's name:

Signature: Date:

Declaration by member of research team:

I have given a verbal explanation of the research project to the participant and have answered the participant's questions about it.I believe that the participant understands the study and has given informed consent to participate.

Researcher's name:

Signature: Date:

Appendix B. Child Information Sheet and Consent Form

Parent/Legal Guardian Information Sheet

Study title:	**Prevalence and impact of genetic muscle disorders in New Zealand**		
Locality:	**New Zealand**	Ethics committee ref.:	**14/NTB/118**
Lead investigator:	**Alice Theadom**	Contact phone number:	**0800 MDPREV**

You are invited to take part in a study that is looking at how many people are affected by genetic muscle disorders in New Zealand. We would also like to find out how people and their significant others are affected by these conditions.

Whether or not you take part is your choice. If you don't want to take part, you don't have to give a reason, and it won't affect the care you or your child receives. If you do want to take part now, but change your mind later, you can pull out of the study at any time.

This information sheet will help you decide if you'd like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide today whether or not you will participate in this study. Before you decide you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this.

If you agree to take part in this study, you will be asked to sign the consent form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

This document is 7 pages long, including the Consent Form. Please make sure you have read and understood all the pages.

WHAT IS THE PURPOSE OF THE STUDY?

We are a team of researchers who work in universities, hospitals and community organisations across New Zealand, with an interest in supporting people with neuromuscular conditions.
The purpose of this study is to find out how many people are affected by genetic muscle disorders in New Zealand. We would also like to find out how peoples' everyday lives are affected and to explore the impact on those around them. We hope that by finding out this information and identifying areas of unmet need, will help us to improve the support and treatment children, adults and their family/whānau receive. Even if your child is not experiencing any effects from their condition, this is just as important for us to know as if they do.

This study is funded by the Health Research Council of New Zealand.

If you have any questions about the study please contact the Study Manager, Kerry Walker:

Telephone: 0800 MDPREV (637738)
Mobile: 021 2458597
E mail: kwalker@aut.ac.nz

This study has been approved by the Health and Disability Ethics Committee reference: 14/NTB/118

WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?

Your child has been identified as someone who may have a genetic muscle disorder. We are inviting everyone with a genetic muscle disorder in New Zealand to participate in this study (about 1200 people). This will enable us to explore the services and supports people receive across the country.

If you would like to take part in this study, we would like to arrange a time to come and talk to you and your child. You will be asked questions about how they find completing everyday activities, socializing and about any symptoms they experience. We would then like to ask some questions about your own quality of life. All researchers who will be asking these questions have been specially trained for this project. We can arrange for a member of the team to visit you and your child at your home or other convenient location such as at your local GP surgery, at the child's school or a private room in a public library. You can also complete some questions yourself on a questionnaire or over the phone if you prefer.

When a researcher comes to visit you, you will have the opportunity to ask any questions you may have about the study. If you are happy to take part, you will be invited to sign the consent form. The assessment should take about one hour to complete.

You will be able to have support people with you during the assessment and we can complete the assessment over several sessions if you prefer.

We aim to finish collecting data for this study by the end of March 2016.

WHAT ARE THE POSSIBLE BENEFITS AND RISKS OF THIS STUDY?

Taking part in this study will take some of your time and require you to answer a series of questions. There are no known risks caused by this study, however you may feel uncomfortable or embarrassed by some of the questions. You do not have to answer any questions you do not wish to do so. All our researchers have received training in administering these assessments and working with people who have a genetic muscle disorder.

Your (or your child's) usual medical care will not be affected in any way by participating in the study, or withdrawing from the study at any stage. Your (and your child's) participation in this study will be stopped should any harmful effects appear or if the doctor feels it is not in your best interests to continue. Similarly your doctor may at any time provide you (or your child) with any other treatment he/she considers necessary.

As part of the study we will be working with health care and service providers about the findings of the study. We aim to identify areas of unmet need for people living with these conditions to improve service delivery. We will also be in contact with your GP or neurologist about your child's diagnosis and if any information that may be of benefit to you and your child emerges during the study we will let them (and you) know.

WHO PAYS FOR THE STUDY?

There should be no direct costs to you in taking part in this study.

A $20 food/fuel voucher will be provided to you after completion of the assessment (your child will also be given a $20 voucher on completion of their assessment) in acknowledgment of the contributions you and your child have made to this study.

Assessments will be completed at your home or other accessible location. If for some reason you need to travel for the assessment, your mileage or costs will be reimbursed.

WHAT IF SOMETHING GOES WRONG?

It is unlikely that you will be at risk of harm from taking part in this study. If something goes wrong, please contact the study manager as soon as possible on 0800 MDPREV (637738).

WHAT ARE MY RIGHTS?

Your participation is entirely voluntary and you will be able to withdraw from the study at any time without experiencing any disadvantage.

The study files and all other information that you provide will remain strictly confidential, unless information is revealed that indicates you, your child or someone else is at risk. The answers to your questions will be stored separately to any document that has your name and contact details on.

No material that could personally identify you will be used in any reports or discussions about this study. As we will be collecting a lot of valuable information as part of the study we would like to share anonymised data will other international researchers following completion of the study. However we will only share your and your child's data if you agree for us to do so, otherwise your data will be removed before it is shared outside of the study team.

You will be able to access your information collected as part of the study if you wish to do so. If any information that may be of benefit to you emerges during the study we will contact you to let you know

WHAT HAPPENS AFTER THE STUDY OR IF I CHANGE MY MIND?

Upon completion of the study your and your child's information will be stored for 16 years in a locked cabinet at AUT University in Auckland by the lead investigator (Dr Alice Theadom). All computer records will be password protected. Any identifying information will not be shared outside of the research team without seeking your permission.

After 16 years all your electronic information will be deleted and paper forms will be shredded and destroyed with the university confidential waste. Your child's information will be stored for 10 years after they have turned 16 years of age.

After we have looked at all the data we will send you a summary of results if you would like to receive them.

WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?

If you have any questions, concerns or complaints about the study at any stage, you can contact:

Kerry Walker, Study Manager
Telephone number: 0800 MDPREV (637738)
Email: kwalker@aut.ac.nz

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone: 0800 555 050
Fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@hdc.org.nz

For Maori health support please contact :

Te Puna Oranga (Waikato DHB Maori Health Unit),
Hockin Building, Level 1, Pembroke St, P.O.Box 934, Hamilton.
Ph: (07) 834 3644. Fax: (07) 834 3619.

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Phone: 0800 4 ETHICS
Email: hdecs@moh.govt.nz

Please keep this for your information.
Thank you for interest in this study

Registration Number:	Participant Initials:	Date of Birth:

Parent/Guardian Consent Form

If you need an INTERPRETER, please tell us.

I have read, or have had read to me in my first language, and I understand the Parent/Legal Guardian Information Sheet.

I have been given sufficient time to consider whether or not to participate in this study.

I have had the opportunity to use a legal representative, whanau/ family support or a friend to help me ask questions and understand the study.

I am satisfied with the answers I have been given about the study and I have a copy of this consent form and information sheet.

I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my medical care.

I consent to the research staff collecting and processing my information, including information about my health from medical records and health databases.

I consent to the research staff contacting my child's teacher for information about their progress at school

If I decide to withdraw from the study, I agree that the information collected about me (and my child) up to the point when I withdraw may continue to be processed.

I consent to my own or my child's GP or treating clinician being informed about my participation in the study and of any significant abnormal results obtained during the study.

I agree to an approved auditor appointed by the New Zealand Health and Disability Ethic Committees, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.

I understand that my (and my child's) participation in this study is confidential and that no material, which could identify me (or my child) personally, will be used in any reports on this study.

I know who to contact if I have any questions about the study in general.

I understand my responsibilities as a study participant.

I wish to receive a summary of the results from the study. Yes ☐ No ☐

I agree to my own and my child's anonymised data being shared with researchers overseas for further research into neuromuscular conditions Yes ☐ No ☐

Declaration by Parent/Legal Guardian:

I hereby consent for myself and my child, (NAME) _____to take part in this study.

Parent/Legal Guardian's name:

_____

Signature: Date:

_____

Declaration by member of research team:

I have given a verbal explanation of the research project to the participant, and have answered the participant's questions about it.

I believe that the parent/legal guardian understands the study and has given informed consent to participate.

Researcher's name:

Signature: Date:

APPENDIX C. Adult Questionnaire

Questionnaire items relevant to this thesis

MD-PREV

PREVALENCE AND IMPACT OF GENETIC MUSCLE DISORDERS IN NEW ZEALAND

FORM O
Adult Participant

MD-Prev Adult Participant Questionnaire (Form O)

Welcome to the MD-Prev Questionnaire

Thank you for participating in our study. Your feedback is important.

Please try to answer every question.

However if there are questions you don't want to answer, you can simply leave them blank.

If you are unsure of how to answer a question, please make a note of this in the text box on the last page of the questionnaire.

If you fill in an answer which doesn't seem correct (for example; an incorrect date format), you will be prompted to re-think your answer.

Please give one answer per line unless prompted otherwise.

Next

MD-Prev Adult Participant Questionnaire (Form O)

Demographic details

1. Registration number (please leave blank if not known)

2. What is the first initial of your first name?

3. What are the first three letters of your surname?

4. How is this questionnaire being completed?

- ○ With a researcher (in person)
- ○ With a researcer (over the phone)
- ○ Being completed by myself online
- ○ Being completed by myself on paper

5. What is your date of birth?

Date DD / MM / YYYY

6. What is the highest level of education you completed?

- Primary school
- High school (Secondary)
- Polytechnic or college
- University

7. Do you have any children?

- Yes
- No

8. How many children do you have?

9. Do you have a medicalert bracelet?

- Yes
- No

10. Who do you live with?

- Live alone
- Living with family
- Living with partner
- Living with others

11. How many adults do you live with?

12. What type of accomodation are you currently living in?

- Hospital (Inpatient)
- Own home or home owned by friends or family
- Rental property
- Residential care (disability service)
- Retirement village (elderly care facility)
- Other (please specify)

13. What is your current marital status?

- ○ Married/civil union/de facto
- ○ Separated/divorced/widowed
- ○ Never married or single
- ○ Other (please specify)

14. Has your genetic muscle disorder affected your romantic relationships in any way?

Prev Next

MD-Prev Adult Participant Questionnaire (Form O)

Symptoms experienced

People can experience a wide variety of signs or symptoms from their genetic muscle disorder. Please indicate to what extent you experience the symptoms below and tell us if we have missed any out.

1. To what extent do you experience the following symptoms?

	None	Mild	Moderate	Severe
Headaches	○	○	○	○
Muscle weakness	○	○	○	○
Muscle spasms	○	○	○	○
Limited movement in a joint(s)	○	○	○	○
Joint(s) feeling stuck (contractures)	○	○	○	○
Irregular heart beat (e.g. palpitations, faints/blackouts, pacemaker)	○	○	○	○
Muscle weakness of the heart (e.g. shortness of breath, swollen ankles)	○	○	○	○
Respiratory difficulties (e.g. needing oxygen, mucus in the lungs)	○	○	○	○
Ptosis (drooping of the eyelid)	○	○	○	○
Dysphagia (difficulty swallowing)	○	○	○	○
Poor balance	○	○	○	○
Frequent falls	○	○	○	○
Visual impairment	○	○	○	○
Speech impairment	○	○	○	○

Other (please specify)

2. How old were you (in years) when you first started to experience symptoms related to your genetic muscle disorder e.g. muscle weakness?

3. Do you have any other medical conditions?

○ Yes

○ No

4. Please specify

Prev Next

2. Do you require ventilation support?

- ○ Yes, I have this
- ○ No, and I don't need it
- ○ No, but I do need it

Prev Next

MD-Prev Adult Participant Questionnaire (Form O)

Health Care Needs - Ventilation

1. What type of ventilation support do you have?

- ○ Non-invasive (Eg: CPAP, BiPAP)
- ○ Invasive (Eg: tracheostomy, endotracheal tube)

2. Is this ventilation support....?

- ○ Continuous
- ○ Part time/nocturnal

Prev Next

MD-Prev Adult Participant Questionnaire (Form O)

Health Care Needs - Overall

6

1. How satisfied are you with the overall standard of health care you receive?

Very dissatisfied		Dissatisfied		More dissatisfied than satisfied	More satisfied than dissatisfied		Satisfied		Very Satisfied
○	○	○	○	○	○	○	○	○	○

Prev Next

MD-Prev Adult Participant Questionnaire (Form O)

Health care access

We would like to understand more about the health care that you currently use specifically in relation to your genetic muscle disorder or associated complications.

1. Do you currently require any prescription medication (given to you by your GP/clinician)?

- ○ Yes
- ○ No

2. If yes, how many different medications are prescribed for you?

3. What medications do you currently take?

4. If yes, how many times a day do you need to take your medication?
(includes all medication you are taking together)

- 1 to 2 times each day
- 3 to 4 times each day
- More than 4 times each day

5. Are you taking any medications recommended or prescribed for you that are not government funded/subsidised?

- Yes
- No

6. If yes, please specify

7. If yes, how much in NZ dollars do you spend on personally funded medications each week?

8. Are there any medications recommended to you by a clinician that you are not taking because they are not funded by the government/subsidised?

- Yes
- No

9. Please specify

10. Do you currently take any herbal or vitamin supplements?

- Yes
- No

11. If yes, please specify

12. How much in NZ dollars do you spend on herbal or vitamin supplements each week?

13. Are you currently taking any nutritional supplements (e.g. energy drinks)?

- Yes
- No

14. If yes, please specify

15. How much in NZ dollars do you spend on nutritional supplements each week?

16. Are you currently using any complementary therapies e.g. aromatherapy, acupuncture, homeopathic remedies?

- Yes
- No

17. If yes, please specify

18. How much in NZ dollars do you spend on complementary therapies each week?

Prev Next

1. Please tell us how many times you have visited each of the following health care providers in the past 12 months?

	No visits in past 12 months	1-2 visits	3 to 5 visits	6 to 11 visits	Once per month	Once per week	More than once per week
General Practitioner (GP) or family doctor	○	○	○	○	○	○	○
Medical specialist e.g. neurologist	○	○	○	○	○	○	○
Physiotherapist	○	○	○	○	○	○	○
Speech and language therapist	○	○	○	○	○	○	○
Occupational therapist	○	○	○	○	○	○	○
Dietician	○	○	○	○	○	○	○
Accident and emergency department/clinic	○	○	○	○	○	○	○
Nurse	○	○	○	○	○	○	○
Psychologist or counselor	○	○	○	○	○	○	○

Other (please specify)

2. Do you have access to a neurologist who specialises in neuromuscular conditions?

- ○ Yes
- ○ No
- ○ I don't know

3. Have you been taken to hospital in the past year?

- ○ Yes
- ○ No

4. If yes, how many times

5. Have you been hospitalised in the past year?

- ○ Yes
- ○ No

MD-Prev Adult Participant Questionnaire (Form O)

Activity Limitations

Please estimate how difficult or easy you would find performing each of the following activities without any aides or human help (even if you actually use help in daily life).

Three responses are presented. These assess the perception of the difficulty/ease depending on whether the activity is “impossible”, “difficult” or “easy”. If an activity has not been attempted in the last 3 months, tick the question mark.

So, for any activity, the four potential answers are:
- Impossible: You are unable to perform the activity without using any other help
- Difficult: You are able to perform the activity without any help but experience some difficulty
- Easy: You are able to perform the activity without any help and experience no difficulty
- Question mark: You cannot estimate the difficulty of the activity because you have never done the activity

Watch out!! If the activity was never attempted because it is impossible, then it must be scored “impossible” rather than “question mark”.

1. How difficult are the following activities?

	Impossible	Difficult	Easy	?
Putting on a T-shirt	○	○	○	○
Washing one's upper body	○	○	○	○
Dressing one's lower body	○	○	○	○
Taking a shower	○	○	○	○
Sitting on the toilet	○	○	○	○
Taking a bath	○	○	○	○
Opening a door	○	○	○	○
Washing one's face	○	○	○	○
Hanging up a jacket on a hat stand (or hanging a jacket up on a hook)	○	○	○	○
Wiping(drying) one's upper body	○	○	○	○
Carrying a heavy load	○	○	○	○
Getting into a car	○	○	○	○
Closing a door	○	○	○	○
Putting on a backpack	○	○	○	○
Getting on and off the toilet	○	○	○	○
Stepping up and down curbs	○	○	○	○
Getting out of a car	○	○	○	○
Getting out of a bed into a chair	○	○	○	○
Getting up off the floor from lying on your back without help	○	○	○	○

1. How difficult are the following activities?

	Impossible	Difficult	Easy	?
Walking downstairs	○	○	○	○
Stepping out of a bath tub	○	○	○	○
Walking outdoors on ground level	○	○	○	○
Walking upstairs (more than 3 steps)	○	○	○	○
Standing for a long time (more than 10 minutes)	○	○	○	○
Walking more than one kilometre (equivalent to 10 rugby fields)	○	○	○	○
Hopping on one foot	○	○	○	○
Running	○	○	○	○

2. How difficult are the following activities?

	Impossible	Difficult	Easy	?
Standing still on one leg	○	○	○	○
Picking up a cell phone from the floor, from a sitting position	○	○	○	○

1. What is your ability to do the following activities without support?

	Without any difficulty	With a little difficulty	With some difficulty	With much difficulty	Unable to do
Are you able to turn a key in a lock?	○	○	○	○	○
Are you able to brush your teeth?	○	○	○	○	○
Are you able to make a phone call using a touch tone key pad?	○	○	○	○	○
Are you able to pick up coins from a table top?	○	○	○	○	○
Are you able to write with a pen or pencil?	○	○	○	○	○
Are you able to open and close a zipper?	○	○	○	○	○
Are you able to shampoo your hair?	○	○	○	○	○
Are you able to wash and dry your body?	○	○	○	○	○

Prev Next

4. What is the approximate annual income for all people living in your household (before tax).

If you are living in a residential facility please just put your own income.

- ○ Less or equal to $20,000
- ○ Between $20,000 and $40,000
- ○ Between $40,000 and $60,000
- ○ Between $60,000 and $80,000
- ○ Between $80,000 and $100,000
- ○ More than $100,000

MD-Prev Adult Participant Questionnaire (Form O)

To Finish

1. Is there anything else about living with a genetic muscle disorder that you would like to add?

2. Would you be willing to be contacted again in the future for a further follow up?

- ○ Yes
- ○ No

Thank you very much for completing this questionnaire and for participating in the study.

Prev Done

APPENDIX D Example of a parent questionnaire

Questionnaire items relevant to this thesis

MD-PREV

PREVALENCE AND IMPACT OF GENETIC MUSCLE DISORDERS IN NEW ZEALAND

FORM P4

Parents of Children Aged 11-15 years

MD-Prev Parent or Legal Guardian Questionnaire (Form P4, 11-15 years)

WELCOME TO THE MD-PREV QUESTIONNAIRE

Thank you for participating in this study. Your feedback is important.

Please try to answer every question.
However if there are questions you don't want to answer, you can simply leave them blank.

If you are unsure of how to answer any of the questions, please give it your best try. Otherwise you may make a note of the question in the text box on the last page of the questionnaire.

If you fill in an answer which doesn't seem correct (for example; an incorrect date format), you will be prompted to re-think your answer.

Please give one answer per line unless prompted otherwise.

Next

MD-Prev Parent or Legal Guardian Questionnaire (Form P4, 11-15 years)

DEMOGRAPHIC DETAILS

1. Registration number (please leave blank if not known)

2. What is the first letter of your child's first name?
(eg: John = J)

3. What are the first three letters of your child's surname?
(eg: Smith = SMI)

4. What is your child's date of birth?

Date DD / MM / YYYY

5. How is this questionnaire being completed?

- With a researcher (in person)
- With a researcher (over the phone)
- Being completed by myself online
- Being completed by myself on paper

Prev Next

MD-Prev Parent or Legal Guardian Questionnaire (Form P4, 11-15 years)

ABOUT YOU

1. What is your relationship to the child?

- Mother
- Father
- Grandparent
- Legal Guardian
- Other (please specify)

2. What is your ethnicity?

- NZ European
- Other European
- Maori
- Samoan
- Cook Island Maori
- Tongan
- Niuean
- Chinese
- Indian
- Other (please specify)

3. What is your date of birth?

Date DD / MM / YYYY

4. What is your gender?

- Male
- Female

5. What is the highest level of education you completed?

- Primary school
- High (Secondary) school
- Polytechnic or college
- University

6. What is the approximate annual income for all people living in the child's household (before tax).

- Less or equal to $20,000
- Betwen $20,000 and $40,000
- Between $40,000 and $60,000
- Between $60,000 and $80,000
- Between $80,000 and $100,000
- More than $100,000

7. Has your financial situation changed since the child developed symptoms of a genetic muscle disorder?

- Improved
- Remained the same
- Worsened

8. What is your marital status?

- Married, civil union, de-facto
- Seperated, divorced, widowed
- Never married (single)
- Other (please specify)

MD-Prev Parent or Legal Guardian Questionnaire (Form P4, 11-15 years)

ABOUT THE CHILD

1. What type of accommodation does your child currently live in?

- ○ Hospital (Inpatient)
- ○ Own home or home owned by friends or family
- ○ Rental property
- ○ Residential care (disability service)
- ○ Retirement village (elderly care facility)
- ○ Other (please specify)

2. Are you or your child receiving any financial benefits to support their care, such as disability allowance?

- ○ Yes
- ○ No

3. If yes, what benefits are you receiving?

- [ ] Disability allowance
- [ ] Unemployment
- [ ] Accomodation supplement
- [ ] Community services card
- [ ] Course participation assistance
- [ ] Jobseeker support
- [ ] Other (please specify)

4. Does your child have a medicalert bracelet?

- ( ) Yes
- ( ) No

5. Does your child attend school?

- ( ) Yes
- ( ) No

6. Have any changes been required to enable your child to attend school?

- ( ) Yes
- ( ) No

7. If yes, what changes have been required to enable the child to attend school?

Prev Next

MD-Prev Parent or Legal Guardian Questionnaire (Form P4, 11-15 years)

SYMPTOMS EXPERIENCED

People can experience a wide variety of signs or symptoms from their condition. Please tell us if we have missed any out.

1. Please indicate to what extent you believe the child experiences the symptoms below.

	None	Mild	Moderate	Severe
Headaches	○	○	○	○
Muscle weakness	○	○	○	○
Muscle spasms	○	○	○	○
Limited movement in a joint(s)	○	○	○	○
Joint(s) feeling stuck (contractures)	○	○	○	○
Irregular heart beat (e.g. palpitations, faints/blackouts, pacemaker)	○	○	○	○
Muscle weakness of the heart (e.g. shortness of breath, swollen ankles)	○	○	○	○
Respiratory difficulties (e.g. needing oxygen, mucus in the lungs)	○	○	○	○
Ptosis (drooping of the eyelid)	○	○	○	○
Dysphagia (difficulty swallowing)	○	○	○	○
Poor balance	○	○	○	○
Frequent falls	○	○	○	○
Visual impairment	○	○	○	○
Speech impairment	○	○	○	○
Other	○	○	○	○

(Please specify)

2. How many years old was your child when you first started to notice that they were experiencing symptoms related to the genetic muscle disorder e.g. muscle weakness (if the child has no symptoms, please put "no symptoms")

3. Does your child have any other medical conditions?

○ Yes

○ No

4. Please specify

2. Does your child require ventilation support?

- ○ Yes, we have this
- ○ No, and we don't need it
- ○ No, but we do need it

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MD-Prev Parent or Legal Guardian Questionnaire (Form P4, 11-15 years)

HEALTH CARE NEEDS - VENTILATION SUPPORT

1. What type of ventilation support does your child require?

- ○ Non-invasive (Eg: CPAP, BiPAP)
- ○ Invasive (Eg: tracheostomy, endotracheal tube)

2. Is this ventilation support....?

- ○ Continuous
- ○ Part time/nocturnal

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MD-Prev Parent or Legal Guardian Questionnaire (Form P4, 11-15 years)

HEALTH CARE ACCESS

We would like to understand more about the health care that your child receives specifically in relation to their genetic muscle disorder or associated complications.

1. Do they currently require any prescription medication (given to them by their GP or neurologist)?

- ○ Yes
- ○ No

2. If yes, how many different medications are prescribed for them?

3. What medications do they currently take?

4. If yes, in general, how many times a day do they need to take their medication?

- ○ 1 to 2 times each day
- ○ 3 to 4 times each day
- ○ More than 4 times each day

5. Are they taking any medications recommended or prescribed for them that are not government funded?

- Yes
- No

6. If yes, please specify

7. If yes, how much in NZ dollars do you spend on personally funded medications each week?

8. Are there any medications recommended for your child by a clinician that they are not taking because they are not funded by the government?

- Yes
- No

9. Please specify

10. Do they currently take any herbal or vitamin supplements?

- yes
- No

11. If yes, please specify

12. How much in NZ dollars do you spend on herbal or vitamin supplements each week?

13. Are they currently taking any nutritional supplements (e.g. energy drinks)?

- Yes
- No

14. If yes, please specify

15. How much in NZ dollars do you spend on nutritional supplements each week?

16. Are they currently using any complementary therapies e.g. aromatherapy, acupuncture, homeopathic remedies?

- ○ Yes
- ○ No

17. If yes, please specify

18. How much in NZ dollars do you spend on complementary therapies each week?

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2. Does your child have access to a paediatric neurologist?

- ○ Yes
- ○ No
- ○ I don't know

3. Has your child been taken to hospital in the past year?

- ○ Yes
- ○ No

4. If yes, how many times

5. Has your child been hospitalised in the past year?

- ○ Yes
- ○ No

6. If yes

How many times were they admitted to hospital in the past year?

On average, how long was each stay in days?

7. Has the child spent the night at a respite centre in the past year?

- ○ Yes
- ○ No

8. If yes, how many nights did they stay on average?

9. Has the child required any surgery or surgical procedures in the past year?

- ○ Yes
- ○ No

10. If yes, what surgery or surgical procedures did they have?

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MD-Prev Parent or Legal Guardian Questionnaire (Form P4, 11-15 years)

ACTIVITY LIMITATIONS (ACTIVLIM)

Please estimate how difficult or easy it would be for your child to perform each of the following activities without any aides or human help (even if the patient actually uses help in daily life).

Three responses are presented. These assess the perception of the difficulty/ease depending on whether the activity is "impossible", "difficult" or "easy". If an activity has not been attempted in the last 3 months, tick the question mark.

So, for any activity, the four potential answers are:
• Impossible: The child is unable to perform the activity without using any other help
• Difficult: The child is able to perform the activity without any help but experiences some difficulty
• Easy: The child is able to perform the activity without any help and experiences no difficulty
• Question mark: The child cannot estimate the difficulty of the activity because he has never done the activity

Watch out!! If the activity was never attempted because it is impossible, then it must be scored "impossible" rather than "question mark".

1. How difficult are the following activities for your child?

	Impossible	Difficult	Easy	?
Putting on a T-shirt	○	○	○	○
Washing one's upper body	○	○	○	○
Dressing one's lower body	○	○	○	○
Taking a shower	○	○	○	○
Sitting on the toilet	○	○	○	○
Taking a bath	○	○	○	○
Opening a door	○	○	○	○
Washing one's face	○	○	○	○
Hanging up a jacket on a hat stand (or hanging a jacket up on a hook)	○	○	○	○
Wiping one's upper body (drying)	○	○	○	○
Carrying a heavy load	○	○	○	○
Getting into a car	○	○	○	○
Closing a door	○	○	○	○
Putting on a backpack	○	○	○	○

2. Is your child able to stand up without support for at least 5 seconds?

○ Yes

○ No

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MD-Prev Parent or Legal Guardian Questionnaire (Form P4, 11-15 years)

ACTIVITY LIMITATIONS (ACTIVLIM)

1. How difficult are the following activities for your child?

	Impossible	Difficult	Easy	?
Getting on and off a toilet	○	○	○	○
Stepping up and down curbs	○	○	○	○
Getting out of a car	○	○	○	○
Getting out of bed into a chair	○	○	○	○
Getting up off the floor from lying on their back, without any help	○	○	○	○

2. How difficult are the following activities for your child?

	Impossible	Difficult	Easy	?
Walking downstairs	○	○	○	○
Stepping out of a bath tub	○	○	○	○
Walking outdoors on ground level	○	○	○	○
Walking upstairs	○	○	○	○
Standing for a long time (more than 10 minutes)	○	○	○	○
Walking more than one kilometre	○	○	○	○
Hopping on one foot	○	○	○	○
Running	○	○	○	○

3. How difficult are the following activities for your child?

	Impossible	Difficult	Easy	?
Standing still on one leg	○	○	○	○
Picking up a cell phone from the floor, from a sitting position	○	○	○	○

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1. Please respond to each question or statement by marking one box per row.

Is your child able to do the following....

	Without any difficulty	With a little difficulty	With some difficulty	With much difficulty	Unable to do
Turn a key in a lock?	○	○	○	○	○
Brush their teeth?	○	○	○	○	○
Make a phone call using a touch tone key-pad?	○	○	○	○	○
Pick up coins from a table top?	○	○	○	○	○
Write with a pen or pencil?	○	○	○	○	○
Open and close a zipper?	○	○	○	○	○
Wash and dry their body?	○	○	○	○	○
Shampoo their hair?	○	○	○	○	○

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Thank you very much for taking the time to complete the questionnaire and for supporting this study

Prev Done

APPENDIX E Ethics Approval Letter Health and Disability Ethics Committee

Health and Disability Ethics Committees

Health and Disability Ethics Committees
Ministry of Health
133 Molesworth Street
PO Box 5013
Wellington
6011

0800 4 ETHICS (0800 4 384427)
hdecs@moh.govt.nz

16 January 2019

Dr Alice Theadom
AUT North Shore Campus
Auckland 1142

Dear Dr Theadom,

Re:	**Ethics ref:**	**14/NTB/118/AM06**
	Study title:	Prevalence and impact of genetic muscle disease

I am pleased to advise that this final report has been *approved* by the Northern B Health and Disability Ethics Committee. This decision was made through the HDEC Expedited Review pathway.

Please don't hesitate to contact the HDEC secretariat for further information.

Yours sincerely,

Chairperson
Northern B Health and Disability Ethics Committee

Encl: appendix A: documents submitted
appendix B: statement of compliance and list of members

Appendix A
Documents submitted and approved

Document	Version	Date
Final report: Final Report	1	10 January 2019
Post Approval Form	AM06	10 January 2019

Appendix B
Statement of compliance and list of members

Statement of compliance

The Northern B Health and Disability Ethics Committee:

- is constituted in accordance with its Terms of Reference
- operates in accordance with the *Standard Operating Procedures for Health and Disability Ethics Committees*, and with the principles of international good clinical practice (GCP)
- is approved by the Health Research Council of New Zealand's Ethics Committee for the purposes of section 25(1)(c) of the Health Research Council Act 1990
- is registered (number 00008715) with the US Department of Health and Human Services' Office for Human Research Protection (OHRP).

List of members

Name	*Category*	*Appointed*	*Term Expires*	*Present on 31/12/2019?*	*Declaration of interest?*
Mrs Maliaga Erick	Lay (consumer/community perspectives)	01/07/2015	01/07/2018	No	No
Mr John Hancock	Lay (the law)	14/12/2015	14/12/2018	No	No
Dr Nora Lynch	Non-lay (health/disability service provision)	24/07/2015	24/07/2018	No	No
Miss Tangihaere Macfarlane	Lay (consumer/community perspectives)	20/05/2017	20/05/2020	No	No
Mrs Kate O'Connor	Lay (ethical/moral reasoning)	14/12/2015	14/12/2018	Yes	No
Mrs Stephanie Pollard	Non-lay (intervention studies)	01/07/2015	01/07/2018	No	No
Mrs Leesa Russell	Non-lay (intervention studies), Non-lay (observational studies)	14/12/2015	14/12/2018	No	No
Mrs Jane Wylie	Non-lay (intervention studies)	20/05/2017	20/05/2020	No	No

Unless members resign, vacate or are removed from their office, every member of HDEC shall continue in office until their successor comes into office (HDEC Terms of Reference)

http://www.ethics.health.govt.nz

APPENDIX F: Ethics Approval Letter AUTEC

AUT UNIVERSITY
TE WĀNANGA ARONUI O TAMAKI MAKAU RAU

A U T E C

S E C R E T A R I A T

6.1.1.1

11 September 2014

Alice Theadom

Faculty of Health and Environmental Sciences

Dear Alice

Ethics Application: **14/296 Prevalence and impact of genetic muscle disorders in New Zealand (MD-Prev).**

Thank you for submitting your application for ethical review to the Auckland University of Technology Ethics Committee (AUTEC. I am pleased to confirm that the Chair and I have approved your ethics application for three years until 11 September 2017

As part of the ethics approval process, you are required to submit the following to AUTEC:

- A brief annual progress report using form EA2, which is available online through http://www.aut.ac.nz/researchethics. When necessary this form may also be used to request an extension of the approval at least one month prior to its expiry on 11 September 2017;
- A brief report on the status of the project using form EA3, which is available online through http://www.aut.ac.nz/researchethics. This report is to be submitted either when the approval expires on 11 September 2017 or on completion of the project;

It is a condition of approval that AUTEC is notified of any adverse events or if the research does not commence. AUTEC approval needs to be sought for any alteration to the research, including any alteration of or addition to any documents that are provided to participants. You are responsible for ensuring that research undertaken under this approval occurs within the parameters outlined in the approved application.

AUTEC grants ethical approval only. If you require management approval from an institution or organisation for your research, then you will need to obtain this.

To enable us to provide you with efficient service, we ask that you use the application number and study title in all correspondence with us. If you have any enquiries about this application, or anything else, please do contact us at ethics@aut.ac.nz.

All the very best with your research,

Kate O'Connor

Executive Secretary

Auckland University of Technology Ethics Committee