Protocol

Treatment of Mild Cognitive Impairment: Systematic Review and Meta-analysis

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Review methods

Key Questions

1. Do pharmacological or non-pharmacologic interventions for MCI in older adults improve: 1) cognition, 2) function, 3) behaviour, 4) global status, or 5) mortality?

    a. How effective are the screening tools validated for Canadian populations (e.g. MoCA) in improving: 1) cognition, 2) function, 3) behaviour, 4) global status, or 5) mortality?

2. What are the adverse events (AE) (serious including hospitalization or death and psycho-social harms such as depression, lack of independence, etc.) of pharmacological or non-pharmacologic interventions for MCI?
3. What are the diagnostic properties of screening tools validated in a Canadian population of adults older than age 65?
    a. What are the cut-offs for mild cognitive impairment in adults 65 years and over and how well they work (i.e. examine how well the screening tools differentiate between no cognitive impairment and mild cognitive impairment, and between mild and severe cognitive impairment).

Contextual Questions

Patient Preferences and Values

1. People's willingness to be screened for MCI and elements that factor into this decision process (I am willing because…; I am not willing because…)

2. People's willingness to be diagnosed for MCI (i.e. interest in knowing the diagnosis if MCI was found (given available treatment options) and elements that are factored into this decision process (I am willing because…; I am not willing because…)

Searches

Our search is based on the search conducted by the USPSTF for their 2013 systematic review entitled: Screening for Cognitive impairment in Older Adults: An Evidence Update for the U.S. Preventive Services Task Force. We are modifying their strategy to narrow it to those with MCI. We will search Medline and the Cochrane Databases of Systematic Reviews for the period of Dec 2012-Dec 2014.

The USPSTF put forward a recommendation for cognitive impairment in general (i.e. they didn't separate MCI from other types of cognitive of impairment (e.g. mild or moderate dementia)). Individuals with MCI have a level of cognitive impairment that does not interfere with their independence in daily living, which is a key difference between MCI and the other types of cognitive impairment. MCI and dementia are mutually exclusive.

The CTFPHC decided to develop a recommendation focusing on the MCI population for several reasons. First, there is evidence showing that MCI may predict later dementia (Ref). If clinicians are able to identify individuals with MCI early through screening and either slow down or stop the progression of MCI through effective treatment, the incidence of cognitive impairment (measured through cognition, function, behavior, and global status) may decline. Second, if individuals are identified at the MCI stage, when their comprehension and decision-making capacity and autonomy are not affected, they will have the opportunity to plan for the future in different areas of their lives (e.g. medical, legal, financial). Finally, clinicians may also benefit given that they have the opportunity to put in plan measures to address comorbidities in an effective way and without worsening cognitive impairment.

Condition or domain being studied

For the purpose of this review, cognitive impairment includes mild cognitive impairment (MCI). MCI includes problems with language, thinking, judgment and memory that are noticeable but do not affect daily living, whereas dementia occurs when the problems are sever enough to affect daily living. The Alzheimer's Society of Canada reported that 14.9% in Canadians over the age of 65 years suffered from cognitive impairment in 2011. This number is expected to increase with the aging population.

Participants/ population

Community-dwelling older adults, average age 65 years or older diagnosed with MCI. (MCI can be defined by the study authors or MCI as defined by DSM-V).

Community-dwelling older adults: Adults who live at home or in senior living communities, assisted living, adult foster care, or residential care facilities. This excludes institutionalized people who reside in intermediate care facilities (i.e., rehabilitation centers or skilled nursing facilities).

Intervention(s), exposure(s)

Pharmacologic interventions used to treat MCI for the purpose of preventing cognitive decline: approved drugs for use in Canada. Non-pharmacologic interventions aimed at patients MCI.

Comparator(s)/control

Placebo or usual care

Types of study to be included

RCTs

Context

Primary care, outpatient settings (ambulatory care), and home. This excludes hospitals, emergency departments, or specialty outpatient settings (i.e. memory, dementia, geropsychology, or neurology clinics).

Primary outcome(s)

Global Cognition score: measured with Mini Mental Status Examination (MMSE) or Alzheimer's Disease Assessment Scale — cognition subscale (ADAS-CS)

Adverse Events: Serious (i.e. hospitalization or death) and psycho-social harms (e.g. lack of independence, stress, depression, etc.).

For the outcome of Global Cognition there must be a minimum of 6 months post baseline data; no follow-up duration needed for harms data

Secondary outcomes

Function measured with Alzheimer's Disease Cooperative Study activities of daily living inventory); behaviour measured by Neuropsychiatric Inventory; Global Status (measured by Clinician's Interview-based Impression of Change plus Caregiver) and mortality.

Studies with at least 6 month post baseline data for benefits; no duration of follow-up for harms

Data extraction (selection and coding)

The titles and abstracts of papers considered for the key question and sub-questions will be reviewed in duplicate; any article marked for inclusion by either team member will be moved to full text screening. Full text review will be done independently by two people with consensus required for inclusion or exclusion. Review team members will extract data about population, study design, intervention, analysis and results for outcomes of interest. One team member will complete full abstraction, followed by a second team member who verified all extracted data and ratings.

Risk of bias (quality) assessment

We will be using the Cochrane Risk of Bias tool for quality assessment. High risk of bias studies with major methodological flaws such as inadequate randomization technique or allocation concealment and high attrition rates or drop outs (30% or more with no intention-to-treat analysis) may be excluded following this assessment. In that case, studies with either low or unclear risk of bias will be included in and that will be analyzed.

Strategy for data synthesis

For the continuous outcomes of benefit of treatment and management of mild cognitive impairment such as cognition; function; behaviour; and global status, we will utilize immediate post-treatment data and longest follow-up data (means, standard deviations) and extracted data will be meta-analyzed when appropriate. Where meta-analysis is not possible the data will be provided in a narrative summary.

Analysis of subgroups or subsets

For outcomes of benefit of treatment and management of mild cognitive impairment sub-group and sensitivity analyses based on intervention intensity, length of follow-up, and study risk of bias will be conducted where possible to evaluate statistical stability and effect on statistical heterogeneity. The Cochrane's Q (a=0.05) will be employed to detect statistical heterogeneity and I^2 statistic to quantify the magnitude of statistical heterogeneity between studies where 12>50% represents moderate and 12>75% represents substantial heterogeneity across studies.