BMJ Open What is the best way to keep walking and moving around for individuals with Machado-Joseph disease? A scoping review through the lens of Aboriginal families with Machado-Joseph disease in the Top End of Australia

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ABSTRACT

Objectives Machado-Joseph disease (MJD) is the most common spinocerebellar ataxia worldwide. Prevalence is highest in affected remote Aboriginal communities of the Top End of Australia. Aboriginal families with MJD from Groote Eylandt believe 'staying strong on the inside and outside' works best to keep them walking and moving around, in accordance with six key domains that form the 'Staying Strong' Framework. The aim of this current study was to review the literature to: (1) map the range of interventions/strategies that have been explored to promote walking and moving around (functional mobility) for individuals with MJD and; (2) align these interventions to the 'Staying Strong' Framework described by Aboriginal families with MJD.

Design Scoping review.

Data sources Searches were conducted in July 2018 in MEDLINE, EMBASE, CINAHL, PsychINFO and Cochrane Databases.

Eligibility criteria for selecting studies Peer-reviewed studies that (1) included adolescents/adults with MJD, (2) explored the effects of any intervention on mobility and (3) included a measure of mobility, function and/or ataxia were included in the review.

Results Thirty studies were included. Few studies involved participants with MJD alone (12/30). Most studies explored interventions that aligned with two 'Staying Strong' Framework domains, 'exercising your body' (n=13) and 'searching for good medicine' (n=17). Few studies aligned with the domains having 'something important to do' (n=2) or 'keeping yourself happy' (n=2). No studies aligned with the domains 'going country' or 'families helping each other'.

Conclusions Evidence for interventions to promote mobility that align with the 'Staying Strong' Framework were focused on staying strong on the outside (physically) with little reflection on staying strong on the inside (emotionally, mentally and spiritually). Findings suggest future research is required to investigate the benefits of lifestyle activity programmes that address both physical and psychosocial well-being for families with MJD.

Strengths and limitations of this study

- This is the first review to map interventions trialled for individuals with Machado-Joseph disease (MJD) to enhance walking and moving around and to align findings with the 'Staying Strong' Framework.
- Studies typically focussed on interventions that promote 'staying strong on the outside' (physically), with few targeting 'staying strong on the inside' (emotionally, mentally and spiritually).
- This study is limited by a shortage of high-quality research that includes individuals specifically with MJD.
- This review highlights opportunities for investigating the benefit of lifestyle activity programmes that address both physical and psychosocial well-being for families with MJD.

INTRODUCTION

Machado-Joseph disease (MJD), or spinocerebellar ataxia type 3, is an autosomal-dominant neurodegenerative disease. Individuals with MJD experience progressive cerebellar ataxia and decline in mobility caused by premature cell death in the cerebellum and brainstem.¹ Average life expectancy is 20 years from onset of symptoms, with most individuals wheelchair users within 10 years of symptoms emerging.² MJD is the most common spinocerebellar ataxia (SCA) worldwide³ and is most prevalent in remote Aboriginal communities in the Top End of Australia. For example, prevalence estimates for the Groote Eylandt Archipelago in Australia are ~743/100 000, compared with ~39/100 000 for the Azores Archipelago in Portugal, where MJD is also common.⁴⁻⁷

Many trials are underway to find a cure for a range of SCAs.^{8,9} Other research efforts have focused on physiotherapeutic interventions to address impairments and activity limitations resulting from a range of hereditary ataxias (HAs).^{10–13} These interventions have been shown to enhance mobility and potentially delay symptom progression.¹⁴ For people with MJD, current recommended physiotherapeutic interventions are based on findings from studies on other SCAs.^{13,15–17} A focus on MJD is required, given the differences in pathophysiology and neurochemistry between SCA types,⁹ and to understand what interventions have been previously explored and where gaps lie. This information will provide future direction for targeted interventions for people with MJD to maximise their functional mobility.

Interventions designed to promote mobility for Aboriginal families with MJD from the Top End of Australia, whose culture and lifestyle are uniquely different to those with MJD in other parts of the world, have not been investigated.¹⁸ Importantly, these interventions are unlikely to be effective if they do not incorporate Indigenous views and concepts of physical activity and lifestyle in line with cultural and traditional practices.^{18–20}

Aboriginal families with MJD from the Groote Eylandt Archipelago have experienced the impact of MJD on their families for generations.¹⁸ In a recent study,²¹ these families shared their perspectives on what is important and

what works best to keep walking and moving around.¹⁸ Participants emphasised the importance of ‘staying strong on the inside and outside’ (physically, mentally, emotionally and spiritually) through ‘exercising your body’, ‘keeping yourself happy’, ‘going country’, ‘searching for good medicine’, ‘families helping each other’ and having ‘something important to do’.¹⁸ These domains formed the ‘Staying Strong’ Framework to keep walking and moving around; a framework driven by community and culturally founded needs (table 1).¹⁸ This review set out to explore: (1) What interventions/strategies have been explored to promote walking and moving around for people with MJD (2); How the findings of these explorations align with the perspectives of families with MJD from Groote Eylandt, according to the domains of the ‘Staying Strong’ Framework.¹⁸

METHODS AND ANALYSIS

A scoping review was conducted following the five-step approach recommended by Arksey and O’Malley and further developed by Levac *et al.*^{22,23} A scoping review was chosen to allow a broad range of topics across a range of study types and designs to be explored, to identify the nature and extent of research evidence available.²⁴ The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) extension for Scoping Reviews

Table 1 ‘Staying Strong’ Framework

Domains	Definition
Exercising your body	<ul style="list-style-type: none"> ▶ Having an active lifestyle and keeping your body moving every day keeps you physically strong (ie, going country, walking, hunting, fishing swimming, dancing, doing housework and yard work, riding a bike, walking on a treadmill). ▶ Exercising your body helps you cope with the worries and sadness that come with MJD.
Something important to do	<ul style="list-style-type: none"> ▶ Finding something meaningful to do pushes you to keep your body moving and keep physically strong. ▶ Having something important to do helps you feel you are contributing to your family and community, sets an example for others and builds self-esteem and happiness.
Keeping yourself happy	<ul style="list-style-type: none"> ▶ Finding ways to stay happy and positive, and drawing on family and support services when required, helps you keep persevering in life despite having MJD. ▶ It helps you to keep doing the things you need to do to stay physically strong. ▶ Feeling low and unhappy can make you feel physically weak.
Searching for good medicine	<ul style="list-style-type: none"> ▶ Searching for good medicine or food from the natural environment, or useful clinical medicines, is important for staying physically and emotionally strong. ▶ It is important to find good medicines that help you to manage other illnesses that negatively impact living with MJD (colds, flus, infections and pain). ▶ For Aboriginal people of Groote Eylandt, finding traditional medicines in the bush or beach is important for staying active and keeping physically and emotionally strong.
Going country	<ul style="list-style-type: none"> ▶ Going country means getting out and about, to places meaningful to the individual, to do things that matter, with people that matter, to keep yourself both physically and emotionally strong. ▶ For Aboriginal families of Groote Eylandt, going country involves getting out of the home, visiting their lands, at the bush or beach, often to go hunting or fishing with family.
Families helping each other	<ul style="list-style-type: none"> ▶ Family support is important for having opportunities to keep physically strong and for physical assistance as the disease progresses. ▶ Support from families offers important emotional support, keeping you strong inside. ▶ Family extends to local and trusted service providers.

MJD, Machado-Joseph disease.

Table 2 Search terms (MEDLINE)

Concept	Search terms	Limits
What (interventions)	program* or promot* or interven* or strateg* or approach* or train* or rehab* or princip* or therap* or support* or motivat*	Nil
Works best (promote, enhance)	benefi* or improv* or positiv* or significan* or maint*	Nil
People with MJD (initially broadened search to HAs to ensure all studies that may have included participants with MJD could be screened)	cerebellar ataxia/ or exp spinocerebellar ataxias/ or spinocerebellar degenerations/ or friedreich ataxia/ or olivopontocerebellar atrophies/ or 'spinocerebellar ataxia*' or 'machado joseph disease' or 'friedreich's ataxia' or 'inherited olivopontocerebellar atrophy' or 'cerebello-olivary atrophy' or 'spinocerebellar degeneration' or 'genetic degenerative ataxia' or 'cerebellar ataxia' or 'hereditary ataxia' or 'genetic ataxia' or 'inherited ataxia' or 'dentatorubral pallidoluysian atrophy' or 'trinucleotide repeat dis*' or 'inherited neurodegenerative dis*' or 'degenerative ataxia' or 'hereditary neurodegenerative ataxia*' or 'autosomal dominant hereditary ataxia*' or 'autosomal recessive hereditary ataxia*'	Nil
Walking and moving around (functional mobility)	exp Movement/ or exp Human Activities/ or exp Locomotion/ or Physical Mobility/ or Motor Activity/ or Stair Climbing/ or walk* or mobil* or function* or move* or moving or activit* or step* or stand* or transfer*	Nil

HAs, hereditary ataxias; MJD, Machado-Joseph disease.

Checklist was followed.²⁵ This review was not registered with PROSPERO as scoping reviews are not currently accepted.

Relevant studies

A comprehensive search of peer-reviewed published literature was conducted for studies published from 1990 when genetic confirmation of MJD became possible,^{26 27} until August 2018. The search was repeated prior to publication to identify studies published up to July 2019. Using MEDLINE, EMBASE, CINAHL, PsychINFO and Cochrane Databases, a combination of medical subject headings terms and keywords with truncations were used (table 2). The search was initially broad to include all HAs, to ensure inclusion of studies with participants with multiple aetiologies including MJD would be identified. Studies were chosen if they (1) included human participants with genetically confirmed MJD either exclusively or within the study sample, (2) included adolescents and/or adults, (3) included at least one measure of mobility, function or ataxia and (4) explored the influence of any intervention/strategy on mobility and/or function using objective measures or from the perspective of the participant. In studies that did not disclose the types of SCA of included participants, authors were contacted to confirm inclusion or exclusion on this basis.

Study selection and quality assessment

Database searches were conducted by one reviewer (JJC) and verified by a second reviewer (JQ). Both reviewers (JJC and JQ) independently screened titles and abstracts and reviewed full-text articles. Additional studies screened for inclusion were identified by handsearching reference lists of included studies, literature reviews that met the eligibility criteria and through citations tracked using Google Scholar.^{18 9 11 12 14 28–31} The PRISMA flow diagram outlines

the results of the search (figure 1).³² The second search found no new studies that met the inclusion criteria.

Methodological quality assessment of included studies, not typically required of scoping reviews, was employed to identify gaps in the literature and quality of the studies available.³³ Two reviewers (JJC and MS) assessed methodological quality of included studies using the Mixed Method Appraisal Tool (MMAT)³⁴ and classified them according to the National Health and Medical Research Council (NHMRC) evidence hierarchy.³⁵ The MMAT was selected as this single tool allowed quality appraisal of the range of study designs relevant to this review (qualitative, randomised controlled (RCTs), non-RCTs and quantitative descriptive studies). Joanna Briggs Institute (JBI) Levels of Evidence for Meaningfulness³⁶ was used to grade level of evidence for the qualitative study³⁷ and the expert opinion excerpt.¹ Disagreements were resolved by consensus or referred to a third reviewer (RNB).

Data extraction, collation and analysis

To facilitate analysis and reporting, data were extracted using NVivo V.12³⁸ following a data extraction guide. Data extracted included study characteristics, participant characteristics, intervention characteristics, outcome measures and study outcomes. Data gathered were charted into tables.²² Measures of blood chemistry, neuroimaging or measures of upper limb function were not extracted unless included in composite or functional outcome measures, such as the Spinocerebellar Ataxia Functional Index (SCAFI).

All studies found were collated and then mapped according to the domains they aligned to in the 'Staying Strong' Framework (JJC). Studies that aligned to more than one domain were mapped under the domain to which they most strongly aligned (table 3). A descriptive approach was used to analyse the data collected.³⁹ To

Figure 1 Flow diagram of study selection.

provide an overview, key points that highlight each study's alignment with the different domains were compiled in a separate table (online supplementary table 1). Meta-analysis was not possible due to heterogeneity of outcome measures and interventions in the included studies.

Patient and public involvement

There was no patient or public involvement in this study.

RESULTS

A total of 30 studies met the eligibility criteria and included quantitative (experimental (n=27); observational (n=1)) and qualitative (n=1) designs. One expert opinion excerpt (n=1) that was eligible and included was extracted from a literature review that otherwise did not meet the eligibility criteria. Twelve different countries were represented (Brazil (n=6), Germany (n=4), China (n=3), Japan (n=3), Taiwan (n=3), USA (n=3), India (n=2), Italy (n=2), Spain (n=2), Korea, the Netherlands and Scandinavia. Characteristics of the included studies are outlined in table 3.

Study population

Of the 30 studies, 12 studies included MJD participants exclusively. The remaining 18 included participants with both MJD and other HAs. Mobility status was reported as ambulant in 21 studies, able to stand at a minimum in one study, while eight studies did not report mobility status. Study sample sizes ranged from eight to 295 participants, with a total of 850 participants, 429 with MJD (50.5%). Age ranged from 15 to 76 (average across all studies=46.7 years).

Methodological quality

Seven quantitative studies were graded level II (RCTs) according to NHMRC levels of evidence.^{30 40–45} The remaining studies were graded III-1 (one study),⁴⁶ III-2 (three studies),^{47–49} III-3 (one study)⁵⁰ and IV (16 studies).^{51–66} The qualitative study was graded level 3³⁷ and the expert opinion excerpt was graded level 5¹ in accordance with the JBI Levels of Evidence for Meaningfulness.³⁶ MMAT scores for methodological quality are provided in table 4. Quality scores ranged as follows *(n=1),⁴⁸ ** (n=6),^{41 43 51 54 58 64} *** (n=10)^{30 37 44 45 49 50 53 57 63 66} and **** (n=12).^{40 42 46 47 52 55 56 59–62 65} The expert opinion excerpt was not scored.¹

Outcome measures

Fifty-three different outcome measures were used to investigate interventions in this review. The SARA scale (14/30 studies) was the measure most commonly used. Outcome measures included measures at the impairment level (ataxia, disease severity and depression), measures at the activity level (function, mobility and balance) and measures of quality of life (QOL). No studies included measures at the participation level. Table 5 presents measures used, as well as outcomes that reached statistical significance.

Adverse events

Nine studies reported adverse events, all within pharmacological studies. None were considered serious or life threatening.^{30 41 42 44 45 53 55 64 66} One study reported two-drop outs due to side effects, but details of the effects were not specified.⁶⁴

Table 3 Summary of studies exploring interventions to promote walking and moving around for people with MJD

Study characteristics				Participant characteristics		Intervention		Measurement and Outcomes					
Author, year, country	Design	Level of evidence NHMRC	Quality MMAT	Participants (n=)	Age (y) mean (SD)	Mobility status	Description	Duration (week)	Frequency (week)	Intensity	Outcome measures	Assessment timepoints	Significant outcomes
Wang <i>et al</i> 2018 China	RCT	II	***	n=9; MJD	Exp: 54 (51-60) Control: 57 (44-61)	Ambulant	Exergames training vs conventional balance +coordination training	4	3	40min	▲ SARA (I) ▲ Limit of stability test (A) ▲ Spatiotemporal gait parameters (A)	▲ Pre and post	Between groups: not significant Within group (exp group): ▲ Improved SARA gait-posture (p=0.038)*, SARA total (p=0.042)*
Kaut <i>et al</i> 2014 Germany	Pseudo RCT	III-1	***	n=31; MJD (n=2) SCA1 SCA2 SCA6	Exp: 61.2 (12.3) Control: 57.3 (12.7)	Ambulant	Stochastic vibration therapy vs sham	8 days	4 sessions total	5x60s on/60s off	▲ SARA (I) ▲ SCAH (A) ▲ INAS (I)	▲ Pre and post	Between groups: not significant Within group (exp group): ▲ Improved SARA gait and posture (p<0.01)*, 8MWT (p=0.02)
Conte <i>et al</i> 2017 Italy	Non-randomised experimental trial	III-2	***	n=13; MJD (n=1) SCA1 SCA2 SCA3 SCA6	50.2 (9.5)	Ambulant	Wide BOS walking vs walking between two white lines (width determined by healthy controls)	6x10m walking trials per session, 1 min rest between trials	2 walking sessions on 2 separate days 1week interval between days	Gait speed matched to healthy controls	▲ Spatiotemporal gait parameters (A) ▲ Upper body and lower body kinematics (A) ▲ Muscle coactivation (A) ▲ Energy recovery and expenditure (I)	▲ Each session recorded	Between groups: not significant Within group: ▲ Narrow BOS walking: reduced speed*, step length*, hip and knee ROM*, energy recovery*; increased double support*, gait variability*, trunk oscillation*, ankle joint muscle coactivation* ▲ Widened BOS walking—increased dynamic stability*; reduced compensatory mechanisms*, mechanical energy
Tabbassum <i>et al</i> 2013 India	Non-randomised experimental trial	III-2	*	n=20; MJD (n=1) SCA1 SCA2 SCA3 OPCA	Not reported	Ambulant	Core stability training+balance training+relaxation	4	3	1 hour/day	▲ BES-Test (A) ▲ MFES (Falls) (A)	▲ Pre and post 4 weeks post	Between groups (exp group): ▲ BES-Test each assessment* ▲ Not significant: MFES
Fonteyn <i>et al</i> 2014 The Netherlands	Case series with pretest/post-test outcomes	IV	***	n=10; MJD (n=1) SCA6 SCA9	61.4 (5.7)	Ambulant	Gait adaptability training on treadmill with visual cues on treadmill	5	2	6 gait adaptability exercises for 60min No handrail used. Difficultly gradually progressed	▲ Obstacle avoidance task success rate (A) ▲ SARA (I) ▲ 10MWT (A) ▲ TUG (A) ▲ BBS (A) ▲ EFAP (A) ▲ ABC (A) ▲ No of falls (A) ▲ Experience of training questionnaire (Q)	▲ 1-week pre ▲ 1-week post	Between groups: NA Within group: ▲ Improved SARA and EFAP obstacle subtask*; increased short-step strategy preference (p=0.003)*; Not significant: TUG, ABC, BBS, 10MWT, 8MWT, Avoidance Task
Im <i>et al</i> 2017 Korea	Case series with pretest/post-test outcomes	IV	***	n=19; MJD (n=3) SCA2 SCA6 Idiopathic MSA-C	53.2 (13.8)	Ambulant	Task specific walking training: part practice (weight shifting, stepping-whole practice of walking) Manual support provided and weaned as required	12	2	1.5 hours each session	▲ ICARS (I) ▲ Spatiotemporal gait parameters (A)	▲ Pre and post 3 months post	Between groups: NA Within group: ▲ Improved ICARS each assessment*; reduced spatiotemporal gait parameter variability*
Leonardi <i>et al</i> 2017 Italy	Case series with pretest/post-test outcomes	IV	***	n=9; MJD (n=2) SCA1 SCA2 FA	35.3 (16.3)	Ambulant	Wearable proprioceptive stabiliser-conventional balance training (limit of stability training+external perturbations practice in protected conditions)	Device wear: 3 Usual balance training: 6	Device wear: 5 Usual balance training: 5	Device wear: 3 (hour) Usual balance training: 40	▲ SARA (I) ▲ 6MWT (A) ▲ Spatiotemporal gait parameters (A)	▲ Pre and post 3 weeks of device wear (T1)+usual training ▲ 3 weeks postdevice discontinuation+usual training only (T2)	Between groups: NA Within group: ▲ Improved SARA*, 9HPT-dominant hand*, PATA*, 6MWT*, spatiotemporal gait parameters (T1)*, length of gait cycle (T2)*
de Oliveira <i>et al</i> 2018 Brazil	Case series with pretest/post-test outcomes	IV	**	Stage 1: n=9 Stage 2: n=5 MJD (n=6) SCA1 SCA7	43 (11)	Ambulant	PBVS treadmill training: Stage 1: CV training Stage 2: dynamic balance training	Stage 1:8 Stage 2:10	2 (days)	50min	▲ CPET (A) ▲ BORG (A) ▲ BBS (A) ▲ DGI (A) ▲ SARA (I) ▲ BARS (I) ▲ Katz ADL (Q) ▲ Treadmill inclination (A)	▲ Prestage 1 (S0) ▲ Poststage 2 (S1) ▲ Poststage 2 (S2)	Between groups: NA Within group: ▲ S1: Improved DGI (p=0.03)*, CPET duration (p<0.01)*; treadmill inclination (p<0.01)* ▲ S2: Improved BBS compared with S1 (p=0.04)* ▲ Not significant: SARA, Katz ADL, BARS, VE peak/VO2 max
de Oliveira <i>et al</i> 2015 Brazil	Case series with pretest/post-test outcomes	IV	***	n=11; MJD (n=8) SCA2 SCA7	46.1 (range 28-59) SD not reported	Ambulant	Balance training	4	2-3	1 (hour)	▲ BBS (A)	▲ Pre and post	Between groups: NA Within group: ▲ Improved BBS (p=0.0034)*
Sawant and Gokhale 2015 India	Case series with pretest/post-test outcomes	IV	***	n=3; MJD (n=1) Hereditary SCA	24.6 (3.4)	Ambulant	Occupational therapy+intensive functional physical training (tailored programme meaningful to participant)	12	5 (supervised-3; home/unsupervised-2)	45min-1 hour	▲ BBS (A) ▲ FIM+FAM (A)	▲ Pre and post	Between groups: NA Within group: ▲ Improved BBS (p=0.05)*, FIM+FAM (p=0.01)*

Continued

Table 3 Continued

Staying strong domain: exercising your body													
Study characteristics			Participant characteristics			Intervention		Measurement and Outcomes					
Author, year, country	Design	Level of evidence NHMRC	Quality MMAT	Participants (n=); diagnosis	Age (y) mean (SD)	Mobility status	Description	Duration (week)	Frequency (week)	Intensity	Outcome measures	Assessment timepoints	Significant outcomes
Silva <i>et al</i> 2010 Brazil	Case series with pretest/post-test outcomes	IV	***	n=23; MJD	42.4 (10)	Ambulant	Occupational therapy: training priorities on functional limitations	6 months	Once/week: 0-3months Once/month: 3-5months	40 min	FIM (A) Barthel Index (A) Hamilton rating scale (C) WHOOOL-BREF (C) NESSCA (I) SARA (I)	Pre and post Mid intervention	Between groups: NA Within group: ► Improved Hamilton depression score at 6 months (p<0.001)* ► Not significant: FIM, Barthel Index, WHOOOL-BREF
D'Abreu <i>et al</i> 2010 Brazil	Review (expert opinion section)	V (JBI)	NA	n=23; MJD	NA	NA	NA	NA	NA	NA	Recommendations: Physical therapy assessment +exercise programme. Falls assessment and assistive device prescription Trial levodopa for those with dystonia affecting mobility Exercise improve ability to cope, increases self-esteem. Source of pain should be identified and managed appropriately (musculoskeletal/neuropathic/secondary to dystonia/ mixed)	Pre and post Mid intervention	Between groups: NA Within group: ► Improved Hamilton depression score at 6 months (p<0.001)* ► Not significant: FIM, Barthel Index, WHOOOL-BREF
Staying strong domain: searching for good medicine													
Study characteristics			Participant characteristics			Intervention		Measurement and outcomes					
Author, year, country	Design	Level of evidence NHMRC	Quality MMAT	Participants (n=); diagnosis	Age (y) mean (SD)	Mobility status	Description	Duration (week)	Frequency (week)	Intensity	Outcome measures	Assessment timepoints	Significant outcomes
Assadi <i>et al</i> 2007 USA	RCT	II	***	n=19 MJD (n=2) SCA1 SCA2 SCA17 FA Idiopathic	40.5 (17.3)	Not stated	Bupropione HCl 30mg twice daily vs placebo Crossover after 4 week washout	Each treatment arm: 12 weeks of each arm consisted of titration period.	Twice daily	NA	► ICAPS (I)	► Pre and post each treatment phase	Between groups: not significant
Lei <i>et al</i> 2016 China	RCT	II	**	n=34 MJD	Multidose exp: 800mg: 36.5 (5.4) 1200mg: 33.9 (7.1) Sham: 33.9 (4.5)	Ambulant	Valproic acid low-dose VPA (800 mg/day), high-dose VPA (1200 mg/day) vs placebo	12	Twice daily	NA	► SARA (I)	► Predose ► Week 4 ► Week 8 ► Week 12	Between groups: ► Improved SARA in 1200mg/day group (-2.05) compared with 800 mg/day (-1.58) and placebo (-0.75) (p=0.021)* ► Improved SARA subscores in placebo and VPA groups (800mg/day and 1200mg/day) (p<0.05)
Saite <i>et al</i> 2014 Brazil	RCT	II	***	n=60 MJD	Exp: 40.5 (9.6); sham: 40.4 (9.2)	Ambulant	Lithium carbonate vs placebo	48	300mg once/day; increased to twice daily until 0.5-0.8 mEq/L	NA	► NESSCA (I) ► SARA (I) ► 8MWT (A) ► SCAFI (A) ► CCFS (A) ► Barthel Index (A) ► WHOOOL-BREF (C) ► BDI (C) ► PGI (C)	► Pre dose ► 24 weeks ► 48 weeks	Between groups (exp group): ► Improved SCAFI (24, 48 week)*; CCFS (48 week)* ► Not significant —NESSCA, SARA, 8MWT, 9HPT, BDI, Barthel Index, WHOOOL-BREF, PGI
Schulte <i>et al</i> 2001 Germany	RCT	II	**	n=20 MJD	44.7 (11)	Standing (minimum)	Trimethoprim-sulfamethoxazole trimethoprim (160mg)+sulfamethoxazole (800mg) 2/52; trimethoprim (80mg)+sulfamethoxazole (400mg) remainder of 6months	Phase 1: 6months exp or placebo Washout: 4 Phase 2: crossover to alternate preparation.	Twice daily	NA	► Posturography (A) ► ACRS (I) ► SF36 (C)	► Pre ► Post 2/52 ► Post each 6 months treatment phase	Between groups: not significant
Wessel <i>et al</i> 1997 Germany	RCT	II	***	n=18 MJD (n=2) SCA1 Idiopathic CA	46.8 SD not reported	Not stated	Physostigmine (30 mg) patch vs sham patch	Each treatment arm: 4 Washout: 1	Patch worn continuously	24 hour/day	► ACRS (I) ► Posturography (A)	► Pre and post each treatment phase	Between groups: not significant
Zesiewicz <i>et al</i> 2012 USA	RCT	II	***	n=13 MJD	Exp: 47.44 (10.83); Sham: 53.78 (11.18)	Not stated	Varenicline 4weeks for titration and 4weeks at 1mg twice daily	8	Max dose, twice daily	NA	► SARA (I) ► T25FMT (A) ► BDI (Q) ► BAI (Q) ► CGI (I) ► PGI (C) ► SF36 (C)	► Pre and post	Between groups (exp group) ► Improved SARA subs scores (gait, stance, rapid alternating movements)*, T25FMT*, BDI (p<0.05)* ► Not significant: CGI, PGI, BAI, SF36

Continued

Table 3 Continued

Staying strong domain: searching for good medicine

Study characteristics				Participant characteristics			Intervention	Measurement and outcomes					
Author, year, country	Design	Level of evidence NHMRC	Quality MMAT	Participants (n=)	Age (y) mean (SD)	Mobility status	Description	Duration (week)	Frequency (week)	Intensity	Outcome measures	Assessment timepoints	Significant outcomes
Shiga <i>et al</i> 2002, Japan	Non-randomised experimental trial	III-2	***	n=74 MJD (#) SCA1 SCA6	Exp: 58.63 (1.47) Sham: 56.31 (1.96)	Ambulant	TMS over cerebellum vs sham	21 days	Once daily	10 pulses Pulse duration: 0.1 ms Output adjusted to 100% of maximum output	10MWT (A) Walking capacity (A) Standing capacity (A) Tandem steps (A)	Pre and post	Between groups (exp group): ► Improved 10MWT time (p<0.05)*; 10m steps (p<0.05)*; tandem steps (p<0.005)*, standing capacities (p<0.05)* Within group (sham group): ► Improved 10m time (p<0.05)*, 10m steps (p<0.05)*, standing capacities (p<0.05)
Liu <i>et al</i> 2005, Taiwan	Interrupted time series without a parallel control	III-3	**	n=6 MJD	27 SD not reported	Ambulant	Lamotrigine	Week 0-1: No meds Week 2-7: LTG (6 weeks) Week 8-9: Withdrawal	25 mg daily	NA	TGI (A) OLS (A)	Weekly (1-9 weeks)	Between groups: NA ► Within groups: ► Improved TGI with LTG (p<0.05; week 4, 5, 6, 7; OLS scores (p<0.05; week 7) but not during withdrawal
Alpa <i>et al</i> 2015, Spain	Case series with pretest/post-test outcomes	IV	***	n=12 MJD (7) SCA7	51 (13)	Not stated	Human IGF-1 (subcutaneous administration)	2 years	Twice daily	0.05 mg/kg	SARA (I)	Pre 4 months 9 months 16 months 20 months 24 months	Between groups: NA ► Within group: ► Improved SARA for SCA3 after IGF-1 treatment at 8 months (p<0.005)
Giordano <i>et al</i> 2013, Germany	Case series with pretest/post-test outcomes	IV	**	n=14 MJD (2) SCA1 SCA6 ADCA FCDG SCA3	60 (11.3)	Ambulant	Slow release 4-Aminopyridine	14 days	Once daily	2x-10 mg	SARA (I) EQ-5D (Q) 8MWT (A) SCAFI (A)	Pre 4 hour post 4-AP 14 days post 4-AP	Between groups: NA Within group: ► Improved SCAFI after 4 hours and after 14 days (p<0.01)*; 8MWT after 14 days*, but not after 4 hours (p<0.01)* ► Not significant: SARA, 9HPT, EQ-5D
Monte <i>et al</i> 2003, Brazil	Case series with pretest/post-test outcomes	IV	**	n=13 MJD	41 (13)	Ambulant	Fluoxetine	6	Once daily	20 mg	EDSS (A) UPDRS (A)	Pre and post	Between groups: NA Within group: not significant
Sanz-Gallego <i>et al</i> 2014, Spain	Case series with pre/post-test outcomes	IV	***	n=26 MJD (n=19) SCA6 SCA7	SCA3: 50.3 (13) Total: 49.3 (14.1)	Ambulant	IGF-1 therapy	12 months	Twice daily	NA	SARA (I) SF36 (Q)	Pre 4 months 8 months 12 months	Between groups: NA Within group: ► Improved SARA (p=0.013), 8 and 12 months) in SCA3* and SCA7 subgroups after 12 months (p values not provided)* ► SF36: 18.5% were dissatisfied, 14.8% had poor satisfaction, 37% had fair satisfaction, and 29.6% showed high satisfaction over study durations
Takei <i>et al</i> 2004, Japan	Case series with pretest/post-test outcomes	IV	***	n=10 MJD	41.9 (2.4)	Ambulant and non-ambulant	Tandospirone 15 mg/day, increased to 30 mg/day after 1 week	7 Week 0-1: NI therapy Week 1-4: Tandospirone Week 5: Withdrawal Week 6-7: Follow-up with Tandospirone	Once daily	NA	ARS (I) TLT (A) SDS (Q) Leg pain questionnaire (I)	► ARS: Week 0, 4, 5, 7 ► SDS: Week 0, 4, 5, 6 ► Leg pain questionnaire: Week 0, 4, 5, 6 ► TLT: Week 0-7	Between groups: NA Within group: ► Improved ARS (from week 3) and SDS (from week 2) (p<0.05)*; increased ICARS in withdrawal but decreased significantly to lower than pre-therapy level after restart (p<0.05)* ► TLT reduced in 5/7 patients more than 10% ► Leg pain alleviated in 5/7 patients (significance level not provided) ► Not significant: SDS
Takei <i>et al</i> 2010, Japan	Case series with pretest/post-test outcomes	IV	**	n=39 MJD (n=14) SCA1 SCA2 SCA6 MSA-C MSA-P	52.4 (14.5)	Ambulant	Tandospirone 15 mg/day	4	Once daily	NA	ICARS (I) TLT (A) SDS (Q)	Pre and post	Between groups: NA Within group: ► Improved ICARS (p=0.005) (MJD)*, TLT (p=0.002) (MJD)*, SDS (significance not reported; 5/14 MJD scored=50 indicating depression; 3/5 improved to<50 after therapy
Tsai <i>et al</i> 2017, Taiwan	Case series with pretest/post-test outcomes	IV	***	n=7 MJD (n=6) MSA-C	41.57 (range 21-69) SD not reported	Not stated	Adipose mesenchymal stem cells	Once	Once	NA	SOT—posturography (A) SARA (I)	► 1 month before baseline ► 0.5, 1, 3, 6, 9 and 12 months after AD-MSC	Between Groups: NA Within group: ► Improved SOT (p<0.05 at 3 and 6 months) (MJD)* ► Not significant: SARA
Yang <i>et al</i> 2011, China	Case series with pretest/post-test outcomes	IV	**	n=30 MJD (n=5) SCA1 SCA2 SCA6 Unknown FA	43.14 (12.77)	Not stated	Stem cell treatment+balance training	4-6 weeks	Stem cells: 4-6 times (5-7 day interval) Balance training: 30min/session Twice daily	Stem cells; 15-30min training; 30min/session	BBS (A)	Pre and post	Between groups - NA Within group: ► Improved BBS (p=0.0001)*

Continued

Staying strong domain: searching for good medicine

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Table 4 Quality assessment of included studies using the Mixed Methods Appraisal Tool (MMAT)*

Author(s)†	Qualitative				Quantitative RCT				Quantitative non-random				Quantitative descriptive				Total	Score
	Sources of data	Process for analysis	Context	Researchers' influence	Randomisation	Blinding	Outcome data	Dropout rate	Selection bias	Appropriate measurements	Compared groups	Outcome data	Source strategy	Methods of analysis	Context	Reflexivity		
Arpa <i>et al</i> 2015									1	1	1	1					4/4	100
Assadi <i>et al</i> 2007					0	1	1	1									3/4	75
Berntsson <i>et al</i> 2017	0	1	1	1													3/4	75
Conte <i>et al</i> 2017									1	1	1	1					4/4	100
de Oliveira <i>et al</i> 2015									1	1	1	1					4/4	100
de Oliveira <i>et al</i> 2018									1	0	1	0					2/4	50
Fonteyn <i>et al</i> 2014									1	1	1	1					4/4	100
Giordano <i>et al</i> 2013									0	1	0	1					2/4	50
Im <i>et al</i> 2017									1	1	1	1					4/4	100
Kaut <i>et al</i> 2014					1	1	1	1									4/4	100
Lei <i>et al</i> 2016					0	0	1	1									2/4	50
Leonardi <i>et al</i> 2017									1	1	1	1					4/4	100
Liu <i>et al</i> 2005									0	1	1	1					3/4	75
Lo <i>et al</i> 2016													1	1	1	1	4/4	100
Monte <i>et al</i> 2003									0	1	0	1					2/4	50
Sanz-Gallego <i>et al</i> 2014									1	1	1	0					3/4	75
Saute <i>et al</i> 2014					1	1	1	1									4/4	100
Sawant and Gokhale 2015									0	1	1	1					3/4	75
Schulte <i>et al</i> 2001					0	0	1	1									2/4	50
Shiga <i>et al</i> 2002									0	1	1	1					3/4	75
Silva <i>et al</i> 2010									1	1	1	1					4/4	100
Tabbassum <i>et al</i> 2013									0	1	0	0					1/4	25
Takei <i>et al</i> 2004									0	1	1	1					3/4	75
Takei <i>et al</i> 2010									0	1	1	0					2/4	50
Tsai <i>et al</i> 2017									1	1	1	1					4/4	100
Wang <i>et al</i> 2018					1	1	1	1									4/4	100
Wessel <i>et al</i> 1997					0	1	1	1									3/4	75
Yang <i>et al</i> 2011									1	0	1	1					3/4	75
Zesiewicz <i>et al</i> 2012					1	1	1	0									3/4	75

*A mixed-methods studies column was not included as no mixed-method studies were reviewed.

†D'Abreu *et al* 2010 was not scored (expert opinion excerpt).

1, criterion met; 0, criteria not met or unable to determine; RCT, randomised controlled trials.

Study setting

Of the 27 experimental studies, 12 were conducted under supervision of a health professional in the outpatient setting,^{40 46–49 52 56 59 60 62 63} two of which included an additional unsupervised home programme.^{52 63} In the remaining 15 studies, participants self-administered medications in their homes.^{30 42–45 49–51 53 54 64 65} The

qualitative³⁷ and longitudinal observational studies⁶¹ were conducted face to face in an outpatient Neurology clinic. Study setting was not relevant to the expert opinion excerpt.¹ Assessments were carried out in the inpatient setting in three studies,^{41 55 57} outpatient setting for 12 studies,^{30 42–45 49–51 53 54 64 65} both in two studies,^{41 57} while all follow-up took place in the outpatient setting.

Table 5 Summary of outcome measures and results+

[illegible]

Table 5 Continued

[illegible]

Symbols: *, significant difference within groups or significant difference presingle and postsingle group; †BG, significant difference between groups; ‡, significant change in VE peak or VO2 max; †, activity and impairment measure; #, includes measures for depression, well-being and overall health; +, Note: only outcome measures clinically relevant to function and mobility shown (ie imaging results for brain glucose metabolism and brain metabolite ratios have been excluded); X, relationship between variables assessed only. Nil intervention. See table 3 for findings.

Interventions

A range of interventions have been explored, both pharmacological and non-pharmacological. Overall, no pharmacological interventions are currently recommended for use by individuals with MJD. Non-pharmacological, exercise-based interventions, have had a positive impact on walking and moving around. Intervention types have been described under each of their corresponding domains in the 'Staying Strong' Framework (see [table 3](#) and online supplementary table 1). In relation to the International Classification of Functioning, Disability and Health framework,⁶⁷ no interventions in this review targeted the participation level, but focussed predominantly on the body functions and structures level and activity level.

Exercising your body

Thirteen studies discussed interventions which aligned with 'exercising your body'.^{1 40 46–48 52 56–60 62 63} Exercise in general was reported to be beneficial in one study.¹ Specific interventions could be separated into three types of training: (1) walking training, (2) task specific training and (3) balance training. All studies related to 'exercising your body' reported significant findings, although only three of the 13 studies had a control group. Interventions varied in type, duration and frequency. Intervention sessions occurred on average for 51 min duration, 2.7 times a week for 8 weeks. Dosages such as repetitions completed per session or intensity, in terms of effort per session, were not reported. Rest periods were reported in one study.⁴⁷

Walking practice

Four studies investigated interventions that aligned to walking practice^{47 56 58 59} including training on a treadmill,^{56 58} over ground walking⁵⁹ and walking with a wide base of support.⁴⁷ All significantly improved either balance,^{47 58} ataxia^{56 59} and/or walking ability.^{47 56 59}

Task-specific training

Two studies investigated task-specific training through ADL training alone⁵² or in combination with strength, balance, coordination, walking and cycling training.⁶³ ADL training alone significantly improved depression scores,⁵² but when combined with other task-specific training, balance and function also improved significantly after 12 weeks.⁶³

Balance practice

Six studies explored interventions to challenge balance: balance training alone⁶² or in conjunction with 'exergames'⁴⁰; a wearable proprioceptive stabiliser⁶⁰; core stability training⁴⁸; stochastic vibration therapy⁴⁶ and task-specific training.⁶³ Significant improvements (both between and within groups) in balance,^{48 62} ataxia severity^{40 46 60} and walking^{46 60} were found. One study combined stem cell therapy with balance training (see below in 'searching for good medicine').⁵⁷

Searching for good medicine

Seventeen studies evaluated interventions that aligned with 'searching for good medicine'. Fourteen different pharmacological interventions were explored, one in combination with balance training,⁵⁷ as well as one non-pharmacological intervention (transcutaneous magnetic stimulation (TMS)). No studies evaluated traditional medicine or complementary medicine use.⁶⁸ One study (expert opinion) recommended medications to minimise the sequelae of impairments as a result of MJD (ie, levodopa for dystonia, pain relief for pain).¹ While some therapies demonstrated potential to reduce ataxia (valproic acid,⁴¹ lithium carbonate,⁴² varenicline)⁴⁵ and improve function (lithium carbonate,⁴² TMS),⁴⁹ efficacy had not been demonstrated. None of the interventions were recommended for use by individuals with MJD⁹ ([table 3](#)).

Keeping yourself happy

Two studies aligned with 'keeping yourself happy'.^{37 61} Depression was found to have a significant negative impact on functional status and QOL, independent of ataxia, with suicidal ideation more common in MJD than in SCA1, SCA2 or SCA6.⁶¹ Participants living with ataxia shared the devastating impact of the disease on their social life, mood, parental roles, ADLs and employment, but recommended living in the present and taking 1 day at a time.³⁷ Exercise was reported to help individuals with MJD cope and gain a sense of control over their disease.¹ However, only one study explored individualised interventions designed to promote both physical and psychosocial well-being.⁵² Nine studies included measures of QOL or depression to evaluate their intervention^{42 43 45 52–54 58 64 66} but only two studies^{53 54} demonstrated significant improvements in those measures ([table 5](#)).^{53 54} The remainder reported either non-significant findings or did not report significance levels.

Something important to do

Two studies aligned with having 'something important to do'. Support from employers was important to maintain work roles.³⁷ Loss of meaningful employment, lack of support from employers or changes to roles as a parent or provider had a negative impact on mood and identity.³⁷ Only one study evaluated an intervention tailored to the goals/needs of the participant.⁵² Depression scores improved, but measures of function and QOL failed to reach significance.⁵² No other included studies explored goal orientated or task-specific training or training based on individual goals/priorities/interests.

Going country

No studies aligned with 'going country'. All studies were conducted either in a hospital or research facility with the exception of two studies that included an unsupervised home programme.^{52 63} No studies were found that explored 'going country', community participation, community engagement, vocational rehabilitation, outdoor mobility, sport and/or recreation in relation to mobility for individuals with MJD.

Families helping each other

No studies aligned with 'families helping each other'. No studies considered the influence of family support, interventions or rehabilitation with family, or the role of families in supporting mobility and function for individuals with MJD.

DISCUSSION

The purpose of this review was to map the range of interventions/strategies trialled for people with MJD to enhance walking and moving around and to align those interventions with the 'Staying Strong' Framework developed by individuals and families with MJD from the Groote Eylandt Archipelago. Studies were typically of low quality and focused on what is largely staying strong on the outside: 'exercising your body' (walking training, balance training or task-specific training) and 'searching for good medicine' (various oral medicines, injectable medicines and non-pharmacological medicines). Few studies explored the impact on mobility of having 'something important to do' (ie, goal orientated, or task specific training based on individual goals/priorities/interests) or strategies for 'keeping yourself happy'. No studies in this review considered the impact on mobility of 'going country' (community participation, outdoor mobility, sport/recreation) or 'families helping each other' (the impact or relationship of family support on functional mobility). This review thereby highlights an opportunity for meaningful, individualised, person-centred interventions to promote physical and psychosocial function, consistent with the views of families with MJD in Australia,¹⁸ and those living with ataxia in other parts of the world.^{69 70}

Exercising your body

Overall, exercise or physical activity interventions were found to have positive effects on mobility for individuals with MJD and to be generally safe, inexpensive and in current use. The most effective interventions and the optimal dosage could not be determined, due to heterogeneity of outcome measures and study designs. However, studies that engaged participants in at least 50 min training, at least 2–3 times each week, for approximately 4 weeks, demonstrated improvement. This finding is consistent with ataxia research more broadly, that has shown higher intensity rehabilitation to be more effective (60 min, 2 days per week) than less intensive training.¹¹ Interestingly, no studies evaluated incidental physical activity or participants' level of activity outside of the intervention, unlike studies in other progressive conditions including Huntington's disease (HD), multiple sclerosis and Parkinson's disease (PD) literature.^{71 72} Programmes and interventions that promote participation and an active lifestyle have well known benefits on mobility and well-being for individuals living with neurological disorders.⁷³ Yet the amount of exercise suggested to bring benefit for people with MJD and other ataxias¹¹

suggests that lifestyle-orientated programmes that extend well beyond a 4-week intervention are required.⁷⁴

Searching for good medicine

Consistent with perspectives of families with MJD from the Groote Eylandt Archipelago,¹⁸ this review highlights the continued search for good medicine for individuals with MJD. The impact of traditional medicines or nutritional supplements on functional mobility for those with MJD has not been studied as it has in HD and PD.^{75 76} Furthermore, none of the many medications that were evaluated are currently indicated for MJD with most studies assessing drug safety with small samples. Notwithstanding, in this review, individuals with MJD were better represented in pharmacological studies than in studies on physiotherapeutic interventions. While large sample size recruitment is an inevitable challenge in rare disease research,¹⁶ sample homogeneity within studies will be important moving forward to generate strong clinical recommendations for those with MJD.⁹ Consistent with other ataxias, current recommendations for pharmacological management for those with MJD relate largely to managing the sequelae of disease, such as spasticity, sleeping difficulties and incontinence.¹⁹

Going country

In this study and across all SCAs, research to explore community-based interventions in the context of an individual's environment or lifestyle is lacking, despite known benefits of engagement in sport, recreation and leisure activities for those with disabilities.⁷⁷ Dance and participation in sport are some activities that have been evaluated for those with other neurodegenerative conditions.^{78 79} While *going country* may be culturally and contextually specific to Aboriginal families with MJD in the Top End of Australia, individuals with ataxia in other parts of the world share similar views, relevant to their own context.⁸⁰ Participation in outdoor sports, self-developed exercises, team sports or community-based exercise classes, while beneficial physically, have also been found to promote self-esteem and well-being.⁷⁰ Outdoor activities have helped individuals with ataxia manage depression and focus on living life to the fullest.⁷⁰ Individuals with MJD generally remain ambulant up to 10 years following onset of symptoms,⁴ leaving opportunities for engagement in sport and recreational activities outside of a facility and in the community. Impairment focused intervention programmes restricted to indoor clinical facilities may overlook functional benefits that could be gained through participation in interventions that are fun, enjoyable and meaningful to the person.^{70 81} Research to evaluate the benefits of such interventions on mobility is warranted, for those with MJD and HAs more broadly.

Something important to do and keeping yourself happy

Disappointingly, having 'something important to do' and 'keeping yourself happy' were discussed minimally in the literature. The impact of depression on QOL for people

with SCAs is alarming, particularly the significantly higher rates of suicidal ideation for those with MJD.⁶¹ While a number of studies in this review included measures of depression and QOL,^{42 43 45 52–54 58 64 66} interventions tested appeared to have little impact on either. The sensitivity of the measures used over the generally short intervention period should be taken into consideration.⁸² On the other hand, this may highlight a need for more individualised interventions that target both physical and psychosocial well-being more effectively. The importance of self-selected meaningful exercise has been echoed by individuals with other degenerative ataxias, finding self-chosen activities that offer physical challenge and personally meaningful rewards, provide a sense of achievement, satisfaction and motivation to carry on.⁷⁰ While evaluation of the efficacy of individualised interventions does present challenges,⁸³ programmes such as ParkFIT for PD in the Netherlands^{84 85} and Engage-HD for people with HD in the UK⁷¹ have provided examples on how these challenges can be overcome.⁷³

Families helping each other

It is perhaps surprising, considering MJD is an autosomal-dominant disease, that no studies discussed the inclusion of family members as study participants. The devastating impact families face with autosomal-dominant neurodegenerative diseases is well known.^{86–88} While family support, peer socialisation and support through physical activity is a facilitator for engagement in physical activity for people with neurodegenerative diseases,⁸⁹ no studies in this review discussed these factors. Furthermore, no studies evaluated group-based interventions, although the involvement of peers or family members in physiotherapeutic interventions can enhance motivation, social support and long-term participation in physical activity.⁹⁰ There is no doubt that the role of families is worthy of further investigation.

Outcome measures

Consensus and validation of outcome measures for individuals with MJD is required, with consideration given to outcomes in terms of all the domains of the 'Staying Strong' Framework. Reaching agreement on recommended outcome measures for people with MJD will be an important step for future clinical trials and development of clinical guidelines for management of MJD over the course of the disease. Guidelines for people with inherited ataxias have been developed,⁹¹ as have guidelines for those with Friedreich's ataxia,⁹² but the particular issues individuals and their families with MJD face require specific attention.

Limitations

There were few studies that contained participants exclusively with MJD, so it is difficult to draw conclusions specifically for people with MJD. However, the findings do highlight the dearth of evidence relating to walking and moving around for individuals with MJD. While there may be interventions trialled that have had a positive impact on functional mobility, they are yet to be evaluated.

Additional studies may exist that focus on domains such as having 'something important to do', 'keeping yourself happy' and 'families helping each other', but these may not have been found on initial searches if they did not include a functional mobility-related keyword. However, search strategies in this review were used to identify interventions that promoted functional mobility through staying strong both on the inside and outside.

CONCLUSION

This scoping review mapped studies that investigated the range of interventions to keep people with MJD walking and moving around. Findings were compared with 'what works best' according to families with MJD from the Groote Eylandt Archipelago. Interventions which aligned with their 'Staying Strong' Framework¹⁸ were largely limited to staying strong on the outside (physically), with little reflection on staying strong on the inside (emotionally, mentally and spiritually). The findings of this review suggest future research is required to investigate the benefit of lifestyle activity programmes that address both physical and psychosocial well-being for families with MJD. Detailed reporting on the physical and psychosocial aspects of these interventions, and on the development and delivery of these programmes will help guide programme implementation for health service providers and clinicians working alongside families with MJD. The 'Staying Strong' Framework presented community and culturally founded needs that provided a way to identify significant gaps in the literature and highlight where those needs have not been met. Considerably more effort in culturally informed research is required.

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REFERENCES

- D'Abreu A, França MC, Paulson HL, *et al.* Caring for Machado-Joseph disease: current understanding and how to help patients. *Parkinsonism Relat Disord* 2010;16:2–7.
- Massey L, Jane A, Lindop N, *et al.* Disability Audit – NE Arnhem Land/NT Gulf – A Snapshot of Indigenous Australian Disability in the Very Remote Communities of the Groote Eylandt Archipelago (Angurugu, Umbakumba, Milyakburra), Elcho Island (Galiwin'ku), and Ngukurr (including Urapunga). *Australian Indigenous Health Bulletin* 2013;13.
- Ruano L, Melo C, Silva MC, *et al.* The global epidemiology of hereditary ataxia and spastic paraplegia: a systematic review of prevalence studies. *Neuroepidemiology* 2014;42:174–83.
- MJD Foundation. MJD Foundation – Disability Service Delivery Model – A review of the MJD Foundation's disability service delivery model: contrast and comparison to traditional disability service models. Alyangula, Northern Territory: MJD Foundation, 2018.
- de Araujo M, Raposo M, Kazachkova N, *et al.* Trends in the epidemiology of spinocerebellar ataxia type 3/Machado-Joseph disease in the Azores Islands, Portugal. *JSM Brain Sci* 2016;1.
- MacMillan J. Machado Joseph Disease SCA3. [lecture notes on the Internet] Herston. Australia: Genetic Health Queensland, 2011. <http://mjd.org.au/2-what-is-mjd.html> [Accessed 1 Jan 2018].
- Australian Bureau of Statistics. 2075.0 – Census of Population and Housing – Counts of Aboriginal and Torres Strait Islander Australians, 2016. Table 11: Census Counts, Indigenous Regions – Northern Territory, 2016: Australian Bureau of Statistics; 2017 [cited 3 Apr 2018]. Available: <http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/2075.02016?OpenDocument> [Accessed 3 Apr 2018].
- Ilg W, Bastian AJ, Boesch S, *et al.* Consensus paper: management of degenerative cerebellar disorders. *Cerebellum* 2014;13:248–68.
- Zesiewicz TA, Wilmot G, Kuo S-H, *et al.* Comprehensive systematic review summary: treatment of cerebellar motor dysfunction and ataxia: report of the Guideline development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology* 2018;90:464–71.
- Fonteyn EMR, Keus SHJ, Verstappen CCP, *et al.* The effectiveness of allied health care in patients with ataxia: a systematic review. *J Neurol* 2014;261:251–8.
- Milne SC, Corben LA, Georgiou-Karistianis N, *et al.* Rehabilitation for individuals with genetic degenerative ataxia: a systematic review. *Neurorehabil Neural Repair* 2017;31:609–22.
- Saute JAM, Jardim LB. Machado Joseph disease: clinical and genetic aspects, and current treatment. *Expert Opin Orphan Drugs* 2015;3:517–35.
- Miyai I, Ito M, Hattori N, *et al.* Cerebellar ataxia rehabilitation trial in degenerative cerebellar diseases. *Neurorehabil Neural Repair* 2012;26:515–22.
- Synofzik M, Ilg W. Motor training in degenerative spinocerebellar disease: ataxia-specific improvements by intensive physiotherapy and exergames. *Biomed Res Int* 2014;2014:583507.
- Ilg W, Brötz D, Burkard S, *et al.* Long-Term effects of coordinative training in degenerative cerebellar disease. *Mov Disord* 2010;25:2239–46.
- Ilg W, Schatton C, Schicks J, *et al.* Video game-based coordinative training improves ataxia in children with degenerative ataxia. *Neurology* 2012;79:2056–60.
- Ilg W, Synofzik M, Brötz D, *et al.* Intensive coordinative training improves motor performance in degenerative cerebellar disease. *Neurology* 2009;73:1823–30.
- Carr JJ, Lalara J, Lalara G, *et al.* 'Staying strong on the inside and outside' to keep walking and moving around: perspectives from Aboriginal people with Machado Joseph disease and their families from the Groote Eylandt Archipelago, Australia. *PLoS One* 2019;14:e0212953.
- Gray C, Macniven R, Thomson N. Review of physical activity among Indigenous people. *Australian Indigenous HealthInfoNet* 2013;13:1–17.
- Dahlberg E, Hamilton S, Hamid F, *et al.* Indigenous Australians' perceptions of physical activity: a qualitative systematic review. *Int J Environ Res Public Health* 2018;15:1492.
- Machado Joseph Disease Foundation. About us: what we do: MJD Foundation; 2017 [cited 16 Mar 2017]. Available: <http://mjd.org.au/7-about-us.html> [Accessed 12 Mar 2017].
- Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol* 2005;8:19–32.
- Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. *Implement Sci* 2010;5:69.
- Munn Z, Peters MDJ, Stern C, *et al.* Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. *BMC Med Res Methodol* 2018;18:143.
- Tricco AC, Lillie E, Zarin W, *et al.* PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Ann Intern Med* 2018;169:467–73.
- Kawaguchi Y, Okamoto T, Taniwaki M, *et al.* CAG expansions in a novel gene for Machado-Joseph disease at chromosome 14q32.1. *Nat Genet* 1994;8:221–8.
- Takiyama Y, Nishizawa M, Tanaka H, *et al.* The gene for Machado-Joseph disease maps to human chromosome 14q. *Nat Genet* 1993;4:300–4.
- Trujillo-Martín MM, Serrano-Aguilar P, Montón-Álvarez F, *et al.* Effectiveness and safety of treatments for degenerative ataxias: a systematic review. *Mov Disord* 2009;24:1111–24.
- Braga Neto P, Pedrosa JL, Kuo S-H, *et al.* Current concepts in the treatment of hereditary ataxias. *Arq Neuropsiquiatr* 2016;74:244–52.
- Assadi M, Campellone JV, Janson CG, *et al.* Treatment of spinocerebellar ataxia with buspirone. *J Neurol Sci* 2007;260:143–6.
- Martins C, Rodrigues E, Oliveira L. Physical therapy approach to spinocerebellar ataxia: a systematic review. *Fisioter e Pesqui* 2013;20:293–8.
- Liberati A, Altman DG, Tetzlaff J, *et al.* The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol* 2009;62:e1–34.
- Pham MT, Rajić A, Greig JD, *et al.* A scoping review of scoping reviews: advancing the approach and enhancing the consistency. *Res Synth Methods* 2014;5:371–85.
- National Collaborating Centre for Methods and Tools. Appraising qualitative, quantitative and mixed method studies included in mixed studies reviews: the MMAT Hamilton, ON: McMaster University, 2015. Available: [http://www.nccmt.ca/knowledge-repositories/search/232%20\(accessed%20May%202017](http://www.nccmt.ca/knowledge-repositories/search/232%20(accessed%20May%202017) [Accessed 1 Sep 2017].
- National Health and Medical Research Council. *NHMRC levels of evidence and grades for recommendations for guideline developers*. Canberra, ACT: Australia, 2009.
- Joanna Briggs Institute Levels of Evidence and Grades of Recommendation Working Party. *New JBI levels of evidence*. Joanna Briggs Institute, 2014.
- Berntsson SG, Landtblom A-M, Flensner G. Cerebellar ataxia and intrathecal baclofen therapy: focus on patients' experiences. *PLoS One* 2017;12:e0180054.
- NVivo 12 [program]. Australia 2018.
- Sandelowski M. Whatever happened to qualitative description? *Res Nurs Health* 2000;23:334–40.
- Wang R-Y, Huang F-Y, Soong B-W, *et al.* A randomized controlled pilot trial of game-based training in individuals with spinocerebellar ataxia type 3. *Sci Rep* 2018;8:7816.
- Lei L-F, Yang G-P, Wang J-L, *et al.* Safety and efficacy of valproic acid treatment in SCA3/MJD patients. *Parkinsonism Relat Disord* 2016;26:55–61.
- Saute JAM, de Castilhos RM, Monte TL, *et al.* A randomized, phase 2 clinical trial of lithium carbonate in Machado-Joseph disease. *Mov Disord* 2014;29:568–73.
- Schulte T, Mattern R, Berger K, *et al.* Double-blind crossover trial of trimethoprim-sulfamethoxazole in spinocerebellar ataxia type 3/Machado-Joseph disease. *Arch Neurol* 2001;58:1451–7.
- Wessel K, Langenberger K, Nitschke MF, *et al.* Double-blind crossover study with physostigmine in patients with degenerative cerebellar diseases. *Arch Neurol* 1997;54:397–400.
- Zesiewicz TA, Greenstein PE, Sullivan KL, *et al.* A randomized trial of varenicline (Chantix) for the treatment of spinocerebellar ataxia type 3. *Neurology* 2012;78:545–50.
- Kaut O, Jacobi H, Coch C, *et al.* A randomized pilot study of stochastic vibration therapy in spinocerebellar ataxia. *Cerebellum* 2014;13:237–42.

47. Conte C, Serrao M, Cuius L, *et al.* Effect of restraining the base of support on the biomechanical features in patients with cerebellar ataxia. *Cerebellum* 2018;17:264–75.
48. Tabbassum K, Zia N, Singh S, *et al.* Core stability training with conventional balance training improves dynamic balance in progressive degenerative cerebellar ataxia. *Indian J Physiother Occup Therapy* 2013;7:136–40.
49. Shiga Y, Tsuda T, Itoyama Y, *et al.* Transcranial magnetic stimulation alleviates truncal ataxia in spinocerebellar degeneration. *J Neurol Neurosurg Psychiatry* 2002;72:124–6.
50. Liu C-S, Hsu H-M, Cheng W-L, *et al.* Clinical and molecular events in patients with Machado-Joseph disease under lamotrigine therapy. *Acta Neurol Scand* 2005;111:385–90.
51. Monte TL, Rieder CRM, Tort AB, *et al.* Use of fluoxetine for treatment of Machado-Joseph disease: an open-label study. *Acta Neurol Scand* 2003;107:207–10.
52. Silva RCR, Saute JAM, Silva ACF, *et al.* Occupational therapy in spinocerebellar ataxia type 3: an open-label trial. *Braz J Med Biol Res* 2010;43:537–42.
53. Takei A, Fukazawa T, Hamada T, *et al.* Effects of Tandospirone on “5-HT1A Receptor-Associated Symptoms” in Patients with Machado-Joseph Disease. *Clin Neuropharmacol* 2004;27:9–13.
54. Takei A, Hamada S, Homma S, *et al.* Difference in the effects of tandospirone on ataxia in various types of spinocerebellar degeneration: an open-label study. *Cerebellum* 2010;9:567–70.
55. Tsai Y-A, Liu R-S, Lin J-F, *et al.* Treatment of spinocerebellar ataxia with mesenchymal stem cells: a phase I/IIa clinical study. *Cell Transplant* 2017;26:503–12.
56. Fonteyn EMR, Heeren A, Engels J-JC, *et al.* Gait adaptability training improves obstacle avoidance and dynamic stability in patients with cerebellar degeneration. *Gait Posture* 2014;40:247–51.
57. Yang W-Z, Zhang Y, Wu F, *et al.* Human umbilical cord blood-derived mononuclear cell transplantation: case series of 30 subjects with hereditary ataxia. *J Transl Med* 2011;9:65.
58. de Oliveira LAS, Martins CP, Horszczaruk CHR, *et al.* Partial body Weight-Supported treadmill training in spinocerebellar ataxia. *Rehabil Res Pract* 2018;2018:7172686.
59. Im S-J, Kim Y-H, Kim K-H, *et al.* The effect of a task-specific locomotor training strategy on gait stability in patients with cerebellar disease: a feasibility study. *Disabil Rehabil* 2017;39:1002–8.
60. Leonardi L, Aceto MG, Marcotulli C, *et al.* A wearable proprioceptive stabilizer for rehabilitation of limb and gait ataxia in hereditary cerebellar ataxias: a pilot open-labeled study. *Neurol Sci* 2017;38:459–63.
61. Lo RY, Figueroa KP, Pulst SM, *et al.* Depression and clinical progression in spinocerebellar ataxias. *Parkinsonism Relat Disord* 2016;22:87–92.
62. Santos de Oliveira LA, Martins CP, Horszczaruk CHR, *et al.* Decreasing fall risk in spinocerebellar ataxia. *J Phys Ther Sci* 2015;27:1223–5.
63. Sawant P, Gokhale P. Functional approach in spino-cerebellar Ataxia-Occupational therapy perspective. *Indian J Physiother Occup Therapy* 2015;9:223–8.
64. Giordano I, Bogdanow M, Jacobi H, *et al.* Experience in a short-term trial with 4-aminopyridine in cerebellar ataxia. *J Neurol* 2013;260:2175–6.
65. Arpa J, Sanz-Gallego I, Medina-Báez J, *et al.* Subcutaneous insulin-like growth factor-1 treatment in spinocerebellar ataxias: an open label clinical trial. *Mov Disord* 2011;26:358–9.
66. Sanz-Gallego I, Rodríguez-de-Rivera FJ, Pulido I, *et al.* IGF-1 in autosomal dominant cerebellar ataxia - open-label trial. *Cerebellum Ataxias* 2014;1.
67. Rimmer JH. Use of the ICF in identifying factors that impact participation in physical activity/rehabilitation among people with disabilities. *Disabil Rehabil* 2006;28:1087–95.
68. World Health Organisation. *WHO traditional medicine strategy: 2014–2023*. Hong Kong, China: World Health Organisation, 2013.
69. Daker-White G, Greenfield J, Ealing J. “Six sessions is a drop in the ocean”: an exploratory study of neurological physiotherapy in idiopathic and inherited ataxias. *Physiotherapy* 2013;99:335–40.
70. Cassidy E, Naylor S, Reynolds F. The meanings of physiotherapy and exercise for people living with progressive cerebellar ataxia: an interpretative phenomenological analysis. *Disabil Rehabil* 2018;40:894–904.
71. Quinn L, Trubey R, Gobat N, *et al.* Development and delivery of a physical activity intervention for people with Huntington disease: facilitating translation to clinical practice. *J Neurol Phys Ther* 2016;40:71–80.
72. Schmidt AL, Pennypacker ML, Thrush AH, *et al.* Validity of the StepWatch step activity monitor: preliminary findings for use in persons with Parkinson disease and multiple sclerosis. *J Geriatr Phys Ther* 2011;34:41–5.
73. Quinn L, Morgan D. From disease to health: physical therapy health promotion practices for secondary prevention in adult and pediatric neurologic populations. *J Neurol Phys Ther* 2017;41:S46–54.
74. Motl RW. Lifestyle physical activity in persons with multiple sclerosis: the new kid on the MS block. *Mult Scler* 2014;20:1025–9.
75. Satoh T, Takahashi T, Iwasaki K, *et al.* Traditional Chinese medicine on four patients with Huntington’s disease. *Mov Disord* 2009;24:453–5.
76. Kim T-H, Cho K-H, Jung W-S, *et al.* Herbal medicines for Parkinson’s disease: a systematic review of randomized controlled trials. *PLoS One* 2012;7:e35695.
77. Lord E, Patterson I. The benefits of physically active leisure for people with disabilities: an Australian perspective. *Annals of Leisure Research* 2008;11:123–44.
78. Aguiar LPC, da Rocha PA, Morris M. Therapeutic dancing for Parkinson’s disease. *Int J Gerontol* 2016;10:64–70.
79. Donze C, Massot C, Hautecoeur P, *et al.* The practice of sport in multiple sclerosis: update. *Curr Sports Med Rep* 2017;16:274–9.
80. Thompson Coon J, Boddy K, Stein K, *et al.* Does participating in physical activity in outdoor natural environments have a greater effect on physical and mental wellbeing than physical activity indoors? A systematic review. *Environ Sci Technol* 2011;45:1761–72.
81. Kleim JA, Jones TA. Principles of experience-dependent neural plasticity: implications for rehabilitation after brain damage. *J Speech Lang Hear Res* 2008;51:S225–39.
82. Payakachat N, Ali MM, Tilford JM. Can the EQ-5D detect meaningful change? A systematic review. *Pharmacoeconomics* 2015;33:1137–54.
83. Beck C, McSweeney JC, Richards KC, *et al.* Challenges in tailored intervention research. *Nurs Outlook* 2010;58:104–10.
84. van Nimwegen M, Speelman AD, Smulders K, *et al.* Design and baseline characteristics of the ParkFit study, a randomized controlled trial evaluating the effectiveness of a multifaceted behavioral program to increase physical activity in Parkinson patients. *BMC Neurol* 2010;10:70.
85. Speelman AD, van Nimwegen M, Bloem BR, *et al.* Evaluation of implementation of the ParkFit program: a multifaceted intervention aimed to promote physical activity in patients with Parkinson’s disease. *Physiotherapy* 2014;100:134–41.
86. Vámos M, Hambridge J, Edwards M, *et al.* The impact of Huntington’s disease on family life. *Psychosomatics* 2007;48:400–4.
87. Maxted C, Simpson J, Weatherhead S. An exploration of the experience of Huntington’s disease in family dyads: an interpretative phenomenological analysis. *J Genet Couns* 2014;23:339–49.
88. Jona CMH, Labuschagne I, Mercieca E-C, *et al.* Families affected by Huntington’s disease report difficulties in communication, emotional involvement, and problem solving. *J Huntingtons Dis* 2017;6:169–77.
89. Newitt R, Barnett F, Crowe M. Understanding factors that influence participation in physical activity among people with a neuromusculoskeletal condition: a review of qualitative studies. *Disabil Rehabil* 2016;38:1–10.
90. Morris J, Oliver T, Kroll T, *et al.* The importance of psychological and social factors in influencing the uptake and maintenance of physical activity after stroke: a structured review of the empirical literature. *Stroke Res Treat* 2012;2012:195249.
91. Bonney H, de Silva R, Giunti P. *Management of the ataxias towards best clinical practice*. 3rd edn. Ataxia UK, 2016.
92. Corben LA, Lynch D, Pandolfo M, *et al.* Consensus clinical management guidelines for Friedreich ataxia. *Orphanet J Rare Dis* 2014;9:184.