



# PHYSICAL ACTIVITY GUIDELINES FOR OLDER AUSTRALIANS WITH MILD COGNITIVE IMPAIRMENT OR SUBJECTIVE COGNITIVE DECLINE

A DCRC FUNDED PROJECT

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## Disclaimer

The views expressed in this work are the views of its author/s and not necessarily those of the Australian Government.

## Acronyms

AD	Alzheimer's Disease
ADAS-Cog	Alzheimer's Disease Assessment Scale-Cognition
ADLs	Activities of Daily Living
ADAPTE	Guideline Adaptation Resource Toolkit
AGREE II	Appraisal of Guidelines for Research Evaluation Instrument
AUPOA	Academic Unit for Psychiatry of Old Age
CALD	Culturally and Linguistically Diverse
CDR	Clinical Dementia Rating
CRAHW	Centre for Research on Ageing, Health & Wellbeing

CRE	Centre of Research Excellence in Cognitive Health
DCRCs	Dementia Collaborative Research Centres
IADLs	Instrumental Activities of Daily Living
METs	Metabolic equivalents
MCI	Mild cognitive impairment
MMSE	Mini–Mental State Examination
MRI	Magnetic Resonance Imaging
NARI	National Ageing Research Institute
NIA-AA	National Institute on Aging–Alzheimer's Association
NZ	New Zealand
PA	Physical activity
PRT	Progressive Resistance Training
RCT	Randomised Controlled Trial
SCD	Subjective cognitive decline
UK	United Kingdom
USA	United States of America
UoM	University of Melbourne
WHO	World Health Organisation

## Tables and Figures

Table 1 Effects of physical activity in older adults with MCI or SCD
Figure 1 Guideline adaptation process
Figure 2 Literature screening process



## Executive summary

The global population is ageing in most geographical regions, including Australia. Currently, Australians aged 65 years and older account for 15.3% of the population. This figure is projected to exceed 20% by 2054 <sup>1</sup>.

Mild Cognitive Impairment (MCI) and Subjective Cognitive Decline (SCD) both represent continuous early phases of cognitive decline. They may lead to the development of dementia in some individuals. Individuals with MCI or SCD may experience changes in complex physical and cognitive activities that are key to performing important occupational and social roles <sup>2</sup>. They may experience poorer mobility <sup>3</sup>, higher falls risk <sup>4</sup>, poorer balance <sup>5</sup>, poorer physical fitness <sup>6</sup>, depressive symptoms <sup>7, 8</sup>, neuropsychiatric symptoms <sup>9</sup> and poorer quality of life <sup>10</sup>, compared to those who do not have MCI or SCD. Individuals with MCI or SCD are also likely to use more health care services as a direct or indirect consequence of MCI or SCD <sup>11</sup>, which can impose a significant burden on individuals, families and society <sup>12</sup>.

There is well-established evidence regarding the benefits of physical activity (PA) across the lifespan. Many countries, such as Canada, the United Kingdom (UK), the United States of America (USA) and New Zealand (NZ), as well as the World Health Organisation (WHO) have developed population-based PA guidelines across different age groups, including for healthy older adults <sup>13-16</sup>. There is growing evidence that many of the reported benefits of PA also apply to older adults with MCI or SCD <sup>17, 18</sup>; however, there are no specific PA guidelines for this cohort. Through participating in appropriate levels and types of PA, individuals with MCI or SCD may experience improved health outcomes, which may help to alleviate the economic and emotional burden on themselves and their families. This may also lessen the public health burden associated with MCI or SCD.

The overall purpose of the Physical Activity Guidelines for Older Australians with MCI or SCD (hereafter our guidelines) is to inform older adults, health care providers, and policy makers about the current evidence on the health benefits of PA for older adults with MCI or SCD. Our guidelines are relevant to individuals aged 60 years and over, who have MCI or SCD. The main questions addressed in the guidelines are: “What are the benefits of PA in older adults with MCI or SCD?” and “What is the most beneficial PA type, frequency, intensity, duration and setting?” The

guidelines also provide practical advice on enablers and barriers to participating in PA for this group. However, the guidelines do not address any chronic conditions beyond MCI or SCD.

The current PA guidelines for older adults with MCI or SCD were adapted from the Canadian Physical Activity Guidelines for Older Adults (Canadian Guidelines)<sup>15</sup> by incorporating recent, high-quality evidence specifically regarding the target population, identified through a comprehensive literature review. The development and reporting of the guidelines followed the process outlined by the Guideline Adaptation Resource Toolkit (ADAPTE) and the Appraisal of Guidelines for Research Evaluation (AGREE II) Instruments. An independent advisory panel was established and advisory panel members served the role of external reviewers of the guidelines, consistent with established best practice<sup>19, 20</sup>.

The process undertaken by the project team in preparation of the Physical Activity Guidelines for Older Australians with MCI and SCD is summarised below:

**(1) Setup phase. Key activities included:**

- Decision on the guideline topic
- Establishment of a multidisciplinary research team best suited to this topic
- Assessment of feasibility of guideline adaptation
- Identification of necessary resources and skills
- Completion of the research protocol/adaptation plan.

**(2) Guideline Adaptation phase. Key activities included:**

- Determination of the health questions to be addressed by the guidelines
- Search and screening of existing PA guidelines, identifying six potentially relevant guidelines developed by the WHO, USA, UK, NZ, and Australia
- Assessment of the rigour of the six guidelines and exclusion of WHO, UK and Australian guidelines
- Full assessment of the USA, Canadian and NZ guidelines
- Review of guideline assessment results and decision that the Canadian Guidelines were best suited for adaptation
- Search and screening of the literature relating to PA for older adults with MCI or SCD
- Decision on modifying the recommendations of the Canadian Guidelines and use of the evidence from the literature to develop the guideline recommendations
- Preparation of draft guidelines
- Team meeting in Melbourne to discuss the draft guidelines



### **(3) Guideline Finalisation phase. Key activities included:**

- Review of draft guidelines by advisory panel members
- Consultation with endorsement bodies
- Acknowledgement of the source documents
- Plan for aftercare of the guidelines, including dissemination and the timeline and strategy for updating the guidelines
- Production of the final guideline document and a lay version of the guidelines for consumers

The Guideline Adaptation phase identified 22 PA guidelines for older adults. Using AGREE II as a guide, we assessed the Canadian Guidelines as the most appropriate for adaptation.

A comprehensive literature review, including development of a literature search strategy and study selection criteria, a literature search in Medline and CINAHL and a rigorous literature screening and review by the project team, identified 25 trial studies (including 24 randomised controlled trials (RCTs)) and 16 observational studies that were relevant to PA for older adults with MCI or SCD. These studies provided evidence about the benefits of PA on cognitive function and other health outcomes, adverse effects of PA, and/or enablers and barriers to participation in PA in older adults with MCI or SCD.

The benefits of PA for cognitive and other health outcomes identified from the literature included:

**Cognitive outcomes:** The studies included consistently demonstrated beneficial effects of PA interventions for global cognition<sup>21-33</sup>. There was some but inconsistent evidence of benefit for memory and executive function from studies measuring domain-specific outcomes. There were insufficient data to comment on other cognitive domains.

**Physical health and function:** The most frequently demonstrated benefit of PA for older adults with MCI or SCD was improved aerobic fitness<sup>28, 34-37</sup>. There was emerging evidence for improvements in strength<sup>35</sup> and mixed results for improvements in activities of daily living and balance<sup>26, 35, 36</sup>. Three studies examined physical health parameters such as weight, blood pressure, glucose metabolism and lipid levels: two studies showed benefits<sup>34, 37</sup> but a third did not<sup>24</sup>.

**Mental health:** Two studies showed decreased depressive symptoms, as measured by the Cornell Scale for Depression in Dementia (CSSD)<sup>25, 26</sup>, while one found benefits using the Memorial University of Newfoundland Scale of Happiness (MUNSH) and the Perceived Stress Scale (PSS)<sup>10</sup>. Studies using the Beck Depression Inventory (BDI) and Neuropsychiatric Inventory (NPI) did not show any benefits<sup>21, 26</sup>.

**Quality of life:** A limited number of studies specifically investigated quality of life outcomes. Pre-post data from both an aerobic PA intervention study<sup>28</sup> and a multimodal PA intervention study<sup>27</sup> reported some improvements in subsets of Quality of Life scales. However, no benefit was shown in another study of a predominantly aerobic intervention<sup>21</sup>.

**Biomarkers:** Four imaging studies examined Magnetic Resonance Imaging (MRI) outcomes, all demonstrating some evidence of positive effects on brain structure<sup>29, 30, 36, 38</sup>. Two studies reported increases in brain derived neurotrophic factor (BDNF)<sup>34, 39</sup>, which may provide some insight into the underlying mechanism of the benefits of PA for the brain. Two studies examined inflammation, with one finding reduction in inflammatory markers tumour necrosis factor alpha (TNF- $\alpha$ ) and interleukin-6 (IL-6)<sup>40</sup> and the other showing a positive change in genes related to inflammation<sup>41</sup>. Three studies reported improved insulin sensitivity, associated with metabolic outcomes, and/or cortisol regulation, a biomarker for stress, inflammation and the hypothalamic-pituitary-adrenal axis<sup>34, 39, 42</sup>. One study found that activation of the noradrenaline system by exercise might influence consolidation of memory<sup>43</sup>.

#### **Barriers, enablers and adverse events:**

Few studies specifically explored enablers, barriers and strategies for increasing PA and/or maintaining increased PA levels in older adults with MCI or SCD, although some discussed these issues in the context of study results. Targeted educational material<sup>27, 31, 37, 44, 45</sup> and incorporating social interaction into PA interventions<sup>32</sup> were reported to facilitate participation in or adherence to PA interventions. Health complaints (including injuries) and practical barriers (time and location) were the most significant of identified barriers to PA participation, with the former reported as a more important barrier in a moderate intensity, outdoor intervention in comparison with a low intensity, indoor intervention<sup>46</sup>. Identified strategies to increase PA

included modification of environment and duration; graded intensity and practice factors. Strategies to accommodate cognitive impairment included longer time for learning, mirror image teaching and practice. Strategies to promote participation included seated options, live rather than video instruction, music, recording and playback, supervision, social activities and feedback <sup>44</sup>.

Consistent with the findings of the Canadian Guidelines <sup>15, 47</sup>, our literature review showed that adverse events were infrequent for older adults with MCI or SCD participating in PA or exercise. While the majority of adverse events were musculoskeletal injuries, serious adverse events were extremely rare.

Overall, the evidence for PA in older adults with MCI and SCD is generally consistent with the Canadian Guidelines. Based on the evidence, four recommendations of the Physical Activity Guidelines for Older Adults with MCI or SCD are provided in the box below:

**Recommendation 1**

Older adults who have MCI or SCD should participate in aerobic PA of moderate intensity for at least a total of 150 minutes per week, or vigorous intensity for at least a total of 90 minutes per week. This recommendation is in addition to incidental light intensity activities of daily living.

**Recommendation 2**

In addition to aerobic PA (as outlined in recommendation 1), older adults with MCI or SCD should engage in progressive resistance training (PRT) activities on at least two days per week. This is in addition to continuing incidental activities that help with strength.

**Recommendation 3**

Older adults with MCI or SCD should engage in activities that help to improve or maintain balance. This is particularly important, as older adults with MCI or SCD often have poorer balance and mobility as well as an increased falls risk, compared to older adults without MCI or SCD.

**Recommendation 4**

PA and exercise should be individually tailored, with consideration given to factors such as health problems, physical capacity and environment. Older adults with MCI or SCD are advised to consult with their healthcare professional for advice before

undertaking PA and exercise.
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## **Interpretation of evidence and justification for the Recommendations**

**Recommendation 1:** Participating in at least 150 minutes of aerobic PA per week has been shown to have significant benefits for brain health and function as well as for physical health and function, including reduced risk of chronic disease such as type-two diabetes, in older adults with MCI or SCD. Findings from several RCTs supported the benefits of aerobic PA in older adults with MCI or SCD. Furthermore, the majority of the evidence base examined a frequency and duration consistent with the strong evidence of a systematic review used to support the Canadian Guidelines <sup>48</sup>.

**Recommendation 2:** The review of the evidence found a number of RCTs supporting beneficial effects of PRT for both brain and physical health and function for older adults with MCI or SCD. The evidence base is smaller than that for aerobic PA but is consistent with the evidence for older adults in general <sup>48</sup>. It is anticipated that the evidence for older adults in general can be extrapolated to those with MCI or SCD. Additionally, multiple RCTs of multimodal PA reported similar benefits, providing further support for the recommendation to undertake both aerobic and resistance training interventions.

**Recommendation 3:** There are no research trials examining balance PA interventions specifically in older adults with MCI or SCD. This recommendation has been extrapolated from the evidence base for older adults in general <sup>48</sup> as well as indirect evidence from five RCTs that included balance interventions as part of a multimodal intervention for older adults with MCI. In studies of older adults in general, balance PA interventions have been associated with health benefits that may be of particular relevance to individuals with MCI or SCD <sup>48</sup>.

**Recommendation 4:** There is evidence to suggest that people with cognitive impairment may prefer “simple and safe” physical activities in an “accessible” location <sup>49</sup>. There is evidence from observational studies indicating that adherence rates to PA interventions are higher when social interaction is explicitly incorporated <sup>27, 32</sup> and when the intervention is of low intensity <sup>50</sup>. However, evidence

from RCTs suggests that adherence rates remain similar across low, moderate and high intensity interventions<sup>29, 36, 51</sup>. Some authors suggest graduating PA intensity supports ongoing adherence, although this has not been specifically tested. Some studies suggested that modifying exercise to account for cognitive impairment might result in improved adherence to interventions<sup>27, 44</sup>. A comprehensive example is the Resources and Activities for Life Long Independence (RALLI) exercise intervention<sup>27</sup>, which broke down exercises into small steps, sequenced and linked with cues to help older adults with memory loss to remember each step. These modification strategies facilitated high adherence to a PA intervention in a sample of older adults with memory loss<sup>30</sup>. Supervision is a commonly used strategy that may be of particular benefit for this group due to the potential impact of MCI or SCD on the ability of an individual to initiate and adhere to PA interventions. While the studies reviewed showed no clear difference in adherence to supervised interventions compared to non-supervised interventions, there is some indirect observational evidence supporting this<sup>46, 47, 52</sup>.

## **Conclusion**

There is increasing evidence that it is feasible and safe for older adults with MCI or SCD to participate in PA and exercise. In addition, older adults with MCI or SCD who participate in PA can gain health benefits such as improving cognitive outcomes, physical health and physical function. However, to ensure safety and to optimise health benefits, it is recommended that older persons with MCI or SCD and/or their family members discuss the older persons' health conditions and appropriate PA options (type, duration, frequency and intensity) with relevant health professionals such as general practitioners, physiotherapists, occupational therapists and accredited exercise physiologists. The roles of carers and of health and exercise professionals in supporting initiation and maintaining PA may be particularly important for this group due to the potential impact of MCI or SCD on the ability of individuals with these conditions to do so independently.

## Introduction

### 1.1 Background and significance

#### 1.1.1 Physical activity and older adults

The population is ageing in many geographical regions, including Australia <sup>1</sup>. Concurrently, there has been a shift in the global burden of morbidity and mortality away from infectious diseases to non-communicable disease (NCD), including conditions such as type-two diabetes mellitus, cardiovascular and neurodegenerative diseases <sup>53</sup>. On an individual level, the burden of NCD tends to accumulate over the lifespan. Thus, the combined effects of demographic change and the increasing burden of NCD have resulted in significant global public health policy challenges.

Physical inactivity has been recognised as a key contributor to many NCDs and is now identified as the fourth leading risk factor for mortality globally <sup>54</sup>. Conversely, there is strong evidence that increasing physical activity (PA), across the lifespan, can have significant health benefits. PA has been shown to have beneficial effects on most broad measures of health, including physical, mental and cognitive functioning, as well as on quality of life <sup>16, 55, 56</sup>. Thus, the individual, social and health economic benefits of PA for older people are compelling.

Dementia is one of the many medical conditions associated with physical inactivity, with 17.9% of the population-attributable risk of dementia in Australia ascribed to low levels of PA alone <sup>57</sup>. This is consistent with data from the USA, Europe and the UK <sup>58</sup>. Evidence from observational studies and meta analyses has shown that participating in PA, even in later life, can have a protective effect against cognitive decline and is associated with reduced risk of developing dementia. This applies to primary prevention (in cognitively healthy individuals) as well as secondary prevention (in individuals who do not have dementia but who are already experiencing cognitive decline) <sup>59</sup>.

Given the multiple benefits of PA, many national governments, non-governmental organisations (NGOs) and the WHO have developed population-based guidelines for PA across the lifespan, including for older people. Whilst there are some differences

between individual guidelines, most are consistent in recommending that, in order to experience health benefits, older adults should <sup>13-16</sup>:

- Increase aerobic activities to a frequency of at least four days per week or accumulate at least 150 minutes of moderate-intensity aerobic PA throughout the week. Seventy five to ninety minutes per week of vigorous-intensity aerobic PA is usually suggested as equivalent
- Undertake muscle-strengthening activities, involving major muscle groups, on two or more days a week
- Include flexibility activities regularly as part of PA
- Incorporate PA aimed at improving balance and preventing falls, especially if mobility is poor
- Be as active as comorbidities and abilities allow, even if the recommended amounts cannot be achieved.

These guidelines often do not accommodate the needs or vulnerabilities of specific groups who already have chronic health conditions or some form of functional limitation, such as people experiencing cognitive decline. These individuals, their families, clinicians and policy makers are, therefore, left uncertain about the benefits that PA may offer, how to optimally harness these and how to minimise the risk of ineffective or, at worst, harmful PA. Guidelines that are specifically tailored for individuals with MCI or SCD may facilitate greater engagement in effective PA and optimise the outcomes achieved.

### 1.1.2 Mild cognitive impairment (MCI)

#### *Definition*

The concept of MCI has been viewed as an intermediate clinical stage between normal cognitive function and a dementia syndrome. It was originally developed to allow for early diagnosis and development of effective interventions to prevent or delay progression to dementia, with a specific focus on Alzheimer's disease (AD) pathology. However, no effective pharmacological treatment has been identified for people with MCI. Nevertheless, the classification of MCI has been adopted by many clinicians as a useful concept for explaining clinical changes and risk factor optimisation to patients and their families.

Substantial diversity persists in the specific criteria used to operationalise this concept. Notwithstanding, most definitions reflect the core features described in the consensus statement of the International Working Group on MCI <sup>60</sup>:



- No dementia
- Subjective and/or objective evidence of cognitive decline beyond that expected for age and education level. Subjective evidence is usually described as a complaint or concern from an individual and/or a carer
- Objective impairment is not specifically defined but consensus statements note that scores on cognitive testing are typically 1-1.5 standard deviations (SD) below the mean for age and education matched peers <sup>61</sup>
- Functioning in Activities of Daily Living (ADLs) is preserved
- Functioning in more complex activities is preserved or only minimally impaired.

According to the consensus statement <sup>60</sup>, MCI can also be divided into sub-types according to whether memory is affected and whether more than one aspect of cognition is affected, such as attention, language, executive functions, praxis or visuospatial functions. The four subtypes of MCI are:

- Amnestic MCI Single Domain
- Amnestic MCI Multiple Domain
- Non-Amnestic MCI Single Domain
- Non-Amnestic MCI Multiple Domain

### *Epidemiology*

Data regarding prevalence and incidence of MCI vary considerably and are influenced by the age of the study population, the population setting and methods used to operationalise criteria. Prevalence rates in one review of population based studies exploring the impact of different definitions varied between 0.1% and 42% <sup>62</sup>. Prevalence rates are generally quoted as between 14%-18% of the population over 70 years of age <sup>63</sup>, while Australian data suggest a prevalence of approximately 9% for adults in their sixties <sup>64</sup>. Another recent study applying uniform criteria to harmonised data from geographically diverse cohorts suggested overall rates of between 6% and 12% for people over 60 years of age <sup>65</sup>.

Similarly, incidence rates for MCI vary widely. One systematic review reported a range of incidence rates between 21.5 and 71.3 per 1000 person-years, combining data from studies examining populations with a minimum age of between 60 and 75 years <sup>66</sup>. Incidence rates also rise with age. Anstey et al., (2013) reported an incidence of approximately 19 per 1000 person-years for Australians in their 60s, while another Australian study, examining a population aged 70 to 90 years, reported a much higher rate of 105 per 1000 person-years <sup>67</sup>.

Most studies have found that non-amnesic MCI is more common than amnesic MCI<sup>65, 68-70</sup> and the most common risk factors are increasing age and lower levels of education<sup>64, 65, 68, 70, 71</sup>. Additional risk factors identified in the aforementioned Australian population in their 60s included: past smoking and overall vascular risk, taking anxiety/depression medications or higher baseline depression, and either abstinence or hazardous alcohol consumption<sup>64, 72</sup>. Other reported risk factors from international studies, such as APOE e4 genetic susceptibility, female gender and specific vascular or psychosocial risk factors have demonstrated less consistent associations<sup>68, 71, 73, 74</sup>.

### *Natural history and relationship to dementia*

While often conceptualised as a transitional phase between normal cognition and dementia, progression from MCI to the latter is not inevitable. Some individuals will return to normal cognitive functioning and others follow a fluctuating course: developing MCI, returning to normal cognitive functioning then later converting again to MCI and/or to dementia<sup>73</sup>. Thus, a diagnosis of MCI is usually considered unstable, particularly in younger populations<sup>64</sup>. Both the likelihood and rate of progression to dementia are influenced by the type of MCI, with the highest rate of progression seen in multi-domain MCI, followed by amnesic single domain MCI. Conversion rates in population based studies range between 5% and 10% per year while those reported from clinical samples are generally 10-15% per year<sup>75-77</sup>. These conversion rates are clearly higher than the reported 1-2% incident dementia rates in the general population of cognitively healthy older adults.

### *Related concepts*

Although the concept of MCI is widely recognised and utilised, there have subsequently been several attempts to better identify and describe those individuals for whom MCI is a transitional phase eventually progressing to dementia, particularly of Alzheimer's type. The National Institute on Aging–Alzheimer's Association (NIA-AA) consensus group developed a classification system of MCI due to AD<sup>61</sup>, in which individuals are categorised according to how likely MCI is due to AD. Categories are: unlikely due to AD; intermediate likelihood; and, high likelihood. This approach also incorporates biomarker information.

Other publications from the NIA-AA workgroup on diagnostic guidelines for AD <sup>78</sup> and those of Dubois et al., (2010) suggest criteria to identify individuals in the pre-clinical stage of AD, before symptoms of MCI have emerged <sup>79</sup>. While each of these classifications relate to the generally accepted definition of MCI, they identify different groups of individuals.

Finally, it should be noted that neither the most recent version of the International Classification of Diseases (ICD-10) <sup>80</sup> nor that of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) <sup>81</sup> includes the concept of MCI as described above. The syndromes of Mild Cognitive Disorder (in ICD-10) <sup>80</sup> and Mild Neurocognitive Disorder (DSM-5) <sup>81</sup> approximate but remain distinct from MCI.

### 1.1.3 Subjective cognitive decline (SCD)

SCD refers to a person's experience of cognitive decline which may or may not be reflected in decline in performance on objectively measured cognitive tests. There are a number of terms used interchangeably with SCD, including Subjective Cognitive Impairment (SCI), Subjective Memory Impairment (SMI), Subjective Memory Complaints (SMC), and Subjective Cognitive Complaints (SCC). The cause of SCD is non-specific and may be related to normal ageing, personality traits and stressors, psychiatric conditions, neurologic and medical disorders, substance use, medication or a combination of various factors <sup>82</sup>.

The Subjective Cognitive Decline Initiative (SCD-I) has proposed research criteria for pre-MCI SCD <sup>82</sup>:

The presence of both 1 and 2, below, are required to meet the criteria.

1. "Self-experienced persistent decline in cognitive capacity in comparison with a previously normal status and unrelated to an acute event".
2. "Normal age-, gender-, and education-adjusted performance on standardised cognitive tests, which are used to classify MCI or prodromal AD".

Exclusion criteria:

- "MCI, prodromal AD, or dementia"
- "Can be explained by a psychiatric or neurologic disease (apart from AD), medical disorder, medication or substance use"

A recent systematic review by Mendonca et al., (2016) reported that SCD has an unstable and unpredictable course over time<sup>83</sup>. It is associated with a 1.5 to 3-fold higher risk of progression to MCI or dementia but can also revert to normal cognition. Factors that increased the risk of progression from SCD to dementia were individuals who were worried, those who described an impact on their ADLs and those whose complaints are noticed by an informant.

While MCI and SCD have different definitions, for many people both represent continuous early phases on the spectrum of cognitive impairment, prior to the onset of dementia. We therefore developed our PA guidelines targeting older adults with MCI or SCD. Often individuals in these two groups will already have some neuropathological changes and should be offered targeted recommendations for secondary prevention approaches.

#### 1.1.4 Impacts of MCI or SCD

Individuals with MCI or SCD, by definition, do not experience severe functional impairment in day-to-day tasks, but can experience changes in more complex activities that are key to performing, amongst other things, important occupational and social roles. Thus, the 'real-world' functional impact of MCI or SCD can be significant for some individuals<sup>2</sup>.

MCI is associated with poorer mobility<sup>3</sup>, higher falls risk<sup>4</sup>, poorer balance<sup>5</sup>, and poorer physical fitness<sup>6</sup>. Although the relationship is complex and likely bidirectional, depressive symptoms are more common in people with MCI than in cognitively healthy peers<sup>7,8</sup>. A variety of other neuropsychiatric symptoms, such as mild psychomotor changes<sup>9</sup> have also been reported as more common in MCI than in those without objective cognitive impairment<sup>84</sup>.

In relation to overall quality of life impacts, MCI and SCD are associated with lower happiness and higher perceived stress<sup>10</sup>. In studies of individuals with MCI, qualitative data have identified the uncertainty that is inherent to the diagnosis, stigma and loss of self-confidence as key issues<sup>85</sup>. Some authors have shown an adverse impact on psychological well-being for individuals and carers<sup>86-88</sup> but others have not demonstrated any clear decline of overall quality of life, measured through life satisfaction, mastery, affect and social interaction<sup>85, 89</sup>. Importantly for quality of

life, individuals with MCI appear to be able to use diverse compensatory and emotional coping strategies successfully<sup>71, 85</sup>.

In contrast to dementia, there is little known about the economic cost of MCI or SCD. The Personality and Total Health Through Life (PATH) study in Australia reported increased GP usage amongst those with any mild cognitive disorder, including individuals with MCI or SCD<sup>11</sup>. Increasing health costs are also suspected on the basis of data demonstrating an association between declining cognition and direct medical costs among those with MCI<sup>90</sup> and increased health care costs for individuals in the year prior to an incident dementia diagnosis<sup>91</sup>. Other authors have also demonstrated, in a UK health service, that early detection and intervention in the pre-clinical stages of AD (including MCI and SCD) have the potential to provide substantial cost savings, particularly where interventions halt decline<sup>12</sup>.

## **1.2 Physical activity and falls**

### **1.2.1 What is physical activity?**

The terms “physical activity” (PA) and “exercise” are often used interchangeably but each has its own specific characteristics and meanings. The definitions used in this document are in the main those used by the American College of Sports Medicine in their position statements on exercise for healthy older adults<sup>92, 93</sup>.

PA is defined as “any bodily movement produced by skeletal muscles that results in energy expenditure”<sup>94</sup> “above resting (basal) levels”<sup>95</sup>. In this context, PA broadly includes all forms of structured and unstructured exercise, sports, recreational or leisure activities and physical activities involved in one’s occupation, daily living and active transport.

Exercise is a sub-category of PA. Exercise is defined as “planned, structured, and repetitive movement to improve or maintain one or more components of physical fitness”<sup>92</sup>. In our guidelines, PA includes activities that would be considered exercise as well as those that do not meet this definition.

Physical fitness is “the ability to carry out daily tasks with vigour and alertness, without undue fatigue and with ample energy to enjoy [leisure] pursuits and to meet unforeseen emergencies”<sup>94</sup>. Physical fitness is operationalised as “[a set of]

measurable health and skill-related attributes” that include cardiorespiratory fitness, muscular strength and endurance, body composition and flexibility, balance, agility, reaction time and power <sup>94</sup>. An improvement in physical fitness is usually seen with the accumulation of PA and participation in exercise. In this context, physical fitness is further described “as a state of well-being with a low risk of premature health problems and energy to participate in a variety of physical activities” <sup>92</sup>.

Physical function is defined as “the capacity of an individual to carry out the PA of daily living. Physical function reflects motor function and control, physical fitness, and habitual PA <sup>96, 97</sup> and is an independent predictor of functional independence <sup>98</sup>, disability <sup>99</sup>, morbidity, and mortality <sup>100</sup>”. This is also termed functional fitness.

Exercise or PA can refer to aerobic activity, resistance training, balance training and flexibility training, either singularly or in combination (multimodal PA or exercise). These terms are based on the components of fitness that they primarily target.

Aerobic exercise or activity “refers to exercises in which the body’s large muscles move in a rhythmic manner for sustained periods” <sup>92</sup>. Aerobic exercise can be defined as a use of oxygen that adequately meets the demands of exercise <sup>101</sup>. This form of activity uses large muscle groups such as arms and legs, and increases heart rate and breathing. Examples of aerobic activity include walking, running, swimming, cycling and dancing and many sports. Aerobic activity is also referred to as endurance activity or cardiovascular exercise.

Resistance activity (or training or exercise) is defined as “exercise that causes muscles to work or hold against an applied force or weight” <sup>92</sup> and is designed to increase strength. This type of exercise is also called “strength exercise or training”. The resistance can be achieved by various approaches including using weights, a resistance band or a person’s body weight. Progressive Resistance Training (PRT) is defined as “applying a load to a movement to increase strength and/or power, and regularly adjusting this load as muscle adaptation occurs” <sup>102</sup>. For safety reasons, this is the most appropriate approach to resistance exercise, especially for older people. In our guidelines, resistance training or resistance exercise refers to PRT, unless otherwise stated.

Flexibility exercise refers to “activities designed to preserve or extend range of motion around a joint”<sup>92</sup>. These activities are also called stretching exercise.

Balance exercise or training is a “combination of activities designed to increase the ability of an individual to maintain their line of gravity within their base of support”, including when in a fixed posture (static balance) and during movement (dynamic balance)<sup>103</sup>.

While some health benefits are achievable through any form of PA, each type of PA/exercise also has some specific benefits and health outcomes and may be less effective (or not effective at all) for other outcomes. For example, balance exercises should be used to improve balance but this may not have any impact on outcomes of strength, flexibility or endurance. This is referred to as specificity of training<sup>16</sup>.

### 1.2.2 Other terms related to physical activity and exercise

Energy expenditure is “the total amount of energy (gross) expended during exercise, including the resting energy expenditure (resting energy expenditure + exercise energy expenditure). Energy expenditure may be articulated in Metabolic equivalents (METs), kilocalories or kilojoules”<sup>104</sup>.

MET is a term denoting an index of energy expenditure. “[A MET is] the ratio of the rate of energy expended during an activity to the rate of energy expended at rest. One MET is the rate of energy expenditure while sitting at rest. By convention, 1 MET is equal to an oxygen uptake of 3.5 milliliters per kilogram of body weight per minute”<sup>16</sup>.

MET-minutes quantifies the total amount of PA performed and energy expended in a standardized manner across individuals and types of activities<sup>16</sup>.

MET-minutes of PA by an individual is calculated by taking “the product of the number of METs associated with one or more PA and the number of minutes the activities are performed (i.e., METs x minutes). This is usually standardised per week or per day”<sup>93</sup>.

Moderate intensity aerobic exercise is defined as 3-6 METs<sup>105</sup>.

Vigorous intensity aerobic exercise is defined as >6 METs<sup>105</sup>.



Active transport or commuting is defined as “traveling to or from work or school by a means involving PA, such as walking or riding a bicycle” <sup>106</sup>.

Sedentary behaviour is a state “that involves little or no movement or PA, having an energy expenditure of about 1–1.5 METs. Examples are sitting, watching television, playing video games, and using a computer” <sup>107</sup>.

Sedentary living is defined as “a way of living or lifestyle that requires minimal PA and that encourages inactivity through limited choices, disincentives, and/or structural or financial barriers” <sup>92</sup>.

### 1.2.3 Physical activity and falls

A fall is defined as “an unexpected event in which the participant comes to rest on the ground, floor, or lower level” <sup>108</sup>. Falls are a common health problem among older people, with one in three people aged over 65 years experiencing one or more falls in a 12 month period. The risk of falling is increased further in people with MCI <sup>109</sup>. Falls most commonly occur during walking related activities, and are often caused by a combination of intrinsic factors (health factors within the individual, such as vision impairment, muscle weakness, or poor balance) and extrinsic factors (environmental factors such as uneven or slippery surfaces, poor lighting).

While falls commonly occur during walking, this and other forms of PA or exercise can be beneficial for older people in maintaining or improving function, independence, and other health benefits such as reducing the risk of some chronic diseases. Walking as a form of PA does not reduce the risk of falling (although it does have many other health benefits for older people). It is important to note that some but not all forms of PA or exercise can reduce the risk of falling for older people, including those with varying levels of cognitive impairment <sup>109, 110</sup>. In particular, current evidence suggests that there is a need for PA to include a component of challenging balance if it is likely to reduce falls (e.g., tai chi, group or home exercise programs that have some balance training exercises) <sup>111</sup>. Advice from a health professional such as a physiotherapist or accredited exercise physiologist can assist in ensuring that a proposed PA will incorporate a challenge to balance, as required to reduce falls, and determining how this can be achieved safely for older people with MCI or SCD.

## 2. Development of physical activity guidelines for older adults with MCI or SCD

### 2.1 Importance of developing physical activity guidelines for older adults with MCI or SCD

The development of specific guidelines for PA in older people with MCI or SCD was deemed important on the basis of the following key points, largely arising from our narrative review of the relevant evidence.

Individuals with MCI or SCD are at increased risk of adverse health and functioning outcomes compared to cognitively healthy older individuals. This includes an increased risk of developing dementia, increased risk of poor mental health, increased risk of falls, poorer mobility and increased mortality. Physical inactivity in this group of individuals is associated with at least some of these poor outcomes<sup>3, 4 5 6</sup>. The impacts of physical inactivity for people with MCI or SCD speak to broader public health concerns and key Commonwealth and State Government health policy priority areas, such as in general population-wide health promotion and in specific prevention of dementia.

There is strong evidence that PA can have beneficial health effects for individuals with MCI or SCD<sup>17, 18</sup>, although the evidence base for several specific health outcomes needs further development. There is evidence that PA is safe for individuals with MCI or SCD but adaptation of PA may be of benefit in light of increased risk of certain adverse outcomes.

There is evidence that the barriers and facilitators for PA in this population may be both qualitatively and quantitatively different to those in the cognitively healthy population. Changing physical inactivity in this group may be difficult<sup>112</sup> and syndrome specific advice may be necessary to overcome barriers<sup>49</sup>.

Dissemination of current knowledge regarding PA in individuals with MCI or SCD is limited and a need for more educational material regarding this has been expressed by health professionals<sup>45</sup> and by consumers<sup>49</sup>.

## 2.2 Purpose and scope

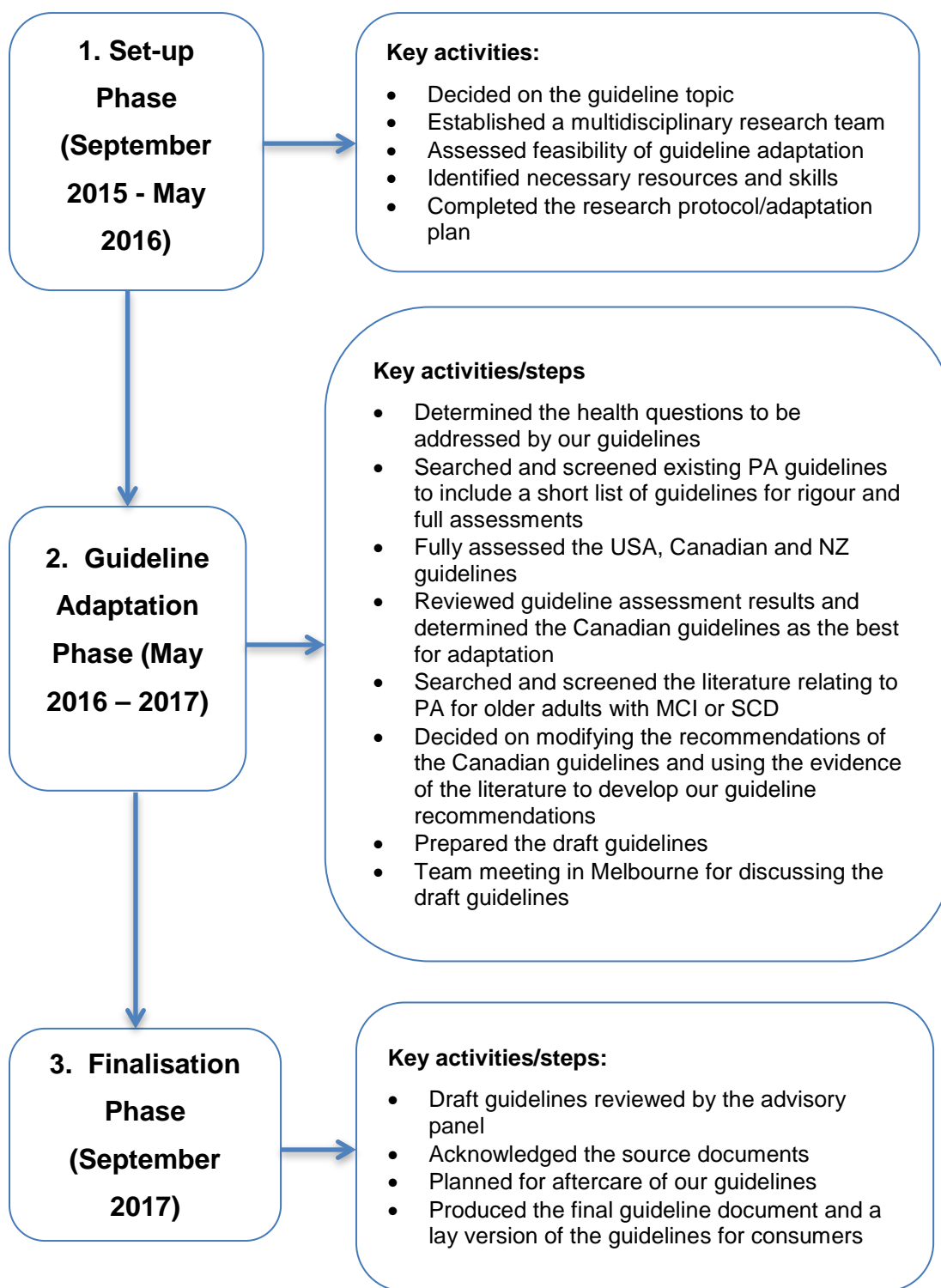
The overall purpose of our PA guidelines is to provide individuals with MCI or SCD, health care providers and policy makers with a practical approach to applying the current evidence regarding the benefits of PA, particularly for cognitive function. The guidelines apply to older adults aged 60 years and over (based on the WHO definition of older adults), who have MCI or SCD. However, our guidelines do not specifically address issues associated with other chronic conditions.

The main questions addressed in the guidelines are: “What are the benefits of PA in older adults with MCI or SCD?” and “What is the most beneficial PA type, frequency, intensity, duration and format?” The primary outcome of interest is cognitive function. The secondary outcomes of interest include mental and physical health outcomes and biomarkers.

Our guidelines provide practical advice and strategies for older adults with MCI or SCD to overcome barriers to participating in PA. However, the development of approaches and interventions to promote PA for those with MCI or SCD is outside the scope of our guidelines.

## 2.3 Guideline development approach and process

Given the existence of several PA guidelines for older adults by peak bodies nationally and internationally, as well as the project timeline and resources, we implemented an adaptation approach to developing our guidelines. The Guideline Adaptation Resource Toolkit (ADAPTE) provided us with a guide throughout the guideline adaptation process <sup>19</sup>. An overview of the guideline adaptation process adopted to develop our PA guidelines is shown in Figure 1 below (Please contact the authors for the detailed process).



**Figure 1 Guideline adaptation process**

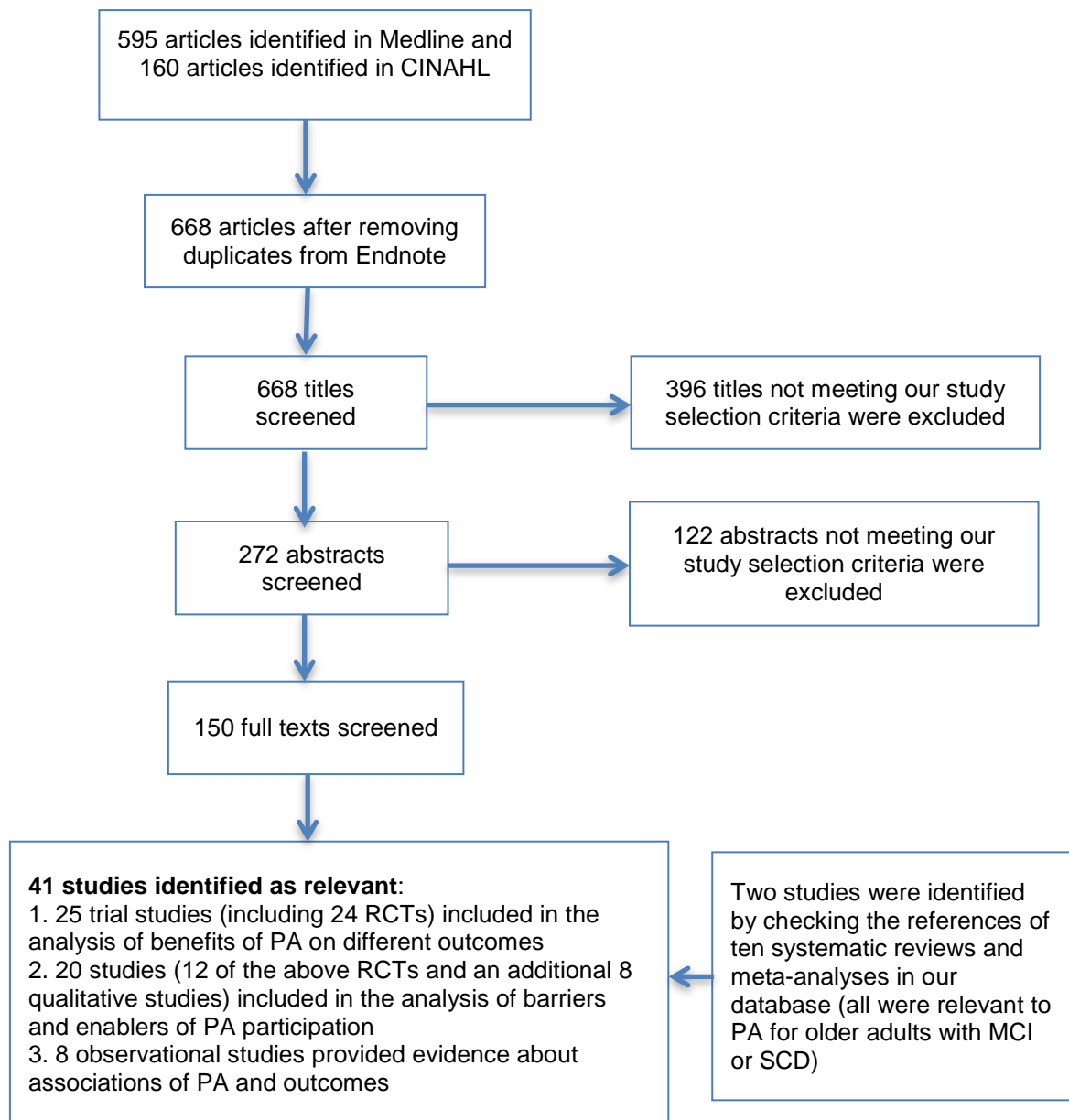
Following the **Set-up** phase, the first step in the Guideline Adaptation Phase was to search relevant PA guidelines for older adults. Following the process outlined by

ADAPTE, together with the advice of the PA experts in our team, we systematically searched published PA guidelines for older adults nationally and internationally. This search yielded 22 PA guidelines for older adults; however, none specifically considered older adults with MCI or SCD. We then used the Appraisal of Guidelines for Research and Evaluation II Instrument (AGREE II) (focusing on its Rigour domain with eight items) to assess the rigour of all 22 guidelines. We rated the USA, NZ and Canadian Guidelines to have good quality. Following this step, we used AGREE II (focusing on all of its six domains with 23 items) to fully assess the three guidelines. Ultimately, we determined the Canadian Guidelines as the most appropriate. Recommended by the ADAPTE tool, AGREE II provided a guide for us to report our guidelines<sup>20</sup>.

To incorporate recent evidence specifically relating to older adults with MCI or SCD into our guidelines, we concurrently conducted a systematic literature search in Medline Complete and CINAHL Complete. This search yielded 668 studies. After the literature screening and review, and quality assessment, we finally identified 25 trial studies (24 were RCTs) examining the effects of PA on cognitive and non-cognitive health outcomes (see Table 1). The literature screening and review process is shown in Figure 2 (Please contact the authors for more details).

We divided those 25 trial studies according to outcome, effect (statistically significant differences in outcomes favouring the intervention group), quality level<sup>15</sup>, and type of PA, in order to assess the evidence regarding the benefits of PA, as described in **Section 3.1** below. We also grouped these trial studies by type of PA and used the same process to analyse and interpret these studies. Please contact the authors for additional information on methodology, adherence, adverse events, supervision, format (group vs. individual) and setting.

We identified eight observational studies investigating associations between PA and health outcomes, which were treated as additional evidence about the benefits of PA. We also identified 20 studies (12 of the 24 RCTs noted previously and eight qualitative studies) providing some information on barriers and enablers of participation in PA, although none of these studies primarily investigated this topic (Please contact the authors for more details about these studies).



**Figure 2 Literature screening process**

**Table 1. Effects of physical activity in older adults with MCI or SCD**

Outcomes	Studies	Type of PA	Yes statistically significant positive effect	No significant effect	Level of quality
<b>1.Cognition</b>					
Global function	Fiatarone Singh et al., 2014	PRT	Yes		1
Global function	Hildreth et al., 2015	Aerobic	Yes		1
Global function	Lam, et al., 2015	Multimodal (Tai Chi)	Yes		1
Global function	Lautenschlager et al., 2008	Aerobic	Yes		1
Global function	Suo et al., 2016	PRT	Yes		1
Global function	Suzuki et al., 2013	Multimodal (Aerobic, Resistance, Balance)	Yes		1
Global function	Barnes et al., 2013	Multimodal (Aerobic, Resistance, Stretching)	Yes		2
Global function	Lam et al., 2012	Multimodal (Tai Chi)	Yes		2
Global function	Law et al., 2014	Multimodal (Functional)	Yes		2
Global function	Suzuki et al., 2012	Multimodal (Aerobic, Resistance)	Yes		2
Global function	Wei & Ji, 2014	Multimodal (Handball Training)	Yes		2
Global function	Logsdon et al., 2009	Multimodal (Aerobic, Resistance, Balance)		No	2
Global function	Nakatsuka et al., 2015	Aerobic		No	2
Executive function	Fiatarone Singh et al., 2014	PRT	Yes		1
Executive function	Lam, et al., 2015	Multimodal (Tai Chi)	Yes		1
Executive function	Nagamatsu et al., 2012	PRT	Yes		1
Executive function	Baker et al., 2010	Aerobic	Yes		2
Executive function	Law et al., 2014	Multimodal (Functional)	Yes		2
Executive function	Nakatsuka et al., 2015	Aerobic	Yes		2
Executive function	Suzuki et al., 2012	Multimodal (Aerobic, Resistance)	Yes		2
Executive function	Hildreth et al., 2015	Aerobic		No	1
Executive function	Lautenschlager et al., 2008	Aerobic		No	1
Executive function	Nagamatsu et al., 2012	Aerobic		No	1
Executive function	Van Uffelen et al., 2008	Aerobic		No	1
Executive	Lam et al.,	Multimodal (Tai Chi)		No	2



Outcomes	Studies	Type of PA	Yes statistically significant positive effect	No significant effect	Level of quality
function	2012				
Executive function	Suzuki et al., 2012	Multimodal (Aerobic, Resistance)		No	2
Memory	Hu et al., 2014	Aerobic	Yes		1
Memory	Lam, et al., 2015	Multimodal (Tai Chi)	Yes		1
Memory	Lautenschlager et al., 2008	Aerobic	Yes		1
Memory	Nagamatsu et al., 2012	PRT	Yes		1
Memory	Nagamatsu et al., 2013	Aerobic	Yes		1
Memory	Suzuki et al., 2013	Multimodal (Aerobic, Resistance, Balance)	Yes (aMCI subgroup only)		1
Memory	Lam et al., 2012	Multimodal (Tai Chi)	Yes		2
Memory	Suzuki et al., 2012	Multimodal (Aerobic, Resistance)	Yes		2
Memory	Fiatarone Singh et al., 2014	PRT		Mixed	1
Memory	Hildreth et al., 2015	Aerobic		No	1
Memory	Nagamatsu et al., 2012	Aerobic		No	1
Memory	Suo et al., 2016	PRT		No	1
Memory	Van Uffelen et al., 2008	Aerobic		No	1
Memory	Zuniga et al., 2015	Aerobic vs Multimodal		No (Both Groups)	2
Memory	Baker et al., 2010	Aerobic		No	2
Other	Baker, et al., 2010	Aerobic	Yes		2
Other	Fiatarone Singh et al., 2014	PRT	Yes		2
Other	Van Uffelen et al., 2008	Aerobic		No	1
Other	Lam et al., 2012	Multimodal (Tai Chi)		No	2
Other	Makizako et al., 2012	Multimodal (Aerobic, Resistance)		No	2
Other	Hildreth et al., 2015	Aerobic		No	1
Other	Hu et al., 2014	Aerobic		No	1
Other	Hildreth et al., 2015	Aerobic		No	1
<b>2.Physical function</b>					
ADLs	Hu, et al., 2014	Aerobic	Yes		1
ADLs	Wei & Ji, 2014	Multimodal (Handball training)	Yes		2

Outcomes	Studies	Type of PA	Yes statistically significant positive effect	No significant effect	Level of quality
IADLs	Law et al., 2014	Multimodal (Functional)	Yes		2
IADLs	Fiatarone Singh et al., 2014	PRT		No	1
IADLs	Lam et al., 2015	Multimodal (Tai Chi)		No	1
Aerobic Fitness	Nagamatsu et al., 2012	Aerobic	Yes		1
Aerobic Fitness	Baker et al., 2010	Aerobic	Yes		2
Aerobic Fitness	Nakatsuka et al., 2015	Aerobic	Yes		2
Aerobic Fitness	Uemura et al., 2012	Multimodal (Aerobic, Resistance, Balance)	Yes		2
Aerobic Fitness	Makizako et al., 2012	Multimodal (Aerobic, Resistance)	Yes		2
Aerobic Fitness	Hildreth et al., 2015	Aerobic		No	1
Aerobic Fitness	Nagamatsu et al., 2012	PRT		No	1
Balance	Nagamatsu et al., 2012	Aerobic	Yes		1
Balance	Lam et al., 2012	Multimodal (Tai Chi)	Yes		2
Balance	Nagamatsu et al., 2012	PRT		No	1
Balance	Makizako et al., 2012	Multimodal (Aerobic, Resistance)		No	2
Strength	Makizako et al., 2012	Multimodal (Aerobic, Resistance)	Yes		2
<b>3. Physical health (Metabolic parameters)</b>					
Glucose Metabolism, Lipids, and Adiposity	Baker et al., 2010	Aerobic	Yes		2
BMI, TC, HDL (not fasting); TGL, HbA1C, SBP/DBP	Uemura et al., 2012	Multimodal (Aerobic, Resistance, Balance)	Yes (TC)	No (BMI, BP, HDL, HbA1C)	2
HbA1c, leptin, fasting glucose, fasting insulin, glucose disposal rate, lipids; weight; fat mass; fat-free mass,	Hildreth et al., 2015	Aerobic		No	1

Outcomes	Studies	Type of PA	Yes statistically significant positive effect	No significant effect	Level of quality
BMI, BP					
<b>4.Mental health</b>					
Mental Health	Lam et al., 2015	Multimodal (Tai Chi)	Yes		1
Mental Health	Lam et al., 2012	Multimodal (Tai Chi)	Yes		2
Mental Health	Zuniga et al., 2015	Aerobic vs Resistance/Balance	Yes		2
Mental Health	Lautenschlager et al., 2008	Aerobic		No	1
<b>5.Quality of life</b>					
Quality of life	Zuniga et al., 2015	Aerobic vs Resistance/Balance	Yes (Association only in both groups)		2
Quality of life	Nakatsuka et al., 2015	Aerobic	Yes		2
Quality of life	Logsdon et al., 2009	Multimodal (Aerobic, Resistance, Balance)	Yes (Physical components only)		3
Quality of life	Lautenschlager et al., 2008	Aerobic		No	1
<b>6.Biomarkers</b>					
Plasma	Baker et al., 2010	Aerobic	Yes		2
Plasma	Nascimento et al., 2014	Multimodal (Aerobic, Resistance)	Yes		2
Plasma	Tortosa-Martinez et al., 2015	Aerobic	Yes		2
Genetics	Iyalomhe et al., 2015	Aerobic	Yes		2
MRI	Suzuki et al., 2013	Multimodal (Aerobic, Resistance, Balance)	Yes (aMCI subgroup only)		1
MRI	Nagamatsu et al., 2012	PRT	Yes		1
MRI	Suo et al., 2016	PRT	Yes		1
MRI	Ten Brinke et al., 2015	Aerobic vs Resistance	Yes (Aerobic)	No (Resistance)	2
MRI	Nagamatsu et al., 2012	Aerobic		No	1

Note: PRT = Progressive Resistance Training; TC = Total Cholesterol; BMI = Body Mass Index; BP = Blood Pressure; SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; HDL = High Density Lipoproteins; HbA1C = Haemoglobin A1C

Level of Quality Scale: Level 1: RCTs without important limitations; Level 2: RCTs with important limitations or observational studies (non-RCTs or cohort studies) with overwhelming evidence; Level 3: Other observational studies (prospective cohort studies, case-control studies, case series); Level 4: Inadequate or no data in population of interest, or anecdotal evidence or clinical experience

### 3. Evidence regarding physical activity for older adults with MCI or SCD

As described above, we developed our PA guidelines by adapting the Canadian Guidelines and incorporating specific evidence from the literature through a rigorous literature review. Given that the Canadian Guidelines target healthy older adults, the evidence discussed in this section is primarily from the literature we identified and where relevant the Canadian Guidelines. The findings of the literature are summarised in Table 1, above, and discussed below (Please contact the authors for more details about the findings of the literature).

#### 3.1 Benefits of physical activity

In this section, when discussing the benefits of PA for older adults with MCI or SCD, we specifically focus on health outcomes that have previously been highlighted as benefitting from PA in cognitively healthy older adults. We consider whether there is sufficient evidence to extend the general population guidelines to this specific population.

As discussed in the **Introduction section**, the definitions of MCI and SCD have changed over time. These also varied between studies reviewed. All reviewed studies included participants with subjective cognitive impairment (according to participant and/or informant). Some of the studies reporting participants with MCI may have used definitions that failed to exclude people with SCD. Further, the number of studies relating to MCI far exceeded those relating to SCD. Consequently, our review considered MCI and SCD as one group.

A wide variety of benefits were identified in the literature. In accordance with the goal of our guidelines, we focused particularly on the cognitive impacts of PA for individuals with MCI or SCD. The benefits of specific types of PA were then reviewed in the three categories that are referred to in the Canadian Guidelines; namely, aerobic, resistance training and balance. A fourth category, entitled multimodal, was added to consider PA interventions that consisted of combinations of two or more of the three elements, such as Tai Chi. It is important to note that while there were many studies examining aerobic and multimodal resistance PA interventions in people with MCI or SCD, there were only five studies examining resistance PA

interventions alone<sup>23, 29, 36, 38, 51</sup> and no studies were identified that examined balance PA interventions alone. There were five studies that examined the benefits of balance PA interventions as part of a multimodal PA intervention allowing indirect consideration of the benefits of balance PA interventions<sup>10, 27, 30, 32, 37</sup>. This clearly has implications for the quality of the evidence base for these two modalities, particularly balance interventions.

Moreover, given the increased risk of falls and other health vulnerabilities already noted as associated with MCI, a key consideration was how the general population guidelines may need to be adapted for those with MCI or SCD to minimise the risk of adverse events. Finally, evidence regarding barriers and enablers of PA for individuals with MCI or SCD was reviewed to inform guidance regarding development and adaptation of PA interventions and/or advice for this population.

The studies discussed in this section are limited to RCTs and non-RCT trials deemed to be of sufficient quality by the team as described in the **Guideline development approach and process** section.

Given that our guidelines were developed through a process of adaptation of the Canadian Guidelines, the health outcomes that the Canadian Guidelines focused on when examining the benefits of PA in the general older adult population are described below where appropriate<sup>15, 48</sup>. It should be noted that the Canadian Guidelines only examined three categories of outcomes: morbidity from chronic disease and all-cause mortality, physical independence and disability, and cognitive function. Our comprehensive literature review led to us identifying more categories of outcomes detailed below.

### 3.1.1 Cognition

As shown in Table 1, there is a growing evidence base with 19 studies examining the potential benefits of PA on cognition in older people with MCI or SCD. In these studies, cognition has been considered globally or in specific domains such as memory, executive function, attention, language and visuospatial function. Another frequently used outcome has been progression to dementia, usually measured by the Clinical Dementia Rating Scale (CDR).

The most consistent evidence was for improvement on measures of global cognition. In total, thirteen Level 1 and 2 RCTs examined the effect of PA interventions on global cognitive function using outcome measurements including the Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog), MMSE and CDR <sup>21-33</sup>. Eleven of these studies showed benefits of PA for global cognition. However, when specific domains of cognition were examined, there was some but inconsistent evidence of benefit for memory and executive function. There were insufficient data to comment on other domains.

The pattern of results from reviewing specific types of PA suggests that aerobic, resistance and multimodal interventions all demonstrate benefits for cognition. They show improvements in global cognition and mixed results for specific domains of cognition. The current evidence does not indicate that any particular modality has superior benefit for cognition.

There is some evidence to suggest that at least moderate intensity PA is necessary to obtain cognitive benefits. PA interventions were of moderate or high intensity in all RCTs demonstrating cognitive benefits from PA. In contrast, at least two studies that failed to detect any benefit of PA used a low intensity PA intervention <sup>26, 35</sup>.

Evidence from cross-sectional studies suggests that higher levels of PA may reduce risk of MCI <sup>6, 113</sup> and also risk of progression from MCI to dementia <sup>114</sup>.

### 3.1.2 Physical health and function

In the general population and for older adults, there is consistent evidence supporting the benefits of PA for physical health and function <sup>48</sup>.

On the basis of our review, the evidence base regarding the benefits of PA interventions for physical health and function in people with MCI or SCD is consistent with that for the general population. Outcomes that were examined in this section included aerobic fitness, for example using six-minute walk test, measurements of balance, ADLs, flexibility and strength. The most demonstrated benefit in the literature was for improving level of aerobic fitness <sup>28, 34-37</sup>. There was emerging evidence for improvements in strength <sup>35</sup> and mixed results for improvements in ADLs and balance <sup>26, 35, 36</sup>, which may require further research.

Only three studies examined physical health parameters such as weight, blood pressure, glucose metabolism and lipid levels. Two studies demonstrated benefits, <sup>34, 37</sup> while the third one did not <sup>24</sup>.

The benefits of PA for physical health and function appeared to follow a similar pattern to PA in general regardless of whether the type of PA was aerobic, resistance or multimodal.

### 3.1.3 Mental health

Mental health was mainly measured using depression scales such as the Cornell Scale for Depression in Dementia (CSSD) or Beck Depression Inventory (BDI) or more general scales such as the Neuropsychiatric Inventory (NPI).

There is clear evidence for the benefits of PA for mental health in general populations <sup>115</sup>. There were only four studies that examined the effects of PA interventions on mental health in older people with MCI or SCD <sup>10, 21, 25, 26</sup>. Two of these studies showed a benefit on the CSSD while another found benefits on scales that are less recognised – Memorial University of Newfoundland Scale of Happiness (MUNSH) and Perceived Stress Scale (PSS) <sup>10</sup>. Studies using the BDI and NPI did not show any benefits <sup>21, 26</sup>. There were insufficient studies of mental health outcomes to be able to compare the effects of different types of PA.

Despite the limited evidence base, there is no apparent reason for not extrapolating the mental health benefits of PA for the general population to people with SCD or MCI.

### 3.1.4 Quality of life

There is limited evidence on changes in Quality of Life as a result of PA interventions in older people with MCI or SCD. Pre-post data from both an aerobic <sup>28</sup> and a multimodal PA intervention study <sup>27</sup> showed some improvements in subsets of Quality of Life scales. However, there was no benefit shown in another study of a predominantly aerobic intervention <sup>21</sup>.



### 3.1.5 Biomarkers

The four imaging studies that were identified all used MRI outcomes and all demonstrated some evidence of positive effects on brain structure<sup>29, 30, 36, 38</sup>. The areas of the brain implicated by these studies included the right lingual/occipito-fusiform, right frontal pole and posterior cingulate regions. Furthermore, one study demonstrated reversal of white matter hyperintensities with resistance training, providing a clear link to some of the measures of physical health that involve vascular risk factors<sup>29</sup>. Evidence from cross-sectional studies also provides support for PA being correlated with hippocampal volume and less vascular change and brain atrophy<sup>116, 117</sup>. These findings are therefore encouraging but their clinical significance is unclear at this early stage. The identified studies mostly involved resistance training, with some being multimodal.

There were only a small number of studies examining a number of plasma biomarkers. Two studies demonstrated increases in brain derived neurotrophic factor (BDNF)<sup>34, 39</sup>, which may provide some insight into the mechanism of the benefits of PA for the brain. Cross-sectional evidence for BDNF was mixed<sup>30, 118</sup>. Two studies examined inflammation, which has been hypothesised as being involved in cognitive impairment. One study found a reduction in two inflammatory markers (TNF- $\alpha$  and IL-6<sup>40</sup>) and the other found a positive change in genes related to inflammation<sup>41</sup>. Three studies showed some benefits for insulin sensitivity, linking with the metabolic findings reported above, and for cortisol regulation, linking with stress, inflammation and the hypothalamic-pituitary-adrenal axis<sup>34, 39, 42</sup>. Finally, one study found that activation of the noradrenaline system by exercise may also have an impact on consolidating memory<sup>43</sup>.

### 3.1.6 Physical activity parameters for cognition and physical health and function

The guideline adaptation process involved a review of the literature to ascertain whether the recommendations of the Canadian Guidelines for healthy older adults would be applicable to older adults with MCI or SCD. The recommendations of the Canadian Guidelines include that:

- To achieve health benefits, and improve functional abilities, adults aged 65 years and older should accumulate at least 150 minutes of moderate-to-vigorous-intensity aerobic PA per week, in bouts of 10 minutes or more

- It is also beneficial to add muscle and bone strengthening activities using major muscle groups, at least 2 days per week
- Those with poor mobility should perform physical activities to enhance balance and prevent falls
- More PA provides greater health benefits.

In the following section, we discuss the evidence of different types of PA for older adults with MCI or SCD and where appropriate relate it to the four recommendations of the Canadian Guidelines.

### *Aerobic physical activity*

In the studies using aerobic PA interventions, the majority examined moderate-vigorous intensity aerobic PA, which was often measured by maximum oxygen uptake (VO<sub>2</sub> max) or heart rate. The studies reporting a statistically significant positive effect for cognition were generally in the order of 150 minutes per week in bouts of 10 minutes or more, with three studies at or exceeding 150 minutes<sup>21, 24, 34</sup> and two studies just below this at 120 minutes and 90 minutes per week respectively<sup>51, 119</sup>. The studies showing benefits for physical health and function were also around 150 minutes per week, although they also included a study which used 60 minutes per week<sup>28</sup>. All the PA interventions were 6 months in duration except for two studies, which were 12 months in duration<sup>10, 120</sup>.

### *Resistance training physical activity*

All four of the studies demonstrating cognitive benefits of resistance training used interventions that were at least twice per week<sup>23, 29, 36, 51</sup>, as did the one study that showed physical health benefits<sup>36</sup>. All of these studies had interventions of 6 months duration.

### *Multimodal physical activity*

Substantial variability in the specific activities undertaken as part of multimodal interventions limits the extent to which generalised comments regarding key parameters can be made. The studies that reported improved cognition and physical health and function were consistent with the aerobic and resistance parameters in the Canadian Guidelines except for one study, which consisted of 650 minutes in total over 10 weeks<sup>33</sup>.

## *Balance*

There were no studies that specifically assessed balance interventions for the target population. Some multimodal PA interventions included balance interventions. These studies showed some benefits for cognition<sup>30, 32</sup> or a trend towards benefits<sup>27</sup> as well as benefits for physical health and function<sup>32, 37</sup>.

## *PA frequency, duration and intensity, supervision and setting*

We did not identify any studies that examined whether more PA provided greater health benefits. The majority of the studies included in our review involved group-based, supervised PA undertaken in a centre. A small number of studies involved individual-based PA undertaken in a person's own environment.

### **3.2 Adverse events and safety**

The evidence base clearly describes many health benefits of PA. The Canadian Guidelines concluded that these benefits clearly outweigh risks<sup>15, 47</sup>. A systematic review completed for the Canadian Guidelines reported that the most common adverse events were musculoskeletal injuries, occurring at around one event per 1000 hours of walking and four events per 1000 hours of running. They also reported that serious adverse events were more likely to occur during exercise than rest but were still rare events<sup>121</sup>. The evidence base in RCTs involving older adults with MCI or SCD is consistent with this data. Specifically, adverse events were infrequent but slightly more common in the intervention groups compared to the control groups. The majority of adverse events were musculoskeletal injuries. Serious adverse events were extremely rare. Further, adherence levels were generally high and dropout rates were generally low. Both measures were either similar in the intervention and control groups, or slightly higher in the intervention group. These findings indirectly support the relatively low level of adverse events and safety issues.

### 3.3 Barriers and enablers for participation in physical activity by older adults with MCI or SCD

#### 3.3.1 Evidence and recommendations regarding barriers and enablers for physical activity in healthy older adults

Given that the benefits of PA have been demonstrated, barriers and enablers for participation in PA must be considered to optimise the translation of evidence into practice, particularly as some observational studies suggest that individuals with MCI may engage in less PA than cognitively healthy adults <sup>122</sup>.

While the Canadian Guidelines provided some evidence about barriers or enablers for PA participation in healthy older adults <sup>15</sup>, our review of the literature did not identify direct evidence on this topic in older adults with MCI or SCD. Key findings from the Canadian Guidelines included: increasing PA levels in older adults was difficult; short term adherence to a variety of types of PA was high but fell sharply after a year; and specific enablers and barriers for effective PA interventions remained unknown <sup>121</sup>. The guidelines highlighted heterogeneity in function and culturally based preferences among older adults. Consequently, they recommended that PA guidance for older adults should emphasise flexibility and tailoring and for education and messaging for older adults to be concrete and focus on quality of life and functional outcomes <sup>121</sup>.

Individual studies and findings cited by the Canadian Guidelines in developing their recommendation included:

- Illness (chronic and acute), injury and lack of skills are major barriers to maintaining PA changes and strategies to reduce these may improve adherence <sup>123</sup>
- Fitness and health professionals may lack specific training required to be able to prescribe PA programs to older adults that are tailored to individual goals and capacities <sup>124</sup>
- Older adults may view PA as ‘a recreational pursuit rather than necessary medical therapy’ and lack awareness of the importance of PA for functional outcomes <sup>125</sup>
- Conserving energy between PA bouts, resulting in no net increase in energy expenditure, may be more prevalent in older adults <sup>126</sup>
- Behavioural counselling and self-regulatory models do not currently have evidence of long-term effectiveness and adherence to counselling sessions involved in these interventions is poor <sup>127</sup>

- Making small, simple changes to routine life, incorporating PA into daily life, accumulating small bouts of PA across the day and supporting change through behaviour modification techniques may result in greater benefits and longer maintenance of both increased PA and physical function benefits <sup>128</sup>
- Tailored and targeted education material may enable increased PA <sup>129</sup>
- Activities to enhance group cohesion and socialisation may result in better long-term adherence to group PA <sup>130</sup>.

### 3.3.2 Evidence for applying these recommendations to MCI or SCD population

In our literature review, few studies specifically explored barriers and enablers for participating in PA, increasing levels of PA and/or maintaining increased PA levels in people with MCI or SCD. Most intervention studies reported adherence and/or drop out rates for both intervention and control groups but few examined factors underlying these. Many studies also included specific adjustments to PA interventions to accommodate cognitive impairment but few outlined a rationale for these adjustments or examined the effect of these on adherence to PA interventions <sup>29</sup>. The most common adjustment to accommodate cognitive impairment was supervised exercise. All but one of the studies reviewed incorporated some degree of supervision for at least part of the intervention. It was, consequently, not possible to compare adherence levels between interventions with and without supervision. However, people with MCI or SCD may have greater difficulty with initiating and maintaining a change in behaviour and indirect observational evidence suggests that regular, ongoing supervision and encouragement may be an effective strategy to overcome this challenge <sup>47, 52</sup>.

The Seattle Protocols are evidence based treatment programs that utilise behavioural approaches based on 'social learning and gerontology theories but accommodating the neuropsychological and behavioural changes that occur in individuals with dementia' <sup>131</sup>. Resources and Activities for Life Long Independence (RALLI) is one of these protocols. It specifically focused on adjustments to PA interventions to facilitate better adherence among individuals with MCI. These emphasised incrementally designed exercises, education for both patients and carers, handouts and tracking forms and incorporating both pleasure and use of behavioural techniques into PA <sup>132</sup>. A pilot study using this protocol in people with MCI reported improved PA frequency that was sustained at six months following completion of the intervention <sup>27</sup>.

Chang et al., (2011) reported a qualitative study of factors facilitating adherence to a Tai Chi intervention for older people with MCI. The study suggested strategies for physical safety; strategies to accommodate cognitive impairment; and strategies to promote participation. Specific strategies for physical safety included environment modifications, duration, graded intensity and practice factors. Strategies for accommodating cognitive impairment included longer time for learning, mirror image teaching and practice. Strategies to promote participation included seated options, live rather than video instruction, music, recording and playback, supervision, social activities and feedback <sup>44</sup>.

Van Uffelen et al., (2009) explored factors related to both interventions and participants that may have influenced adherence to PA interventions in a larger RCT <sup>50, 120</sup>. They noted significantly greater dropout rates in higher intensity interventions. There were significant but small effects of baseline cognition on adherence to the PA intervention that differed depending on intervention intensity. However, baseline cognition had no impact on overall attendance. The effect of baseline cognition was also explored in a large RCT of a multimodal PA intervention <sup>25</sup>. The authors noted that better baseline cognition was associated with better adherence to the intervention.

The influence of attitudes to PA may be significant. In a cross-sectional survey of memory clinic patients with a variety of diagnoses and their carers, patients were noted as less likely to endorse belief in health promotion aspects of PA than carers and both carers' and patients' belief in the importance of high intensity exercise for health maintenance significantly predicted engagement in regular PA <sup>52</sup>. Further, a qualitative study reported that the attitudes of healthcare professionals impacted consumer and carer awareness of the potential benefits of PA <sup>45</sup>. The effect of attitude may be mediated by carers and health professionals with positive attitudes offering greater supervision, tailoring and encouragement, although this has not, to our knowledge, been specifically examined.

Preliminary evidence suggests that education may act as an enabler for PA. Focus groups in the study by Neville et al., (2013) highlighted targeted educational material as helpful, as did the report by Chang et al., (2011) <sup>44, 45</sup>. Some intervention studies including specific education for patients and/or trainers also reported high adherence

rates to interventions, although causality cannot be inferred<sup>27, 31, 37</sup>. In contrast, other intervention trials reported poor adherence despite education and training<sup>36, 38, 51, 120</sup>.

Similarly, without demonstrating a causal link, one study highlighted the potential impact of incorporating social interaction into PA interventions as a means of enabling adherence and reported 100% adherence rates to the study intervention<sup>32</sup>.

With regard to barriers to participation in PA, pain and poor mobility were reported barriers<sup>3</sup>, as were higher falls risk<sup>4</sup> and poor balance<sup>5</sup>. Health complaints (including injuries) and practical barriers (time and location) were the most significant barriers found in a study by Tak et al., (2012). The former was noted as a more important barrier in a moderate intensity, outdoor intervention, compared with a low intensity, indoor intervention<sup>46</sup>.

Lack of subjective progress and disappointment with programs has also been identified as a barrier to continuing exercise following completion of a program<sup>46</sup>. This provides further indirect supporting evidence for the potential importance of in-person support and facilitation to sustain participation in this group of individuals.

In summary, similar to that for healthy older adults, evidence regarding barriers and enablers for PA in people with MCI or SCD is limited. The evidence available suggests that tailored education for people with MCI or SCD, carers and both fitness and health professionals may be an important enabler, particularly as negative attitudes regarding the benefits of PA for people with MCI or SCD may be both more prevalent and act as a significant barrier to PA for this population. Tailoring PA programs to accommodate cognitive impairment, including supervision and encouragement, adjustment of the program itself and the use of multimodal memory aids, shows promise as an enabler of both engagement in PA and sustaining behaviour change. As for older adults in general, emphasising pleasure and the social aspects of PA may also be of benefit. Health complaints appear to be a strong barrier to participating in PA for older people.

## 4. Recommendations

### 4.1 Target population and introduction

Our PA guidelines apply to older adults aged 60 years and over who have MCI or SCD, irrespective of gender, race, ethnicity, or income level. The guidelines can be applied to older adults with MCI or SCD who also have comorbid health conditions such as mental illness and chronic disease. The target audience includes older adults, health professionals, health and community services, policy makers and government both in Australia and internationally. Older people diagnosed with dementia should discuss PA options with their GP, physiotherapist or exercise physiologist.

PA is beneficial to older adults with MCI or SCD for brain health and function as well as for physical health and function. It is possibly beneficial to mental health and quality of life when extrapolating findings from the general population, however, there is insufficient evidence to demonstrate this yet in MCI or SCD.

Our guidelines were created using a methodological process involving the adaptation of the Canadian Guidelines for older adults. Where possible, in our guidelines we attempt to provide evidence to extrapolate the Canadian Guidelines to our target population of older adults with MCI or SCD but also to highlight any points of difference. Great consistency between these guidelines and existing guidelines for the general population in this age group should have significant practical benefits for implementation.

### 4.2 Recommendations

#### 4.2.1 Recommendation 1

Older adults who have MCI or SCD should participate in aerobic PA of moderate intensity for at least a total of 150 minutes per week, or vigorous intensity for at least a total of 90 minutes per week. This recommendation is in addition to incidental light intensity activities of daily living.



### *Interpretation of evidence and justification*

This level of activity has been shown to have significant benefits to brain health and function as well as physical health and function in older adults with MCI or SCD. This includes reducing risk of chronic disease such as type-two diabetes and also helping to maintain a healthy body weight. It is expected that the benefit of reduction in premature death in the general population of older adults would also apply to those with MCI or SCD. To obtain these health benefits, it appears that this level of activity should continue for at least 6 months, but ideally be ongoing. It is possible that increasing frequency or intensity may lead to greater benefit.

Our review of the evidence base provided evidence from a number of Level 1 and 2 quality RCTs supporting the benefits of aerobic PA/exercise in older adults with MCI or SCD. These benefits are for cognitive health and function and physical health and function. Furthermore, the majority of PA/exercise interventions were of a frequency, intensity and duration for MCI or SCD consistent with the Canadian Guidelines, although there were some variations in this, as discussed earlier. This evidence is consistent with the strong evidence found in the systematic review that was part of the preparation of the Canadian Guidelines <sup>48</sup>.

#### **4.2.2 Recommendation 2**

In addition to aerobic PA (as outlined in recommendation 1), older adults with MCI or SCD should engage in progressive resistance training (PRT) activities on at least 2 days per week. This is in addition to incidental activities that help with strength.

### *Interpretation of evidence and justification*

Our review of the evidence found a number of Level 1 and 2 quality RCTs supporting the benefits of PRT PA in older adults with MCI or SCD. These benefits are for brain health and function and physical health and function. The evidence base is smaller than that for aerobic PA but is consistent with the evidence for older adults in general <sup>48</sup>. It is anticipated that the evidence for older adults in general can be extrapolated to those with MCI or SCD. Multiple Level 1 and 2 quality RCTs of multimodal PA interventions also reported similar benefits, providing additional support for the recommendation to undertake both aerobic and resistance training interventions.

### 4.2.3 Recommendation 3

Older adults with MCI or SCD should engage in activities that help to improve or maintain balance. This is particularly important, as older adults with MCI or SCD often have poorer balance and mobility as well as increased falls risk, compared to older adults without MCI or SCD.

#### *Interpretation of evidence and justification*

In our literature review we did not find specific research trials examining balance PA interventions in older adults with MCI or SCD. This benefit has been extrapolated from the evidence base for older adults in general <sup>48</sup> as well as indirect evidence from five RCTs that included balance interventions as part of a multimodal intervention <sup>10, 27, 30, 32, 37</sup>.

### 4.2.4 Recommendation 4

PA and exercise should be individually tailored, with consideration given to factors such as health problems, physical capacity and environment. Older adults with MCI or SCD are advised to consult with a healthcare professional for advice before undertaking PA and exercise.

#### *Interpretation of evidence and justification*

There is evidence to suggest that people with cognitive impairment have a tendency to prefer “simple and safe” physical activities in an “accessible” location <sup>49</sup>. There is evidence from observational studies indicating that adherence rates to PA interventions are higher when social interaction is explicitly incorporated <sup>27, 32</sup> and when the intervention is of low intensity <sup>50</sup>. However, evidence from RCTs suggests that adherence rates remain similar across low, moderate and high intensity interventions <sup>29, 36, 51</sup>. Some authors suggest graduating PA intensity supports ongoing adherence, although this has not been specifically tested. In our literature review, some observational studies (Level 3 evidence) suggested that modifying PA to account for cognitive impairment might result in improved adherence to interventions <sup>27, 44</sup>. One example is the RALLI exercise program <sup>27</sup>, which broke exercises into small steps, sequenced and linked with cues to help older adults with

memory loss to remember each step. These modification strategies facilitated adherence to the PA intervention in a sample of older adults with memory loss<sup>30</sup>.

There is a small amount of Level 3 evidence on barriers to undertaking or maintaining PA in people with MCI. These include ignorance of or negative attitudes regarding the potential benefits of PA<sup>45, 52</sup>; concerns regarding adverse effects<sup>4, 45</sup>; and health complaints and practical concerns<sup>46</sup>. There is also a small amount of evidence indicating that the attitudes and health beliefs of carers and health professionals can influence engagement in PA by people with MCI and that negative attitudes may currently be common<sup>45, 52</sup>. More extensive literature regarding barriers for cognitively healthy older persons has described similar findings and could likely be extrapolated to older adults with MCI or SCD<sup>121</sup>. Some important barriers to PA participation identified among cognitively healthy older adults, but unexplored in older adults with MCI or SCD, pertain to the ways in which communities are designed and built and include the lack of safe and convenient places to engage in exercise and transport-related PA<sup>133-135</sup>.

There are multiple enablers that may assist older adults with MCI or SCD to overcome barriers to undertaking PA. This includes provision of tailored education regarding the benefits and safety of PA by healthcare professionals for both patients and carers; and development of PA interventions that are of graded intensity and incorporate supervision, encouragement and social engagement<sup>32, 45, 47, 52</sup>.

Modifying interventions to accommodate cognitive impairment should be considered during development, including the use of multimodal memory aids, supervision, and repetition<sup>30, 44</sup>.

PA can be successfully and safely undertaken by healthy older adults and older people with many health problems, including those with MCI or SCD. However, for older people with MCI or SCD, or other health problems, there is value in discussing the impact of health problems on PA options and participation, and the forms of PA that might optimise benefits without compromising safety in their specific health circumstances, with a doctor or another health professional (e.g., physiotherapist, or accredited exercise physiologist). If walking is the preferred form of PA, consideration of the environment is important - for example, if the area around

the older person's home is hilly and/or has uneven or broken footpaths, it may be worth considering going to a local park with a smooth walking track instead.

## **5. Future research directions**

The process of adapting the Canadian Guidelines and identifying the most recent evidence from the literature in order to develop our PA guidelines has highlighted gaps and limitations in the current PA literature for older adults with MCI or SCD.

Overall, there is insufficient data regarding this topic. More high-quality and large scale RCTs are required to allow study findings to be generalised to a larger group of older adults with MCI or SCD.

Considering the quality of existing studies, there are common methodological issues that need to be addressed to improve the rigour of the research. There are also issues associated with study design (e.g., reliability and validity of the measures), study foci (e.g., lack of research examining ethnic minority groups and some important topic areas such as dose-response relationship, and barriers and enablers of participation in PA), and reporting (e.g., lack of information on adverse effects). These require specific attention in future research.

Addressing these limitations will help to establish quality evidence about the benefits of PA on health outcomes in older adults with MCI or SCD, and the facilitative and inhibitive factors for this older population to undertake PA. This quality evidence could be added to the PA guidelines and improve their applicability in older adults with MCI or SCD, and health promotion practice and policy.

Lastly, we acknowledge the limitations of the process used to develop these guidelines and propose some suggestions for future practice of guideline development.

### **5.1 General methodological issues**

There were similar methodological issues identified in many RCTs. These included: inconsistent definitions of MCI or SCD; inadequate sample size; short duration of PA intervention; lack of follow-up post intervention to detect longer-term effects; participant selection bias; flaws in randomisation; an absence of concealment of allocation or blinding; and high attrition rate. There is a clear need for future studies

to use consistent and accurate definitions of MCI and SCD, allowing improved interpretation and comparison of findings across studies.

## **5.2 Targeted populations**

Given that Australia is a culturally diverse country with about one third of its older population from culturally and linguistically diverse (CALD) backgrounds<sup>136, 137</sup>, there is a pressing need to undertake research involving older CALD populations. In addition, older adults from socially disadvantaged groups, such as those with low income levels, are also under-researched. Thus, we recommend undertaking rigorous quantitative, qualitative or mixed-methods research on relevant PA topics in these populations, including: the uptake of PA (more specifically the type, frequency and intensity); factors affecting the uptake of PA; PA promotion strategies; and outcome evaluation of PA. The research findings will provide evidence for targeted PA guidelines and inclusive public health practice and policy.

## **5.3 Measures and outcomes**

As shown in the PA studies identified, there is significant variability in the measurement of PA and associated health outcomes. For example, self-reported PA was frequently used, potentially leading to some degree of measurement error. Some studies used objective PA measurement technology, which, however, did not capture all aspects of PA. There was a lack of precision regarding the measures of the PA type, frequency, duration and intensity.

There was significant heterogeneity in measures of cognitive outcomes, the primary focus of our guidelines. For both global and domain-specific cognitive function, different tests were used across studies. Some RCTs conducted a comprehensive cognitive evaluation while others assessed outcomes on only specific cognitive domains. We could not compare the benefits of PA on different cognitive domains because we did not undertake a systematic review or meta-analysis. Further, the global cognitive function findings should be considered cautiously as some of the positive findings may be due to methodological issues, such as practice effects. As a result, the evidence for the benefits of PA on some cognitive outcomes is inconsistent across studies. These issues and questions should be considered in

future research. We also suggest that, in future trials, researchers use at least validated PA and outcome measures before testing the benefits of PA interventions.

Issues of confounders in some studies are worth noting. First, it is unclear whether some confounders were selected based on the knowledge of the field or a conceptual framework or causal model. Second, some important confounders were not examined, such as comorbidities. Finally, some confounders were not defined or measured accurately. These issues may lead to incorrect conclusions about the effects of PA on outcomes and therefore need to be addressed in future research<sup>138</sup>.

Of those PA studies identified, the majority examined some aspects of cognitive health outcomes and less often focused on non-cognitive health outcomes such as physical health, mental health and quality of life. This is not surprising because cognitive health outcomes are most relevant to older adults with MCI or SCD. However, to improve the overall health and wellbeing of this older population, other health outcomes should be emphasised. More research investigating broad outcomes is needed to provide strong evidence in support of the PA guidelines.

#### **5.4 Effects of physical activity interventions**

We have identified 24 RCTs investigating the effects of PA, most of which reported positive, statistically significant effects on some health outcomes in older adults with MCI or SCD. However, this does not necessarily signify clinical significance. It is noteworthy that there is a paucity of research examining the effects of balance-related PA compared with other types of PA, such as aerobic exercise and resistance training. In addition, the dose-response relationship is not well examined in different types of PA. Rigorous research on these areas is warranted to establish the evidence, which would increase our confidence in suggesting the benefits of balance-related PA and recommending appropriate levels of different types of PA to optimise benefits for older adults with MCI or SCD.

#### **5.5 Adverse events**

Similar to existing guidelines for older adults in general, our guidelines for older adults with MCI or SCD noted few adverse events for undertaking PA at a certain level. We made this judgement based on the information available in some but not all identified PA studies. We strongly recommend that future studies report adverse

events, including if the frequency is negligible. This will improve transparency of the studies and facilitate guideline developers to make more accurate guideline recommendations.

## **5.6 Pragmatism of randomised controlled trials**

There is debate about the pragmatism of RCTs because the research intervention is usually implemented in a controlled setting with experienced investigators and highly selected participants <sup>139</sup>. Future studies need to explore the benefits of PA in the ‘real world’ where a broader older adult population with MCI or SCD is involved and the PA or exercise is less structured and less supervised.

## **5.7 Balance of research efforts**

While research testing the benefits of PA interventions in older adults with or without health conditions is ongoing, there is clearly a lack of research focusing on PA-related behaviour change, and strategies for translating, disseminating, implementing and scaling up effective public health practice and policy for PA promotion. We did not find a well-designed study primarily examining these topics although we identified some RCTs and observational studies incidentally discussing these issues. It is important that researchers place more focus on undertaking such studies in the future. It is similarly vital that funding agencies facilitate this type of research <sup>140</sup>.

## **5.8 Healthy lifestyle approach**

While there are numerous benefits for undertaking PA, it should be noted that PA is only one part of a healthy lifestyle. It may interact with other positive lifestyle factors or behaviours such as healthy diet, non-smoking, moderate alcohol intake and quality sleep. Some large lifestyle-based multimodal intervention trials, which target individuals at increased risk of dementia, are being undertaken in several countries such as Finland (Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability/FINGER), France (Multidomain Alzheimer Preventive Trial/MAPT), the Netherlands (Prevention of dementia by intensive vascular care/PreDIVA), Europe (Healthy Ageing Through Internet Counselling in the Elderly/HATICE) and Australia (Maintain Your Brain) <sup>141, 142</sup>. Similar large-scale intervention trials could be designed and conducted for older adults with MCI or

SCD. The research findings would inform the development of more comprehensive and targeted guidelines for a larger segment of the older population with MCI or SCD.

## **5.9 Literature review process**

These guidelines are based on the Canadian Guidelines, adapted to incorporate evidence specific to the target population. Consequently, we did not conduct a systematic review or meta-analysis. However, we developed a comprehensive literature search strategy and study selection criteria. We performed the literature search in two representative databases (Medline Complete and CINAHL Complete), both providing access to top-tier biomedical and health journals and covering subjects relevant to our project topic. We also undertook rigorous literature screening and review processes by involving team members who have expertise in guideline development, systematic review methodology, physical activity, cognitive health, mental health and clinical medicine.

We acknowledge the importance of adhering to internationally well-established standards to undertake systematic reviews or meta-analyses. The literature review method and process we used could serve as a starting point for researchers to work towards achieving this ambitious goal in the future.

## **6. Applicability**

### **6.1 Facilitators and barriers to the application of our guidelines**

According to the literature <sup>143</sup>, factors such as stakeholder involvement in the development of the guidelines, evidence synthesis of the guidelines, considered judgement, implementation feasibility, and guideline messages and format are likely to influence use of the guidelines. Although it is beyond the scope of our project to research these factors, we were aware of them during the development of our guidelines. We also made every effort to address the potential barriers associated with these factors.



## **6.2 Dissemination of our physical activity guidelines**

Avenues for the dissemination of our guidelines and relevant materials will include: 1) scientific and health and aged care industry conferences, 2) academic and industry publications, 3) social media, 4) websites of the State and Commonwealth governments, and research institutes/organisations (e.g., NHMRC National Institute for Dementia Research (NNIDR), NHMRC Centre for Research Excellence in Cognitive Health (CRE), DCRC, AUPOA and NARI), 5) education and training programs for health practitioners (e.g., Master of Ageing program provided by The University of Melbourne (UoM) and training programs provided by the UoM Department of Psychiatry and NARI), 6) professional associations (e.g., Sports Medicine Australia) and physical activity provider groups outside the health system (e.g., Healthy Ageing Online Network (HANet)), and 7) mailings to key stakeholders in the areas of aged care, primary care, sports, recreation, exercise physiology, physiotherapy and sports medicine.

## **6.3 Resource implication of applying our physical activity guidelines**

Given the limited timeframe and resources, we did not investigate resource implications of implementing our PA guidelines. This is an area requiring new research in the near future.

## **6.4 Monitoring and/or evaluation of the application of our physical activity guidelines**

The aim of our project was to develop PA guidelines for older adults with MCI or SCD, which did not include monitoring or evaluating the application of the guidelines. Following our project, we propose undertaking further research to evaluate the implementation of the guidelines in professional practice. We also propose initiating population-based measures of PA and evaluating the impact of the guidelines on health outcomes of older adults with MCI or SCD using data from these measures.

## **7. Editorial independence (funding body and conflicts of interests)**

The PA Guidelines project was funded by the NHMRC DCRCs, whose views had no influence on the implementation of this project or any aspects of the guidelines

developed from this project. All members of the PA guidelines project signed a Conflict of Interest Statement and declared no conflict of interests.

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## Appendix 1: Project team members

Team members	Credentials	Expertise/knowledge/skills	Affiliation
Prof Nicola Lautenschlager <b>(Project chair)</b>	MD, FRANZCP	Cognitive health, mental health, psychiatry	AUPOA, University of Melbourne
Prof Kaarin Anstey	PhD, BA (Hons)	Psychology, cognitive health and decline, public health and epidemiology	CRAHW, Australian National University
Prof Keith Hill	PhD, Grad. Dip. Physio. (Neuro), B. App. Sc. (Physio)	Physiotherapy, exercise prescription, guideline development	School of Physiotherapy and Exercise Science, Curtin University
Prof Dimity Pond	PhD	General Practice, guideline development	Discipline of General Practice, University of Newcastle
A/Prof Kay Cox	PhD, MPE, BEd, Dip PE	Exercise physiology, physical activity promotion	School of Medicine, University of Western Australia
A/Prof Kathryn Ellis	PhD, BAppSc (Hons), BAppSc, GradDipPsychAdv	Ageing cognition neuroscience, mental health, cognitive health	AUPOA, University of Melbourne
A/Prof Briony Dow <b>(advisory panel chair)</b>	BSW, MA, PhD	Psycho-social aspects of ageing, social work	NARI
Dr Diane Hosking	PhD	Psychology, cognitive ageing	CRAHW, Australian National University
Dr Terence Chong	MBBS, MPsychiatry, MBA, RANZCP Cert. Old Age Psych	Psychiatry	AUPOA, University of Melbourne
Dr Emily You	PhD, MSocMedHealthServMgmt, BPubMedMgmt	Public health aspects of health and ageing, systematic review methodology	AUPOA, University of Melbourne
Dr Eleanor Curran	MBBS BMedSc MPM FRANZCP Cert Psych Old	Psychiatry	AUPOA, University of Melbourne
Dr Elizabeth Cyarto	PhD, MSc, BSc (Hons Kin)	Healthy ageing and physical activity	Bolton Clarke Research Institute, NARI
Ms Jennifer Southam	BSc (Human Movement); Grad Dip Ed; Grad Dip Health Ed; BBSc, BAppSc (Psychology) (Hons)	Physical activity and cognition in older adults	AUPOA, University of Melbourne

Note: AUPOA: Academic Unit for Psychiatry of Old Age; CRAHW: Centre for Research on Ageing, Health & Wellbeing; NARI: National Ageing Research Institute; RDNS: Royal District Nursing Service

## Appendix 2. Advisory panel members (external reviewers)

Organisation	Representative	Type
Western Australian Department of Sport and Recreation	Ms Kirsty Martin	Policy maker
Victorian Department of Health and Human Services	Ms Diane Calleja, Ms Sarah Yallop	Policy maker
Consumer representatives	Verona Lea, Lora Yeung, Glenn Staunton, Sheila Harris, Ray Dawson, Jean Hendy and Robyn Whiteley	Consumer
Melbourne Health	Dr Dina LoGiudice	Geriatrician
AUPOA, The University of Melbourne	Ms Alissa Westphal	Occupational therapist
Centre for Research in Ageing and Cognitive Health, University of Exeter	Prof Linda Clare	Academic
Faculty of Medicine, The Chinese University of Hong Kong	Prof Linda C.W. Lam	Academic
Dornsife College of Letters, Arts and Sciences, University of Southern California	Prof Laura D. Baker	Academic
Aging, Mobility, and Cognitive Neuroscience Laboratory, The University of British Columbia	Prof Teresa Liu-Ambrose	Academic
Institute for Health and Ageing, Australian Catholic University	Prof Ester Cerin	Academic
Wicking Dementia Research and Education Centre, University of Tasmania	Dr Maree Farrow	Academic
NHMRC partnership Centre on Dealing with Cognitive and Related Functional Decline in Older People/ The university of Sydney	Prof Susan Kurrle	Academic

Note: the seven consumer representatives only reviewed the lay version guidelines rather than this guidelines document.

### Organisation of the advisory panel

Organisation of the advisory panel commenced in August 2016. The panel Chair, A/Prof Dow, sent an invitation letter to the potential panel members in October 2016. Information provided in the letter included the project background and team members, purpose of organising the advisory panel, and the role of the panel

members. All advisory panel members confirmed their participation before the end of May 2017.

The advisory panel consisted of policy makers, consumers, health professionals, and academics with expertise of cognitive health, mental health and/or physical activity. They were independent from the project team and were not involved in any aspects of the development of our guidelines. It should be noted that the Chair of the advisory panel, A/Prof Dow, was part of the project team and participated in the development of the guidelines.