Population screening for dementia in adults: Evidence Map

ADMINISTRATIVE INFORMATION

1. Title

1a. Identification

Evidence map: Population screening for dementia in adults

1b. Update

Update to: Solutions for Public Health (2018) Screening for dementia: External review against programme appraisal criteria for the UK National Screening Committee. October 2018.

2. Registration

As this is an evidence map formal registration (e.g. PROSPERO) is not required. However, in accordance with the funder principles of open science the map will be made accessible via Open Science Framework (OSF) Registries and protocols.io, which presents generic registers open to any study type. The protocol will also be available via the Evidence Synthesis Group (EnSygN - Sheffield) website. Publication timelines will be agreed with the UK NSC.

3. Authors

3a. Contact

Duncan Chambers, Sheffield Centre for Health and Related Research (SCHARR), D.Chambers@sheffield.ac.uk, School of Medicine and Population Health, University of Sheffield, Regent Court, 30 Regent Street, Sheffield, UK S1 4DA

Burak Kundacki, Sheffield Centre for Health and Related Research (SCHARR), University of Sheffield, B.Kundacki@sheffield.ac.uk

Katherine L Jones Sheffield Centre for Health and Related Research (SCHARR), University of Sheffield, K.L.Jones@sheffield.ac.uk

Anna Cantrell, Sheffield Centre for Health and Related Research (SCHARR), University of Sheffield, A.J.Cantrell@sheffield.ac.uk;

Anastasios Bastounis Sheffield Centre for Health and Related Research (SCHARR), University of Sheffield, A.Bastounis@sheffield.ac.uk

Professor Andrew Booth, Sheffield Centre for Health and Related Research (SCHARR), University of Sheffield,, University of Sheffield, A.Booth@sheffield.ac.uk;

3b. Contributions:

Professor Andrew Booth drafted the protocol in conjunction with the UK National Screening Committee (UK NSC) Evidence Team. All other authors contributed to the final protocol. All authors will contribute to production of the review. Professor Andrew Booth will advise on the methodology. Mrs Anna Cantrell will design and conduct the literature searches.

Professor Andrew Booth is the guarantor for the review.

4. Amendments

Amendments will be made as required with the agreement of both the UK National Institute for Health and Care Research (NIHR) and the UK NSC.

5. Support

5a. Sources

Funded under the Evidence Synthesis Group (EnSygN - Sheffield) from the NIHR Evidence Synthesis Programme.

5b. Sponsor

National Institute of Health and Care Research (NIHR) Evidence Synthesis Programme

5c. Role of sponsor or funder

The NIHR identifies topics for review in conjunction with other stakeholders (i.e. the UK NSC). The protocol is developed by academics at the University of Sheffield and the UK NSC Evidence Team. The report will be drafted by the authors and shared with the UK NSC Evidence Team for input. The NIHR and UK National Screening Committee suggests revisions to improve the applicability and scope of the review.

INTRODUCTION

6. Rationale

Dementia is a progressive clinical syndrome characterised by an ongoing decline of brain functioning which interferes with activities of daily living. The United Kingdom is projected to experience an increase in the number of individuals living with dementia from 2019 to 2050, in line with global trends (Nichols et al, 2022). The last UK NSC review of dementia occurred in April 2019 and concluded that there remained key areas of concern regarding screening for dementia. These included uncertainties about the prognosis of Mild Cognitive Impairment (MCI) and its subtypes in relation to dementia, the potential from further research into biomarkers and imaging techniques and the acceptability of screening for dementia in the UK. Therefore, an evidence map will be conducted to determine if further work on the topic is justified.

7. Objectives

The aim of this evidence map is to assess the volume and type of evidence relevant to general population screening for dementia in adults. The key questions are:

1. What is the volume and type of evidence available on the accuracy of screening tests (e.g. sensitivity, specificity etc.) used to detect mild cognitive impairment (MCI) and/or any type of dementia?
2. What is the volume and type of evidence available on the pharmacological and non-pharmacological interventions used to treat asymptomatic or pre-symptomatic adults with MCI and/or any type of dementia identified through screening?

A companion 'horizon scanning evidence map' exploring the available evidence of active/on-going clinical trials, observational studies or systematic reviews investigating innovations in screening and/or diagnostic tests for MCI and/or any type of dementia, including new proposed medical interventions will be conducted alongside this mapping review. It will be a separate protocol in view of differences in the purpose and likely sources between a horizon scanning evidence map and a mapping review.

METHODS

8. Eligibility criteria

The evidence map will include studies from the UK or comparable countries[1] published in English between January 2018 and June 2024. The populations, index tests, target conditions, outcomes and study designs of interest are detailed below.

[1] For the purposes of this map comparable countries comprise: those in North America (United States and Canada), Scandinavia (Denmark, Norway, Sweden), Western Europe (Austria, Belgium, France, Germany, Italy, Liechtenstein, Monaco, Netherlands, Portugal, Spain, Switzerland), Australia and New Zealand.

Question 1: Screening tests/technologies for dementia	**Question 2: Pharmacological and non-pharmacological interventions for dementia**
Population:	**Population:**
• Adults living in the community who are not already suspected of having dementia and/or mild cognitive impairment	• Presymptomatic/asymptomatic adults (early symptomatic if no evidence on presymptomatic/ asymptomatic adults)
• Do not have any co-morbidity affecting cognitive performance	• Ideally, those identified through screening, but if no evidence is found, other early symptomatic/non-screened populations may be considered
Index tests:	**Interventions:**
Any biomarker used as a screening tool (e.g., blood-based)	Any pharmacological approach
Brain imaging, including PET and MRI	Any non-pharmacological approaches (e.g., occupational therapy, social support, assistance with daily activities, home nursing)
Cognitive assessment tools (e.g., Mini-Mental State Examination, clock drawing test)	
Any screening tool/questionnaire that can be self-administered or delivered by a clinician in a primary care setting	
Reference standard: Formal diagnosis of MCI or dementia in accordance with UK guidelines, e.g. criteria from the Diagnostic and Statistical Manual of Mental Disorders' (DSM)	
Target conditions:	**Target conditions:**
a) Dementia	a) Dementia
b) Mild Cognitive Impairment (MCI)	b) Mild Cognitive Impairment (MCI)
Outcomes:	**Outcomes:**
Sensitivity	Reduce cognitive decline
Specificity	Improved physical function
Positive and negative predictive values	Reduced depression
Likelihood ratios	Reduced challenging behaviour (e.g., aggression, restlessness, wandering)
Area under the curve (AUC)	Improved independence and general quality of life (QoL)
	Reduced mortality
	Any other outcomes reported in the studies
Study designs:	**Study designs:**

Priority given to studies in randomly assigned or consecutively enrolled populations	Randomized controlled trials (priority) Cohort studies
Priority given to systematic reviews of these studies	Systematic reviews of the above
If few of these designs are found, other study designs such as case-control studies may be reported	If few of these designs are found, other study designs such as case-control studies may be reported

9. Information sources

Electronic databases including MEDLINE (Ovid) 2018-2024, EMBASE (Ovid) 2018-2024; PsycINFO (Ovid) 2018-2024, Cochrane Library (including: Cochrane Database of Systematic Reviews (CDSR) and Cochrane Central Register of Controlled Trials (CENTRAL)) 2018-2024 and Web of Science 2018-2024. All databases will be searched from January 2018 to June 2024.

Clinical trial registries: ClinicalTrials.gov, ISRCTN, EU Clinical Trials Register, Clinical Trials Information System (CTIS)

All entries from 2018-2024.

Key organisational websites e.g. Alzheimer's Society, Alzheimer's Research UK, Alzheimer's Association, WHO, FDA, EMA etc. . Studies from the UK will be prioritized; studies from comparable countries will be reported if UK studies are absent. A hierarchical approach to study designs will be utilised, prioritising randomized or consecutively enrolled populations and systematic reviews and reporting other study designs if higher-quality designs are not found.

10. Search strategy

[PRESENT DRAFT SEARCH STRATEGY FOR ONE DATABASE INCLUDING LIMITS]

Table A. Medline search terms for key question 1

Database: Ovid MEDLINE(R) Epub Ahead of Print and In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <June 25, 2024>
Search Strategy:

1 *Cognitive Dysfunction/ (35988)
2 (mild* adj2 (cognitive* impair* or cognitive dysfunction*)).ti. (11424)
3 (cognitive* impair* or cognitive dysfunction*).ti. and (adult/ or middle aged/ or young adult/) (9240)
4 *dementia/ or *alzheimer disease/ or exp *dementia, vascular/ or *lewy body disease/ (160247)
5 (dementia*1 or alzheimer*2 or lewy body).ti. (154167)
6 MCI.ti. (1455)
7 *Cognition Disorders/ (47954)
8 1 or 2 or 3 or 4 or 5 or 6 or 7 (256119)
9 mass screening/ or multiphasic screening/ (119364)
10 diagnosis/ or delayed diagnosis/ or early diagnosis/ or Diagnostic Tests, Routine/ or *Prognosis/

11 (screen*3 or detect*3 or test*3 or identif*3 OR predict*3 OR question*5 or instrument*2 or exam*1 or examination*1 or surveillance).ti,ab.
12 (early adj2 diagnos*3).ti,ab. (141276)
13 diagnos*3.ti. (698473)
14 9 or 10 or 11 or 12 or 13 (9034896)
15 exp Neuropsychological Tests/ (195380)
16 ((cognitive assess* or neuropsycholog*) adj2 (tool? or toolkit? or question* or instrument? or interview? or screen*3)).ti,ab. (2351)
17 ("general practitioner assessment of cognition" or gpcog or "memory impairment screen" or mis or mini-cog or "short form of the informant questionnaire on cognitive decline in the elderly" or short 1qcode or "eight-item informa interview to differentiate aging and dementia" or ad8 or "mini-mental state*exam" or mmse or clock drawing).ti,ab. (35991)
18 15 or 16 or 17 (225412)
19 exp Biomarkers/ (909926)
20 exp Neuroimaging/ (201475)
21 brain/ (566443)
22 magnetic resonance imaging/ or exp tomography, emission- computed/ (604762)
23 21 and 22 (109839)
24 (biomarker? or biological marker?).ti,ab. (445807)
25 ((brain or neurolog*) adj5 (magnetic resonance imaging or mri or pet or tomogra*)).ti,ab. (66582)
26 (neuroimag* or neuro-imag*).ti,ab. (68613)
27 19 or 20 or 23 or 24 or 25 or 26 (1505897)
28 exp Animals/ (27292478)
29 humans.sh. (22057783)
30 28 not 29 (5234695)
31 exp "Sensitivity and Specificity"/ (659568)
32 sensitivity.tw. (1035623)
33 specificity.tw. (582032)
34 ((pre-test or pretest) adj probability).tw. (3000)
35 post-test probability.tw. (759)
36 predictive value$.tw. (144819)
37 likelihood ratio$.tw. (20648)
38 31 or 32 or 33 or 34 or 35 or 36 or 37 (1810942)
39 8 and 14 and 18 and 38 (6146)
40 8 and 14 and 27 and 38 (3738)
41 39 or 40 (8761)
42 (editorial or comment or letter).pt. (2257748)
43 41 not 42 (8685)
44 exp Animals/ (27292478)
45 humans.sh. (22057783)
46 44 not 45 (5234695)
47 43 not 46 (8632)
48 limit 47 to english language (8300)
49 limit 48 to yr="2018 -Current" (2743)

Table B. Medline search terms for Questions 2

Database: Ovid MEDLINE(R) Epub Ahead of Print and In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <June 25, 2024>

Search Strategy:

1 *Cognitive Dysfunction/ (35988)

2 (mild* adj2 (cognitive* impair* or cognitive dysfunction*)).ti. (11424)

3 (cognitive* impair* or cognitive dysfunction*).ti. and (adult/ or middle aged/ or young adult/) (9240)

4 *dementia/ or *alzheimer disease/ or exp *dementia, vascular/ or *lewy body disease/ (160247)

5 (dementia*1 or alzheimer*2 or lewy body).ti. (154167)

6 MCI.ti. (1455)

7 *Cognition Disorders/ (47954)

8 1 or 2 or 3 or 4 or 5 or 6 or 7 (256119)

9 mass screening/ or multiphasic screening/ (119364)

10 diagnosis/ or delayed diagnosis/ or early diagnosis/ or Diagnostic Tests, Routine/

11 (screen*3 or detect*3 or test*3 or identif*3 OR predict*3 or question*5 or instrument*2 or exam*1 or examination*1 or surveillance).ti,ab. (8511849)

12 (early adj2 diagnos*3).ti,ab. (141276)

13 diagnos*3.ti. or *Prognosis/

14 9 or 10 or 11 or 12 or 13 (9034896)

15 Cognitive Dysfunction/dh, dt, rh, th [Diet Therapy, Drug Therapy, Rehabilitation, Therapy] (6082)

16 Dementia/dh, dt, rh, th [Diet Therapy, Drug Therapy, Rehabilitation, Therapy] (14413)

17 Alzheimer Disease/dh, dt, rh, th [Diet Therapy, Drug Therapy, Rehabilitation, Therapy] (28236)

18 Dementia, Vascular/dh, dt, rh, th [Diet Therapy, Drug Therapy, Rehabilitation, Therapy] (1169)

19 Lewy Body Disease/dt, rh, th [Drug Therapy, Rehabilitation, Therapy] (564)

20 Cognition Disorders/dh, dt, rh, th [Diet Therapy, Drug Therapy, Rehabilitation, Therapy] (9783)

21 Cholinesterase Inhibitors/ (23425)

22 ((cholinesterase or acetylcholinesterase) adj inhibitor?).ab,ti. (10351)

23 AChE inhibitor*.ab,ti. (2630)

24 Donepezil/ (2988)

25 (donepezil or aricept or adlarity or eisai).ab,ti. (5099)

26 Galantamine/ (1722)

27 (galantamine or reminyl or razadyne or shire).ab,ti. (2329)

28 Memantine/ (2703)

29 (memantine or ebixa).ab,ti. (4198)

30 Rivastigmine/ (1301)

31 (rivastigmine or exelon).ab,ti. (2085)

32 namzaric.ab,ti. (5)

33 donanemab.ab,ti. (107)

34 ((pharmacolog* or drug?) adj2 (therap* or treatment)).ti,ab. (183674)

35 exp Rehabilitation/ (364616)

36 exp Home Nursing/ (9555)

37 exp Social Support/ (81734)

38 rehabilitation.ab,ti. (207840)

39 ((occupational or art or dance or music) adj therap*).ti,ab. (22695)

40 (("activity of daily living" or "activities of daily living" or adl) adj3 (support or service? or intervention? or program*)).ti,ab. (764)

41 "social support".ti,ab. (55962)

42 home nurs*.ti,ab. (1885)

43 ((nonpharmacolog* or non-pharmacolog*) adj2 (treatment or therap*)).ti,ab. (6738)

44 (therap* or treatment or management or intervention).ti. (2831546)

45 ((multicomponent or multi component or multidisciplinary or multi disciplinary or multimodal or multi modal) adj3 (treatment* or program* or intervention*)).ti,ab. (29375)

46 or/15-45 (3522384)

47 8 and 14 and 46 (25818)

48 (MEDLINE or systematic review).tw. or meta analysis.pt. (476631)

49 47 and 48 (1290)

50 randomized controlled trial.pt. or randomized controlled trial.mp. or Epidemiologic studies/ or exp case control studies/ or exp cohort studies/ or Case control.tw. or (cohort adj (study or studies)).tw. or cohort analy*.tw. or (follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or retrospective.tw. or cross sectional.tw. or cross-sectional studies/

51 47 and 50 (3237)

52 49 or 51 (4488)

53 (editorial or comment or letter).pt. (2257748)

54 52 not 53 (4483)

55 exp Animals/ (27292478)

56 humans.sh. (22057783)

57 55 not 56 (5234695)

58 54 not 57 (4464)

59 limit 58 to yr="2018 -Current" (1888)

60 limit 59 to english language (1836)

11. Study records

11a. Data management

Data management: Search results will be collated in EndNote reference management software. Screening decisions will be recorded in Eppi-Reviewer. Review data will be managed through folders in Google Drive.

11b. Selection process

Initial screening: Reviewers will split the titles and abstracts equally. First, each reviewer will independently screen 20% of their allocated set.

Quality control: After initial screening, the reviewers will work in pairs to compare 20% of the other's screened titles and abstracts. This overlap allows for consistency checking without duplicating all work.

Resolving discrepancies: If the agreement on the 20% overlap is high (e.g., >90%), the team members will process the remaining 80% of titles and abstracts between them. If agreement is lower, they will discuss discrepancies and potentially re-screen a portion of the studies.

As this is a mapping review it will not always be necessary to consult with the full text for eligible items. If it has been necessary to consult the full text to identify this relevant information/data, the team will state this. A proportion of eligible full-texts where title/abstract information was incomplete will be split between subteams of two reviewers. Each reviewer will independently assess their allocated full-texts. Full-text quality control: The team will compare 30% of the other's full-text decisions. This higher percentage at the full-text stage helps ensure important studies aren't missed.

Documentation: The team will keep clear records of the number of records identified by database before deduplification, number of studies screened, included, and excluded at each stage. They will note reasons for exclusion at the full-text stage and include these in the PRISMA flowchart.

11c. Data collection process

The review team will develop and pilot a simplified data extraction input form using EPPI-Reviewer focusing on key items relevant to the mapping review questions.

Extraction quality control: Reviewers will cross-check 10% of each other's data extractions, focusing only on the key items. This approach ensures accuracy without the need for full double data extraction.

Discrepancy resolution: If agreement on the cross-checked items is high (e.g., >90%), proceed with analysis. If lower, the team will discuss discrepancies and consider reviewing a larger sample or having a third reviewer arbitrate.

Mapping and synthesis: The review team will use the extracted key items to create evidence summaries. The focus of the mapping review will be on describing the overall landscape of evidence rather than detailed analysis of individual study results.

Documentation: At all times the team will clearly document the process, including the percentage of studies cross-checked at each stage. They will note any limitations of this streamlined approach in the final report.

12. Data items

Key items will include:

- Study design
- Population characteristics
- Intervention/index test/Reference standard
- Main outcomes
- Key findings (briefly summarized)

Abbreviated reference to the study; Study type; Objectives; Components of the study; Outcomes reported; Conclusions; Overall findings of the study.

Outcomes reported, as specified by the commissioning document, for example:

- for diagnostic studies include sensitivity, specificity, PPV, NPV
- for epidemiological studies include prevalence, incidence etc.
- for screening/treatment interventions include quality of life, patient-reported outcomes, improvement of symptoms/development of disease, benefits/harms, adverse effects/unintended consequences, etc and the relevant measures of association and variability
- for cost-effectiveness studies, include cost-effectiveness analyses, technology assessments, systematic reviews and meta-analyses, modelling studies

If outcomes as specified by the commissioning document are not reported in the abstract, this will be stated. Specifically, the following data items will be sought:

- For question 1: Screening test accuracy data including sensitivity, specificity, predictive values, likelihood ratios, AUC
- For question 2: Efficacy/effectiveness outcomes of interventions including cognitive function, physical function, depression, challenging behaviours, independence, quality of life, mortality

Contextual information will be provided to describe each tool/intervention.

13. Outcomes and prioritization

Question 1: Accuracy of screening tests for MCI and dementia	
Main Outcomes:	
Sensitivity: Proportion of people with dementia or MCI who are correctly identified by the screening test.	Rationale: Critical for assessing a test's ability to detect the condition and minimize false negatives.
Specificity: The proportion of people without dementia or MCI who are correctly identified as not having the condition.	Rationale: Important for assessing a test's ability to avoid false positives and unnecessary further testing or anxiety.
Area Under the Curve (AUC): A measure of the test's overall discriminative ability across different thresholds.	Rationale: Provides a single summary measure of test accuracy.
Additional Outcomes:	
Positive Predictive Value (PPV): The probability that a person with a positive test result actually has the condition.	Rationale: Important for understanding the clinical utility of a positive test result.
Negative Predictive Value (NPV): The probability that a person with a negative test result does not have the condition.	Rationale: Important for understanding the clinical utility of a negative test result.
Likelihood Ratios: The ratio of the probability of a given test result in people with the condition to the probability of the same result in people without the condition.	Rationale: Useful for understanding how a test result changes the pre-test probability of having the condition.
Question 2: Effectiveness of interventions for screen-detected MCI or dementia	
Main Outcomes:	
Cognitive decline: Measured changes in cognitive function over time.	Rationale: Primary indicator of intervention effectiveness in slowing or halting dementia progression.
Quality of life: Measures of overall well-being and life satisfaction.	Rationale: Critical for assessing the holistic impact of interventions on individuals' lives.
Independence in daily activities: Ability to perform activities of daily living without assistance.	Rationale: Important indicator of an intervention's ability to maintain functional independence.
Additional Outcomes:	
Physical function: Measures of physical capabilities and performance.	Rationale: Important for assessing interventions' impact on overall health and mobility.
Depression: Measures of depressive symptoms or diagnoses.	Rationale: Common comorbidity in dementia; important for assessing interventions' impact on mental health.
Challenging behaviour: Frequency or severity of behaviours such as aggression, restlessness, or wandering.	Rationale: Important for assessing interventions' impact on symptoms that affect caregivers and quality of life.

Mortality: Death rates or survival times.	Rationale: Ultimate health outcome, though may be less sensitive to short-term interventions.
Caregiver burden: Measures of stress, strain, or quality of life in caregivers.	Rationale: Important for understanding the broader impact of interventions on families and care systems.

14. Risk of bias in individual studies

It is commonly recognised that evidence mapping reviews do not require formal quality assessment. The quality of included studies will be described in epidemiological terms i.e. the study designs being used. Numerical counts for numbers of different study designs mapping to each question or sub-question will be presented within the results.

15. Data synthesis

15a) Criteria for quantitative synthesis

Given the nature of a mapping review and the expected heterogeneity of studies, a full quantitative synthesis (meta-analysis) is not planned. However, some quantitative elements will be incorporated into the synthesis through descriptive statistics and structured tables. The team will consider additional approaches in the Cochrane Handbook Chapter 12 (methods of synthesis where meta-analysis is not possible).

15b) Planned summary measures and methods

The overall evidence map format will include:

- A systematic literature search
- Sifting of titles and abstracts to identify relevant literature
- Full-text review for some references if needed for clarity
- Summary of relevant evidence
- Recommendation on whether evidence is sufficient for in-depth summary

Descriptive Analysis: Analysis will involve counting the number of studies by study design, population characteristics, intervention/index test types, and outcome measures. The reviewers will present these in tables and/or charts to visualize the distribution of evidence.

Structured Evidence Summaries: The team will create individual summaries of key characteristics of included studies.

For screening tests (Question 1), these will include: Abbreviated reference to the study; Study design, Sample size, Population characteristics, Index test, Reference standard, Sensitivity and specificity (with 95% CIs if available), Other relevant performance measures (e.g., AUC, PPV, NPV)type; Objectives; Components of the study; Outcomes reported; Conclusions; Overall findings of the study.

For interventions (Question 2), summaries will include: Abbreviated reference to the study; Study type; Objectives; Components of the study; Outcomes reported; Conclusions; Overall findings of the study.

We will investigate the use of artificial intelligence (AI) to produce structured summaries. We will validate the proposed approach against human-generated summaries for the same studies. If the AI-generated summaries evaluate as being of at least equal quality we will include an agreed percentage of AI-generated summaries in the report. Conversely, if AI-generated summaries fall below the quality of human-generated summaries then all remaining summaries will be human-generated.

15c) Narrative Synthesis

As appropriate to the research questions and commissioning brief, the team will provide a written summary of the main findings, organized by the two research questions and sub-categories (e.g., types of screening tests, types of interventions). The report will be formatted per the UK NSC guidelines, including accessibility requirements. The team will highlight patterns in relevant evidence and discuss the overall direction of findings (e.g., generally positive, mixed, a recommendation on whether evidence requires an in-depth summary. A narrative and tabular summary is planned. Meta-analysis will not be performed.

Gap Analysis: Given that this is an evidence map it will be appropriate to identify and highlight areas where evidence is lacking or of low quality.

16. Meta-bias(es)

While formal investigation of meta-biases will not be feasible within the given timescale the team will scrutinise included reports to produce a qualitative assessment of any likely meta-biases likely to influence overall findings. For example the funding sources of screening methods or interventions will be identified and documented.

17. Confidence in cumulative evidence

Given that this is an evidence map there is no formal requirement to use GRADE

References

Nichols E, Steinmetz JD, Vollset SE, Fukutaki K, Chalek J, Abd-Allah F, et al. Estimation of the global prevalence of dementia in 2019 and forecasted prevalence in 2050: an analysis for the Global Burden of Disease Study 2019. The Lancet Public Health. 2022 Feb;7(2):e105–25. Available from: http://dx.doi.org/10.1016/S2468-2667(21)00249-8

Project Timetable

Beginning on July 1st and delivering the final report on October 22nd:

1. Preparation and protocol development (2 weeks)
    - Protocol draft completion: July 17th
    - Protocol review and finalization: July 18th
    - Sign Off by NIHR/NSC July 26th
2. Project initiation – July 29th
3. Search strategy development and database searches (2 weeks)
    - Search strategy development: July 17th – July 23rd
    - Database searches: July 23rd – July 19th
4. Study screening and selection (4 weeks)
    - Title and abstract screening: July 22nd (pilot) - August 9th
    - Full-text review and study selection: August 12th-August 16th
    - Resolve conflicts and finalize included studies: August 19th – August 23rd
    - **Summary of volume/type of evidence to National Screening Committee**
5. Data extraction (3 weeks)
    - Develop and pilot data extraction form: August 27th – August 30th
    - Data extraction: September 2nd – September 20th
    - **Preliminary summary to National Screening Committee September 23rd**
6. Data synthesis and report writing (3 weeks)
    - Data synthesis: September 23rd – October 4th
    - Draft report writing: October 7th – October 14th
    - Report review and revisions: October 17th – October 22nd

Key deadlines:

- Protocol finalization: June 29th
- Completion of database searches: July 19th
- Finalization of included studies: August 23rd
- Completion of data extraction: September 20th
- **Preliminary summary to National Screening Committee September 23rd**
- Draft report completion: October 14th
- Final report submission: October 22nd

This timetable allows for a more comprehensive mapping process, with 6 weeks allocated for study screening and selection and 4 weeks for data extraction. The data synthesis and report writing phase is allotted 4 weeks to ensure a thorough analysis and review of the findings and a single iteration with UK National Screening Committee.

Given that the population screening evidence map is running alongside the horizon scanning evidence map, the team will coordinate the efforts of both teams to maximize efficiency and avoid duplication of work. Regular communication and collaboration between the teams will ensure both projects stay on track and meet their respective deadlines.

Supplementary Information

Additions to protocol for academic publication

While the priority is to deliver the evidence map according to the above specification, the remit of the Evidence Synthesis Group requires optimisation of the potential for academic publication. This has the following five implications:

1. **Registration:** We will seek to register the protocol(s) with PROSPERO or an alternative register. This may require upgrading the output from an evidence map to an eligible review type.
2. **Data extraction:** The review team may supplement the minimum data extraction requirements with additional data as required for a generalisable publication.
3. **Visual Mapping:** The team will explore the potential to create evidence maps or bubble plots to visually represent the volume and characteristics of evidence. For example, X-axis could represent different types of interventions or tests, Y-axis could represent study designs or population characteristics, and bubble size could represent sample size.
4. **Studies within a review (SWAR):** A formal Study Within A Review protocol is being separately produced. This will involve comparing artificial-intelligence generated and human-generated summaries and has been planned with minimal disruption to the evidence map process. A checkpoint has been built in to evaluate comparative performance of the two approaches **(See Section 15b above).** Detailed comparison of human- and AI-generated summaries will lie outside the review timescales with a planned completion date of March 2025. All data generated by the SWAR will be made available open access through the Open Science Framework.
5. **Equity, diversity and inclusion:** We will apply the PRO EDI framework to the protocol and data extraction in order to meet the wider requirements of the National institute for Health and Care Research.

Version 3.0 July 23rd 2024.

Horizon scanning evidence map: Emerging screening tests and interventions for dementia and mild cognitive impairment

1b. Update

Not applicable

2. Registration

As this is an evidence map formal registration (e.g. PROSPERO) is not required. However, in accordance with the funder principles of open science the map will be made accessible via Open Science Framework (OSF) Registries and protocols.io, which presents generic registers open to any study type. The protocol will also be available via the Evidence Synthesis Group (EnSygN - Sheffield) website. Publication timelines will be agreed with the UK National Screening Committee (UK NSC).

3. Authors

3a. Contact

Duncan Chambers, Sheffield Centre for Health and Related Research (SCHARR), University of Sheffield, D.Chambers@sheffield.ac.uk

Burak Kundacki, Sheffield Centre for Health and Related Research (SCHARR), University of Sheffield, B.Kundacki@sheffield.ac.uk

Katherine L Jones Sheffield Centre for Health and Related Research (SCHARR), University of Sheffield, K.L.Jones@sheffield.ac.uk

Anna Cantrell, Sheffield Centre for Health and Related Research (SCHARR), University of Sheffield, A.J.Cantrell@sheffield.ac.uk

Anastasios Bastounis Sheffield Centre for Health and Related Research (SCHARR), University of Sheffield, A.Bastounis@sheffield.ac.uk

Professor Andrew Booth, Sheffield Centre for Health and Related Research (SCHARR), University of Sheffield, University of Sheffield, A.Booth@sheffield.ac.uk;

CONTACT ADDRESS: Sheffield Centre for Health and Related Research (SCHARR), University of Sheffield, Regent Court, 30 Regent Street, Sheffield, S1 4DA, UK]

3b. Contributions

AB conceived the study and designed the protocol in conjunction with the UK National Screening Committee (UK NSC) Evidence Team. DC will oversee all aspects of the work. AC contributed to search strategy design and conducted the searches. All authors contributed to the protocol design and will undertake study selection, supported by AB. [AB will act as guarantor of the evidence map.]

4. Amendments

Any amendments to this protocol will be documented and dated, with updated versions published on the Open Research register entry. Substantive changes will be agreed by all study authors and the UK NSC Evidence Team.

5. Support

5a. Sources

Funded under the Evidence Synthesis Group (EnSygN - Sheffield) from the NIHR Evidence Synthesis Programme.

5b. Sponsor

National Institute for Health and Care Research (NIHR) Evidence Synthesis Programme

5c. Role of sponsor or funder

The topic has been proposed and defined by the UK NSC Evidence Team. The protocol is developed by academics at the University of Sheffield and the UK NSC Evidence Team. The NIHR and UK NSC Evidence Team had input to the scope of the horizon scanning evidence map and agreed the final protocol. The report will be drafted by the authors and shared with the UK NSC Evidence Team for input. The sponsor and the UK NSC will receive a copy of the final report for comment.

INTRODUCTION

6. Rationale:

Dementia is a progressive clinical syndrome characterised by an ongoing decline of brain functioning which interferes with activities of daily living. Mild cognitive impairment (MCI) is a related condition where cognitive decline is present but not severe enough to impact independent living. Early detection of dementia and MCI through screening could enable timely access to care and support. However, the last UK National Screening Committee review in 2019 concluded there were uncertainties regarding the accuracy of screening tests and effectiveness of interventions for screen-detected disease.

Rapid developments are occurring in this field, with new screening technologies and biomarkers emerging alongside novel pharmacological and non-pharmacological interventions. A horizon scanning evidence map is needed to proactively identify and monitor new and emerging approaches that could impact future screening policy decisions. Systematically collating evidence on active research will inform further targeted evidence reviews and modelling to estimate the potential future impact of introducing these technologies and interventions into clinical use.

7. Objectives

This horizon scanning evidence map aims to systematically identify emerging screening tests and interventions for dementia and MCI. Specifically, it will address the following question:

What is the available evidence of active research or development (including clinical trials, observational studies, evidence syntheses, patents, or opinions) investigating:

- Innovative screening tests, diagnostic tools, care pathways or risk assessment approaches for MCI and dementia
- Novel interventions (both pharmacological and non-pharmacological) to prevent, delay or treat MCI and dementia

METHODS

8. Eligibility criteria

Evidence relating to emerging screening tests, diagnostic tools or interventions for dementia and MCI in adults will be included.

Eligible evidence types include, but are not limited to:

- Clinical trial protocols and registry entries
- Observational study protocols
- Conference abstracts, posters or presentations (as identified from the Web)
- Published study protocols
- Systematic review protocols and prospective register entries
- Patent applications
- Company reports and press releases (as identified from the Web)
- Editorials
- Guidelines and policy documents

Evidence from the UK will be prioritized; evidence from comparable countries[2] will be reported. Studies/trials/projects that include both comparable and non-comparable countries will be included.

9. Information sources

The following sources will be searched from 1 Jan 2018 to the date of searching:

- Preprint servers including MedRxiv, BioRxiv
- Clinical trial registries: ClinicalTrials.gov, ISRCTN, EU Clinical Trials Register, Clinical Trials Information System (CTIS)
- Systematic review protocol registries: PROSPERO
- Patent databases: Espacenet, Google Patents

[2] For the purposes of this evidence map comparable countries will comprise: those in North America (United States and Canada), Scandinavia (Denmark, Norway, Sweden), Western Europe (Austria, Belgium, France, Germany, Italy, Liechtenstein, Luxembourg, Monaco, Netherlands, Portugal, Spain, Switzerland), Australia and New Zealand.

- Company and financial databases: AdisInsight, BioMedTracker
- PCORI Health Care Horizon Scanning System https://www.pcori.org/topics/dementia-and-cognitive-impairment
- Internet search engines: Google Scholar (Using Publish or Perish)
- Grey literature sources:, OAIster, ProQuest Dissertations and Theses Global
- Conference proceedings (most recent two years) of relevant dementia/neurology conferences e.g. Alzheimer's Research UK, Alzheimer Europe, Alzheimer Society International Congress, Dementia World Conference etc
- Key organisational websites e.g. Alzheimer's Society, Alzheimer's Research UK, Alzheimer's Association, WHO, FDA, EMA etc.
- Searching reference lists and citation tracking key papers

NB. Bibliographic databases of published materials will not be searched for this horizon scanning evidence map. Bibliographic searches will be conducted for the companion Evidence map for population screening and items with a forward looking perspective will be "cross-referred" to this horizon scanning map on an individual basis.

11. Study records

11a. Data management

Search results will be collated in EndNote reference management software. Screening decisions will be recorded in Eppi-Reviewer.

11b. Selection process

One researcher will screen all records against the eligibility criteria and a second will independently screen a 20% sample. As this is an evidence map it will not always be necessary to consult with the full text for eligible items. If it has been necessary to consult the full text to identify this relevant information/data, the team will state this. A proportion of eligible full-texts where title/abstract information was incomplete will be split between sub-teams of two reviewers. Each reviewer will independently assess their allocated full-texts. Full-text quality control: The team will compare 30% of the other's full-text decisions. This higher percentage at the full-text stage helps ensure important studies aren't missed Discrepancies will be resolved through discussion or referral to a third reviewer.

11c. Data collection process

A standardised data charting form will be developed in EPPI-Reviewer and piloted on a subset of included records. Two reviewers will independently extract data from all included records. Any disagreements will be resolved through discussion. Missing data will not be pursued due to the expectation that ongoing research may not yet be fully reported.

12. Data items

Details of active trials, studies, reviews investigating new screening tests or interventions. The following information will be extracted where relevant/applicable:

For screening tests, these will include: Abbreviated reference to the study; Study type; Objectives; Components of the study; Outcomes reported; Conclusions; Overall findings of the study.

For interventions , summaries will include: Abbreviated reference to the study; Study type; Objectives; Components of the study; Outcomes reported; Conclusions; Overall findings of the study.

Contextual information will be provided to describe each tool/intervention.

13. Outcomes and prioritization

The main outcomes of interest are:

- The types of novel screening tests and interventions for MCI and dementia currently in development
- The quantity of active research for different screening/intervention approaches
- The stage of evaluation for emerging screening tests and interventions (e.g. early phase trials vs. late phase trials vs. implementation studies)
- Key findings relating to efficacy, safety or implementation of emerging screening/diagnostic tools or interventions (where available)
- Expert commentary on the trajectory and potential future impact of new screening and intervention approaches

All outcomes will be reported on to comprehensively map the research and innovation landscape. However, emerging approaches at a later stage of development (e.g. being tested in phase 3 trials or beyond) will be prioritised during data synthesis and reporting as these are closest to potential real-world implementation.

14. Risk of bias in individual studies

As a horizon scanning evidence map, formal risk of bias assessment will not be undertaken for individual studies. However, the level of evidence will be considered when interpreting the potential future impact of emerging screening tests and interventions, giving greater weight to findings from scientifically robust study designs where applicable.

15. Data synthesis

15a) Criteria for quantitative synthesis

Quantitative synthesis will be limited to a count and proportional breakdown of the different types of evidence identified, intervention/test types, and phase of development. No meta-analysis is planned as this is a horizon scanning evidence map, not an effectiveness review.

15b) Summary measures and methods

Numerical counts and percentages will be calculated to provide a breakdown of the evidence base by key variables. These will be presented using tables and graphs as appropriate to visually map the findings.

15c) Additional analyses

Depending on data volume, evidence on screening tests and interventions may be analysed and reported separately. Subgroup analyses by disease type (MCI and dementia) may also be considered if feasible.

15d) Narrative synthesis

A narrative and tabular summary is planned. The main data synthesis will comprise narrative description of the key characteristics of emerging screening and diagnostic technologies, risk prediction tools, and interventions for dementia and MCI.

In the published version the individual article summaries will be augmented by tabular summaries of the evidence landscape. The value of graphical summaries will be explored particularly in cases of a large volume of studies.

As appropriate to the commissioning brief, the team will provide a written summary of the main findings, organized by sub-categories (e.g., types of screening tests, types of interventions). The report will be formatted per the UK NSC guidelines, including accessibility requirements. The team will highlight patterns in relevant evidence and a recommendation on whether evidence requires an in-depth summary.

16. Meta-biases

Not applicable as no quantitative synthesis planned.

17. Confidence in cumulative evidence

Not applicable as this is a horizon scanning evidence map rather than an effectiveness review.

18. Project management

Regular online meetings between the review team and the UK NSC Evidence Team will be scheduled throughout the duration of the contract. The frequency of these meetings will be decided by the UK NSC in collaboration with the review team. The review team will meet weekly to discuss progress as required.

Project timetable:

Horizon scanning review starting on July 1st and completing by November 30th:

1. Project initiation and protocol development
    - Start date: July 15th
    - Protocol draft completion (pre-prepared): July 15th
    - Protocol review and finalization: July 26th
2. Search strategy development and database searches (2 weeks)
    - Search strategy development: July 15th – July 20th
    - Database searches and other sources: July 26th – August 2nd
3. Study screening and selection (4 weeks)
    - Title and abstract screening: August 2nd – August 22nd
    - Full-text review and study selection: August 23rd – September 11th
    - Finalize included studies: September 9th – September 11th
4. Data extraction (5 weeks)
    - Develop and pilot data extraction form: September 9th – September 11th
    - Data extraction: September 14th - October 25th
5. Data synthesis and report writing (4 weeks)
    - Data synthesis: October 29th - November 8th
    - Draft report writing: November 8th - November 15th
    - Draft Report to UK NSC – November 15th.
    - Report review and revisions: November 22nd - November 30th

Key deadlines:

- Protocol finalization: July 26th
- Completion of database searches: August 2nd
- Finalization of included studies: September 11th
- Completion of data extraction: October 25th
- Draft report completion to UK NSC: November 15th
- Final report submission to NIHR: November 30th

This timetable compresses the study screening and selection phase to 4 weeks and allocates 4 weeks for data synthesis and report writing to ensure the project is completed by November 30th. This is a tight timeline with the team working efficiently to meet the deadlines. Progress will be monitored with adjustments made as needed to ensure the project stays on track.

Version 3.0 23/07/2024