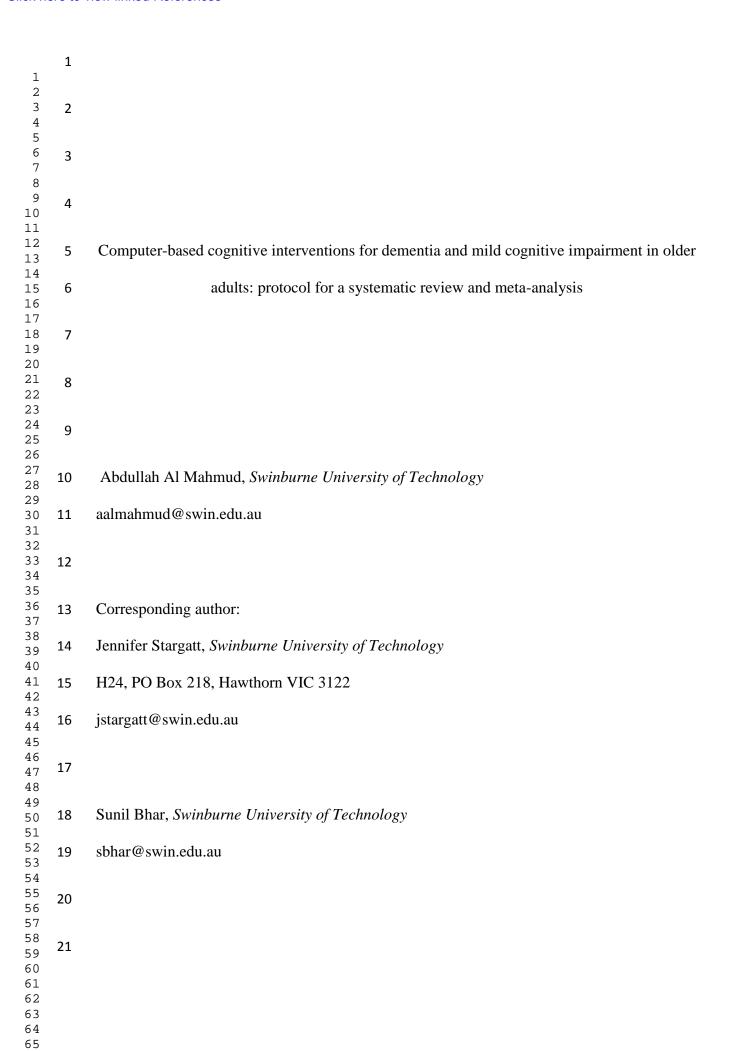
## **Systematic Reviews**

# Computer-based cognitive interventions for dementia and mild cognitive impairment in older adults: protocol for a systematic review and meta-analysis --Manuscript Draft--

Manuscript Number:	SYSR-D-16-00309
Full Title:	Computer-based cognitive interventions for dementia and mild cognitive impairment in older adults: protocol for a systematic review and meta-analysis
Article Type:	Protocol
Abstract:	Background: A growing number of older adults experience neurocognitive disorders such as dementia and mild cognitive impairment (MCI). Recent technological advances allow for traditional cognitive interventions to be administered via computers and other devices. We aim to explore the effect of computer-based cognitive interventions on cognition for older adults with dementia or MCI. Methods: We will systematically search chosen electronic databases to identify randomised and quasi-randomised controlled trials, cluster-randomised trials, and cross-over trials that meet our inclusion criteria. We will screen for studies that examine the use of computer-based cognitive interventions for adults aged over 60 with MCI or dementia at any level of severity and type. Primarily, we will examine the effects of such interventions on cognitive function (e.g., memory, executive function). Secondarily, we will examine outcomes such as mood and quality of life. Risk of bias will be assessed using Downs and Black's checklist for the assessment of the methodological quality of randomised and non-randomised studies. After data extraction we will pool the data and conduct a meta-analysis, with subgroup analysis where possible in order to explore differences for disorder type (dementia vs. MCI) and intervention type (cognitive stimulation, cognitive training, cognitive rehabilitation, cognitive recreation). Finally, we will assess the quality of the evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system.  Discussion: This systematic review will be the first to explore the effect of computer-based cognitive interventions for older adults with dementia and MCI. Results from this review will provide the basis for future research in developing computer-based interventions for this population.  Systematic review registration: PROSPERO CRD42016050236  Keywords: dementia, cognition, impairment, mild cognitive impairment (MCI), computer-based intervention, technology, stimulation, therapy

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22 Abstract

Background: A growing number of older adults experience neurocognitive disorders such as dementia and mild cognitive impairment (MCI). Recent technological advances allow for traditional cognitive interventions to be administered via computers and other devices. We aim to explore the effect of computer-based cognitive interventions on cognition for older adults with dementia or MCI. Methods: We will systematically search chosen electronic databases to identify randomised and quasi-randomised controlled trials, cluster-randomised trials, and cross-over trials that meet our inclusion criteria. We will screen for studies that examine the use of computerbased cognitive interventions for adults aged over 60 with MCI or dementia at any level of severity and type. Primarily, we will examine the effects of such interventions on cognitive function (e.g., memory, executive function). Secondarily, we will examine outcomes such as mood and quality of life. Risk of bias will be assessed using Downs and Black's checklist for the assessment of the methodological quality of randomised and non-randomised studies. After data extraction we will pool the data and conduct a meta-analysis, with subgroup analysis where possible in order to explore differences for disorder type (dementia vs. MCI) and intervention type (cognitive stimulation, cognitive training, cognitive rehabilitation, cognitive recreation). Finally, we will assess the quality of the evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. **Discussion:** This systematic review will be the first to explore the effect of computer-based cognitive interventions for older adults with dementia and MCI. Results from this review will provide the basis for future research in developing computer-based interventions for this population.

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**Keywords:** dementia, cognition, impairment, mild cognitive impairment (MCI), computer-based intervention, technology, stimulation, therapy

48 Background

Globally, the number of older persons—aged 60 and over—is growing faster than any other age group [1]. In line with population aging, the prevalence of later-life cognitive disorders can be expected to increase. Dementia, which is referred to as Major Neurocognitive Disorder in the *Diagnostic and Statistical Manual of Mental Disorders* (5<sup>th</sup> ed.; *DSM-5*), is the significant impairment of cognitive performance in one or more cognitive domains (e.g., complex attention, learning and memory, executive function, language), ultimately resulting in functional incapacity and death [2]. Whilst many forms of dementia exist, the most common form is seen in Alzheimer's disease, where it affects 6-9% of adults aged over 60 worldwide [3]. Similarly, Mild Cognitive Impairment (MCI) involves cognitive decline that is greater than that which occurs in normal aging, but does not significantly interfere with daily functioning [4]. It is estimated that MCI affects 3-42% of older adults, and precedes the onset of dementia in a number of cases [5].

Cognitive interventions for conditions such as dementia and MCI aim to maximise current function and reduce the risk of further cognitive decline [6]. In recent years, advances in computer technology have allowed such interventions to be administered using personal computers, laptops, tablets and other mobile devices, in an increasingly accessible, individualised and cost-effective manner. Studies suggest that such computer-based interventions may be beneficial for improving cognitive abilities such as memory, attentional control, executive function, for both those with dementia and MCI [7-11].

A recently published systematic review and meta-analysis of computer-based cognitive interventions for dementia reported significant improvements in the areas of

cognition, depression and anxiety, and found that computer-based interventions may improve cognition superior to non-computer-based interventions [12]. We plan to build upon the work of García-Casal and colleagues [12] by producing an updated review. As this is a fast-developing field of research, we anticipate that further studies relevant to this review will have been published since 2014. Notably, this review will also include studies of older adults with MCI.

76 Method

### **Objectives**

 The purpose of the systematic review and meta-analysis is to review the current evidence regarding computer-based cognitive interventions for older adults with dementia and MCI. It aims to explore whether computer-based cognitive interventions improve cognitive ability for older adults with dementia and MCI, compared to non-computer-based interventions. The aim of this systematic review protocol is to transparently present the method we will undertake in order to conduct the systematic review, such that it could be adequately replicated. This method includes information regarding eligibility criteria, information sources and search strategy to be used, and the process of data extraction, synthesis, and analysis.

#### **Protocol and registration**

This protocol was developed in adherence with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) guidelines (see additional file 1) [13]. The review will also adhere to the guidelines specified by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [14]. This review has been registered with the International Prospective Register of Systematic Reviews (PROSPERO; CRD42016050236).

#### Eligibility criteria

Types of studies. We will include randomised and quasi-randomised controlled trials, cluster-randomised trials, and cross-over trials. We will exclude single-subject case studies.

**Population.** We will include studies of individuals identified as having MCI and/or any form of dementia at any level of severity and type, such as dementia in Alzheimer's disease, and vascular dementia. Participants of included studies will be at least 60 years of age. Studies that include participants below the age of 60 will be included if the mean age of participants is 60 or over.

**Intervention.** The target intervention is computer-based, that is, utilising screenbased technology such as personal computers, laptops, and other devices such as tablets and mobile phones. The intervention must be designed to address cognition and improve aspects of cognitive function, such as memory, attention and executive function. We will use the classification method specified by García-Casal et al. [12], where interventions were categorised as either cognitive stimulation, cognitive recreation, cognitive rehabilitation, or cognitive training [12]. We will exclude any studies where participants were provided with the target intervention alongside another intervention if results are only given for the interventions combined, due to potential difficulty clarifying whether the outcomes are a result of the target intervention or the other intervention.

**Comparator groups.** The comparator groups are likely to comprise participants receiving care-as-usual, participants receiving a cognitive intervention that is noncomputerised, and participants receiving pharmacological interventions.

**Outcomes.** The primary outcome measures of interest will be those that measure the participants' cognitive ability (e.g., memory, attention, and executive function) using standardised measures such as the Mini Mental State Examination (MMSE) [15]. Secondary

 outcome measures which may be included are those such as participant mood, quality of life, and mental illness such as depression and anxiety, also using standardised measures. Other outcomes may include changes in specific activity-related function. Included studies will report pre- and post-treatment scores.

**Report characteristics.** We will include full-text articles in the English language, and there will be no geographical or date limitation on the included studies.

#### Search methods for identification of studies

We will conduct a systematic search of the following databases: The Cochrane Library, PubMed, EMBASE, MEDLINE, PsycINFO, ScienceDirect, the Specialised Register of the Cochrane Dementia and Cognitive Improvement Group, CINAHL, ACM Digital Library, IEEE Xplore Digital Library, Web of Science, and Springer Link. We will also search the following databases for additional grey literature: Open Grey. Reference lists of relevant literature will be examined in order to find any relevant publications that may have been missed in the initial source. No date restriction will apply. In instances where more information is required, we will correspond with the authors of the publication to obtain such information, where feasible.

A search strategy will be modified from that used by García-Casal et al. We will use key terms relevant to the topic, as identified by García-Casal et al., such as "dementia", "cognition", "computer", and "stimulation". We will add the term "mild cognitive impairment". An example of a database search is shown below:

(((dementia OR alzheimer\* OR "mild cognitive impairment")) AND (cognit\* OR memory OR "reality orientation" OR stimulat\* OR rehabilit\* OR train\*)) AND (comput\* OR technolog\* OR telerehab\*)

#### **Data collection and analysis**

**Selection of studies.** We will independently screen titles and abstracts to identify studies that may be relevant to the review, and full-text copies of the studies identified will be retrieved. We will then screen the full-text publications for their eligibility. We will use online screening and extraction software Covidence to conduct both stages of screening [16]. One reviewer will conduct all screening, and a second reviewer will conduct 20% of the screening at both stages, for the purposes of quality assessment. Discrepancies between the reviewers' decisions will be resolved by reaching consensus, or by obtaining the opinion of a third reviewer. Reasons for excluding any studies from the review at this stage will be noted and reported in the review. A flow chart illustrating the search and selection process of the review will be included.

Data extraction and management. We extract pre-defined data from studies chosen for inclusion in the review using the Covidence software. The following information will be extracted:

- 1. Publication details: authors, title, journal, year, publication type (e.g., peer-reviewed article, conference proceedings), geographical location in which the was conducted, and funding source.
- Study design: type of study (e.g., RCT, quasi-RCT)
- 3. Participant details: sample size, demographic information (e.g., age and gender of participants), condition (e.g., form of dementia and/or MCI).
- 4. Intervention details: technology and software used, aim of the intervention, dosage and timing of the intervention, information regarding the comparator group(s).
- 5. Outcome details: data for primary (cognitive ability) and secondary (e.g., mood, quality of life) outcomes including pre- and post-treatment scores.

 The first reviewer will independently extract data from all chosen studies. The second reviewer will extract data from 20% of the studies for quality assessment purposes. Discrepancies between the reviewers' extracted data will be discussed, and resolved by consensus or with the assistance of a third reviewer if necessary. We will contact study authors to obtain further information where necessary. The data will then be exported into the Review Manager (RevMan) program for further analysis [17].

Assessment of risk of bias in included studies. To assess the risk of bias of individual studies, we will use Downs and Black's checklist for the assessment of methodological quality of the included studies [18]. The checklist assesses study quality in respect to five domains—reporting biases, external validity, internal validity regarding selection bias and potential bias in measurement and outcomes, and statistical power. The checklist has demonstrated high internal consistency (K-R 20: 0.89), test-retest reliability (r = 0.88) and inter-rater reliability (r = 0.75) [18]. We will report on the assessed quality of the included studies overall, and provide summaries for the five quality domains. The second reviewer will assess 20% of included studies for the purposes of quality assessment, and both reviewers will reach consensus regarding the assessment of those studies by discussion or the opinion of a third reviewer.

Measures of treatment affect. Standardised mean differences (SMDs) will be calculated for continuous data where studies report the same outcome using various measures. If studies use the same outcome measure, the mean differences (MDs) will be calculated and used as the measure of treatment effect. If necessary, scores will be modified to ensure the direction of the effect is consistent.

**Dealing with missing data.** If there is missing data, we will attempt to contact the authors of the studies via e-mail for further information. We will also contact study authors to

provide clarification if any key information regarding their studies are unclear. We will indicate to any data that was provided after consultation with study authors.

**Data synthesis.** Studies will be meta-analysed using the RevMan software [17]. We will meta-analyse studies that report our outcomes of interest, primarily cognitive ability, to compare the effects of computer-based cognitive interventions with non-computer-based interventions. The meta-analyses will be conducted using an inverse-variance, random-effects model. We will calculate 95% confidence intervals and two-sided *p* values for each outcome. We will include forest plots to display the results of the meta-analyses. Where it is not appropriate to include studies in a meta-analysis, we will provide a narrative summary.

**Subgroup analysis.** If the data provided in the studies allows, we will also conduct the following subgroup analyses:

- Pre-treatment and post-treatment scores for computer-based interventions.
- Type of cognitive impairment—dementia or MCI
- Classification of computer-based cognitive intervention—i.e., cognitive training, cognitive rehabilitation.

Assessment of heterogeneity. Statistical heterogeneity will be examined using the chi-squared test and the I-squared statistic, and it will be examined for all studies included and for all subgroups analysed. A fixed-effects model will be run for the purposes of sensitivity analysis, and we will report relevant differences between the models.

**Assessment of reporting biases.** We will examine funnel plots of the included studies to evaluate potential publication bias.

**Assessment of the quality of the evidence.** We will use the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach, as

described in the Cochrane Handbook for Systematic Reviews and Interventions to evaluate the quality of the body of evidence [19]. In accordance with GRADE guidelines, rating the quality of the body of evidence for each outcome involves consideration of limitations in study design and implementation, directness of evidence, heterogeneity/inconsistency of results, precision of results demonstrated by confidence intervals, and the probability of publication bias. A summary of evidence based on these guidelines will be provided for all meta-analysed outcomes in the review.

Discussion

The rapidly growing number of older adults worldwide is likely to result in an increase in the prevalence of neurocognitive disorders such as dementia and MCI. Computer-based cognitive interventions may be effective for improving the lives of older adults with dementia and MCI, and may be favoured over traditional interventions for their accessibility and cost-effectiveness.

To our knowledge, this will be the first systematic review and meta-analysis of computer-based interventions for older adults with both dementia and MCI. Observing the methods detailed in this protocol, the review will present up-to-date evidence regarding the effects of computer-based cognitive interventions for older adults with dementia and MCI. The systematic review will be reported according to the PRISMA guidelines [14] and submitted for publication to an appropriate peer-reviewed journal. The findings of the systematic review will serve as a basis for further research regarding the development of computer applications for dementia and MCI.

233 Declarations

Ethics approval and consent to participate

Not applicable.

**Consent for publication** Not applicable. 6 7 Availability of data and materials 10 Not applicable. 13 **Competing interests** The authors have no competing interests. Funding This project received internal funding (Barbara Dicker Brain Science Foundation). **243 Authors' contributions** All authors devised the protocol. JS wrote the manuscript with assistance from other authors. All authors approved the final manuscript. Acknowledgements Not applicable. 40 249 

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