LIVERPOOL REVIEWS AND IMPLEMENTATION GROUP (LRiG)

PROTOCOL

Automated tests for cognitive impairment

This report was commissioned by the NIHR HTA Programme as project number 15/67/01

DOES NOT CONTAIN CIC/AIC

Completed July, 2015

UNIVERSITY OF LIVERPOOL

LIVERPOOL REVIEWS AND IMPLEMENTATION GROUP

A MEMBER OF THE RUSSELL GROUP

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ABBREVIATIONS LIST

AD	Alzheimer's disease
ADL	Activities of Daily Living
DAR	Diagnostic Assessment Review
DORs	Diagnostic Odds Ratio
ICD-10	International Classification of Disease
MCI	Mild Cognitive Impairment
GPCOG	General Practitioner Assessment of Cognition
MMSE	Mini Mental State Examination
QUADAS	Quality Assessment Tool for Diagnostic Accuracy Studies
RCT	Randomised Controlled Trial
ROC	Receiver Operating Characteristic
SAS	Statistical Analysis Software
SROC	Summary Receiver Operating Characteristic

1 TITLE OF THE PROJECT

Automated tests for cognitive impairment

2 TAR TEAM AND PROJECT LEAD

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3 PLAIN ENGLISH SUMMARY

The number of people that are developing problems with their memory and thinking is increasing. The assessment of memory loss is difficult and in the early stages the individual may only show small changes to their memory or ability to think.

In the past, the assessment of memory loss and thinking has been done using pen-and-paper tests and interviews carried out by health care specialists with the individual and often with their families or care givers. Depending on the level of memory loss and thinking, some people were offered treatment, while other people were just be monitored to see if their condition gets any worse.

New tests have been developed that are computer based and that sometimes do not need a specialist to be involved. The purpose of this research is to identify studies that have compared these new computerised tests to the current method of diagnosis to see if they work, and if they do work, can they also monitor changes in the individual's memory and ability to think.

4 DECISION PROBLEM

The aim of this review is to determine whether automated tests accurately identify patients with progressive cognitive impairment and if so, their role in monitoring disease progression or response to treatment.

Specifically the research objectives are to;

1. determine the performance of automated computerised tests, in detecting mild cognitive impairment and early dementia.
2. determine the performance of automated computerised tests in the monitoring of the disease post-diagnosis, specifically in detecting disease progression.
3. identify future research needs.

5 BACKGROUND AND RATIONALE FOR REVIEW

Cognitive impairment in dementia is progressive, and a growing public health concern.[1] It is one of the most distinctive characteristics of all dementias. Consequently assessment of cognitive impairment is an essential element in diagnosis.[2]

Timely recognition of dementia syndromes can be beneficial because some causes of dementia are treatable and fully or partially reversible, for example dementias caused by vitamin B12 deficiency,[3] side effects of medications,[4] metabolic abnormality and certain brain tumours.[5] There is also some evidence from the United States that early recognition and therapy may delay the subsequent need for nursing home care, and reduces the risk of misdiagnosis and inappropriate management.[6] It can also assist in addressing anxiety about

changes in memory, thinking, mood or behaviour for people with suspected dementia and their carers.[7]

A number of pen-and-paper based tools for cognitive assessment are currently used in the United Kingdom, for example the Mini Mental State Examination (MMSE), and the General Practitioner Assessment of Cognition (GPCOG).[8] A few automated cognitive assessment tools are also now available, however, progression of cognitive impairment or response to treatment in these tools has not been evaluated.[9]

The rationale for this review is to determine whether these automated cognitive impairment tests have the potential to lead to an earlier diagnosis, and simplify the ongoing monitoring and assessment process compared to standard practice.

5.1 Population

This review addresses patients in two specific diagnostic categories, those with mild cognitive impairment (MCI) and those suffering from early dementia.

Mild cognitive impairment (MCI)

Evidence from neuropathological and neuroimaging studies suggest that biological changes associated with dementia occur long before the onset of symptoms.[10] Extensive research has been devoted to identify the characteristics of incipient dementia occurring before the onset of the full dementia syndrome.[11,12]

This research has given rise to the concept of Mild Cognitive Impairment (MCI), which is the transitional state between the cognitive changes of normal aging and very early dementia.[13,14] The transitional period has been described using a variety of terms such as mild cognitive impairment (MCI), dementia prodrome, incipient dementia, isolated memory impairment[15] and more recently mild neurocognitive disorder.[11] We will use the term, 'mild cognitive impairment or MCI.

MCI refers to the clinical condition used to describe people whose cognitive function is below that of the normal population for their educational level and age but without any loss of functional abilities or skills.[16-19] The diagnosis of MCI is complicated by the fact that memory complaints in the people above the age of 65 are common.[20] Some of the indicators of dementia for example a reduction in Activities of Daily Living (ADL), decreased attention or ability to plan are absent in MCI.

MCI is a heterogeneous state, with possible trajectories including Alzheimer's disease (AD) and other dementias, and even reversion to normal cognitive functioning.[11] It is also worth noting that a meta-analysis[21] of 41 inception cohort studies reported that the adjusted annual conversion rate (ACR) from defined MCI to dementia was approximately 5-10%. The overall

conversion rate from MCI to AD has been estimated at between 6 and 25% of cases per year[22]. However, these rates vary by subtype of disease and the amnestic subtype has a reported conversion rate of around 30%. The variation in the rates could be explained by the differing disease processes.[12,23]

There has been an effort to subtype MCI in terms of the type and number of cognitive domains affected.[15] The classification of MCI is described in Table 1. Different types of MCI have now been proposed, including 'amnestic form of MCI (A-MCI) when memory is affected and non-amnestic reflecting impairments in a non-memory domain.[15] MCI is also classified as single-domain (sdMCI) or multiple domains (mdMCI) according to the number of cognitive domains with objectively verified impairment.[24]

Table 1 MCI subtypes by aetiology, presentation and long term outcomes

Variable	Amnestic	Non-amnestic
Aetiology	Neurodegenerative disease Apolipoprotein E (ApoE)	Vascular damage Cerebrovascular disease
Presentation	Memory impairment present	Impairment in non-memory domains
Long term outcomes	Alzheimer's dementia (AD)	Non-Alzheimer dementias: Vascular dementia Lewy body, Frontotemporal

Source: Adapted from Roberts R et al., 2013[15]

Early dementia

Early dementia is differentiated from MCI by the level of cognitive decline and change in mood and behaviour. The common changes experienced by people with dementia can be understood in three stages, early, middle and late dementia (Table 2). Individuals diagnosed with early dementia present with multiple cognitive deficits and memory loss sufficient to impact on everyday social and occupational functioning. In the later stages, there is a noticeable deterioration in perception, comprehension and language. This is also often accompanied by impaired ability to recognise objects (agnosia) and an inability to think abstractly and plan, initiate, sequence, monitor and stop complex behaviour.[25,26]

Dementia is caused by a number of conditions, including Alzheimer's disease, vascular conditions (e.g. multiple cortical/subcortical infarcts), fronto–temporal atrophy, lewy body disease, inherited metabolic disorders (e.g. porphyria), or neoplasms (e.g. meningioma). Irrespective of the primary cause, the outlook for most types of dementia is usually poor. Irreversible or untreated dementia usually continues to worsen over time until the person's death.[27,28]

Table 2 Stages of Dementia

Stages of Dementia	Common changes experienced by people with dementia
Early stage	• Become forgetful, especially regarding things that just happened • May have some difficulty with communication • Become lost in familiar places • Lose track of the time, including time of day, month, year, season • Have difficulty making decisions and handling personal finances • Have difficulty carrying out complex household tasks • Mood and behaviour
Middle stage	• Become very forgetful, especially of recent events and people's names • Have difficulty comprehending time, date, place and events • May become lost at home as well as in the community • Have increasing difficulty with communication (speech and comprehension) • Need help with personal care (i.e. toileting, washing, dressing) • Unable to successfully prepare food, cook, clean or shop • Unable to live alone safely without considerable support • Behaviour changes may include wandering, repeated questioning, hallucinations • May display inappropriate behaviour in the home or in the community
Late stage	• Usually unaware of time and place • Have difficulty understanding what is happening around them • Unable to recognize relatives, friends and familiar objects • Unable to eat without assistance, may have difficulty in swallowing • Increasing need for assisted self-care (bathing and toileting) • May have bladder and bowel incontinence • Change in mobility, may be unable to walk or be confined to a wheelchair or bed • Behaviour changes, and include aggression towards carer, nonverbal • Unable to find his or her way around in the home

Source: Adapted from WHO[29]

5.1.1 Epidemiology

Obtaining accurate figures for MCI is difficult since people with memory decline may go undiagnosed. Prevalence and incidence estimates can also vary significantly depending on the definitions that are used. The variance in these estimates then poses a challenge to the understanding of the social burden of this disease. For example, a study utilising data from Medical Research Council Cognitive Function and Ageing Study estimated the prevalence of MCI to range from 2.5–41.0%. In addition, the rates of progression from MCI to dementia varied from 3.7–30.0%.[30]

The most common form of dementia in the United Kingdom is AD.[31] There are an estimated 163,000 new cases of dementia identified each year in England and Wales. The risk of receiving a diagnosis of dementia rises with increasing age, however, a significant portion of those diagnosed are under the age of 65.[32] The incidence of dementia is from 6.7 per 1,000 person years at age 65-69 to 68.5 per 1,000 person years at age 85 and above. There is 3% prevalence by 70 years and prevalence doubles every 5.1 years thereafter.[33] A report

published by the Alzheimer's Society predicts that there will be 1 million people living with dementia in the UK by 2025.[32]

5.2.2 Current diagnostic practice

Recent guidelines from the National Institute for Health and Care Excellence (NICE)[7] place emphasis on early diagnosis of dementia to allow for effective management and planning with patients and carers. The projected increase in prevalence of dementia by the Alzheimer's Society highlights the importance of an equitable and easy access to diagnosis in a population setting.

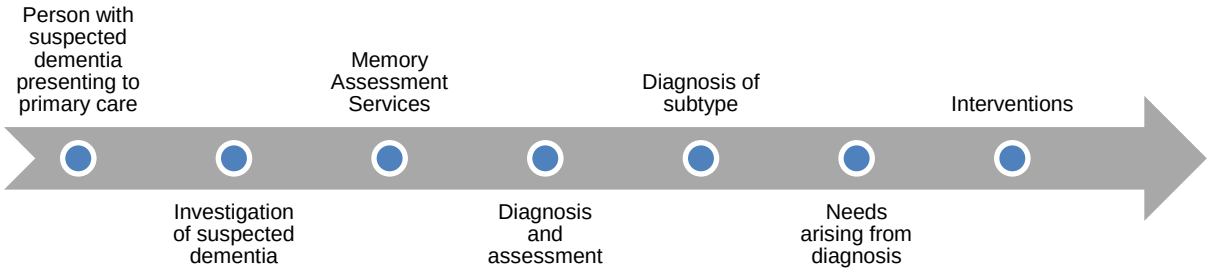


Figure 1 Adapted pathway for dementia diagnosis[8]

A schema of the pathway for the diagnosis of dementia is presented in Figure 1. The first point of contact with health care services for a person with suspected cognitive impairment is primary care. The general practitioner usually takes a brief history, conducts a physical examination and a short test of cognitive function to establish a differential diagnosis for cognitive impairment. NICE guidance[7] recommends the use of the Mini Mental State Examination (MMSE) when aiming to diagnose dementia. It is possible to offer a diagnosis of dementia at this point if it is in an advanced state.[34] However, MMSE is insensitive to early-stage dementia[35] and does not effectively map the transition from MCI to early dementia.[36] The NICE guidance[7] also acknowledges a number of pen-and-paper based tools as suitable tests for screening cognitive impairment. These tests are further discussed in Table 3.

Table 3 Screening tests for cognitive impairment

Test	Administration time	Sensitivity	Specificity
General Practitioner Assessment of Cognition (GPCOG)[7]	5 minutes	82-85%[37]	82-85%[37]
6CIT[7]	3-4 minutes	78.5-83%[38]	77-100%[38]
Mini-cog assessment instrument[39]	2-4 minutes	76-99%[37]	89-96%[37]
Abbreviated Mental Test (AMT)[7]	2-4 minutes	Not validated in a primary care setting	Not validated in a primary care setting
Memory impairment screen[40]	4 minutes	74-86%[37]	96-97%[37]

After this initial screening, the GP refers the patients with suspected MCI or early dementia to a Memory Assessment Services (MAS). The MAS have an important role in clarifying the diagnosis (MCI or dementia; subtype and severity of dementia) and identifying which patients with mild cognitive impairment are at greatest risk of developing dementia and most in need of follow-up. This is established through a detailed clinical history with the patient and a family member or carer, scans (if needed) and cognitive function paper-and-pen diagnostic tests.[41] The different diagnostic tests available for use in this secondary setting are described in Table 4.

Table 4 Diagnostic tests for MCI and early dementia

Test	Administration time	Sensitivity	Specificity
DemTect[42 43]	8-10 minutes	92%[42]	86%[42]
The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool For Mild Cognitive Impairment[43]	10 minutes	90%[44]	87%[44]
Saint Louis University mental status SLUMS[45]	7 minutes.	98–100%[46]	98–100%[46]

5.2 Reference standard

The reference standard can be described as the best available method for identifying patients that have the target condition.[47] Our reference standard will be clinical diagnosis of MCI and early dementia. We recognise that clinical diagnosis itself has a degree of variability but this is not unique to dementia studies and does not invalidate the basic diagnostic test accuracy approach. Clinical diagnosis will include all causes of dementia, except dementia caused by medication, with co-morbidities like learning disabilities, or organic causes like neurological damage caused by stroke or head injury, and brain tumours. Any recognised diagnostic criteria (for example, International Classification of Diseases Edition 10 (ICD-10); Diagnostic and Statistical Manual of Mental Disorders Edition 4 (DSM-IV) can be used.

Dementia diagnosis may specify a pathological subtype. Clinicians may use imaging, pathology, or other data to aid diagnosis, for example, Clinical Dementia Rating[48] which is a gold standard research criterion against which most rating scales have been compared.[49] However, we will not include diagnosis based only on these data without corresponding clinical assessment. We recognise that different iterations of diagnostic criteria may not be directly comparable and that diagnosis may vary with the degree or manner in which the criteria have been operationalised (e.g. individual clinician versus algorithm versus consensus determination). We will explore data on method and application of dementia diagnosis as part of our assessment of heterogeneity.

5.3 Index test

Our index test is an automated assessment of cognitive impairment which can either be self-administered, or interviewer administered. In self-administered tests, patients may require some help with logon identification, simple start-up explanation, and assurance that the patient can see or hear the instructions and test stimuli.

There are several automated tests available for use in the identification of MCI and early dementia. There is limited clinical evidence to demonstrate their equivalence or superiority over standard practice. One UK based review looked at the use of several available computerised automated tests and assessed their sensitivity and specificity for detection of MCI compared to two well-validated paper-and-pencil tests; the Hopkins Verbal Learning Test (HVLT) and the Mini- Mental Status Examination (MMSE).[50] From this review, it was concluded that the HVLT has better sensitivity for the detection of MCI in older adults than the computerised tests, but that one automated test, CogState may enable the identification of cognitive deficits beyond mild impairments in memory.[50] This review, however, did not address whether these test have the potential to improve timely diagnosis or their effectiveness in monitoring disease progression.

Table 5 provides a list of automated tests that were identified by an initial scoping search.

Table 5 Sample of current computerised cognitive test

Tool	Condition	Administration	Duration	Domains
ANAM[51,52]	Cognitively impaired elderly; Alzheimer's	Mouse/keyboard. Self-administered	NR	Memory, attention, psychomotor speed, language, reaction time
CAMCI[51]	MCI	Touch screen computer. Self-administered	20 minutes	Attention, memory, executive function, working memory
CANS-MCI[51,52]	MCI	Touch screen. Self-administered.	30 minutes	Memory, executive function, symbol fluency
CANTAB[51,52]	Early stage Alzheimer's and Parkinson's	Touch screen. Self-administered	30 minutes	Executive function, memory, attention, visuospatial function
CNS vital signs[51,52]	MCI; mild dementia	Keyboard. Self-administered.	30 minutes	Memory, psychomotor speed, reaction time, complex attention, cognitive flexibility
CNTB[51]	Alzheimer's	Keyboard. Technician administered	NR	Language, information processing, motor speed, attention, spatial, memory
COGDRAS-D[51,52]	Dementia; Alzheimer's; Huntington's	Yes/no button. Technician administered.	20-25 minutes	Attention, memory, reaction time
CogState™[51,52]	MCI	Keyboard. Self-administered.	15-20 minutes	Working memory, attention, visuospatial memory
CSI[51,52]	Dementia	Keyboard. Self-administered.	25-35 minutes	Memory, attention, response speed, processing speed
CST[52]	NR	Technician assisted	15 minutes	Learning, memory, executive function
MCIS[51,52]	MCI	Technician records responses or via telephone.	10 minutes	Memory. Executive function, language
MicroCog™[51,52]	MCI	Keyboard/# pad. Self-administered.	>60 minutes/30 minutes short form	Reaction time, memory, attention, mental control, reasoning, spatial processing
Mindstreams™[51,52]	MCI; dementia	Mouse/# pad. Technician administered.	45-60 minutes/30 minutes	Memory, executive function, visual and special ability

MCI – Mild Cognitive Impairment; NC = normal controls

6 METHODS

The methods used in each review will follow the systematic review principles outlined in the Centre for Reviews and Dissemination (CRD)[53] guidance for undertaking reviews in health care, the NICE Diagnostic Assessment Programme Manual[54] and publications from the Cochrane Collaboration diagnostic test accuracy methods[55] working group.

6.1 Search Strategy

The following electronic databases will be searched for published literature using strategies that combine search terms relating to long-term physical illness and synonyms for follow-up:

- Medline (OvidSP)
- Medline in Process (OvidSP)
- Embase (OvidSP)
- Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effectiveness, Health Technology Assessment database
- Cochrane Dementia and Cognitive Improvement Group
- ISI Web of Science- Proceedings (Index to Scientific & Technical Proceedings)
- ISI Web of Science- Science Citation Index Expanded
- PsychInfo

No study design filters will be applied and non-English language reports will be excluded. All databases will be searched from the year 2005 until the latest available version.

Details of the draft search developed in Medline can be found in the Appendix 1.

Grey literature: chosen electronic databases will include assessments of conference proceedings. We will aim to access theses or PhD abstracts from institutions known to be involved in diagnostic and monitoring dementia studies.

Reference lists: We will conduct backward and forward citation tracking for all relevant studies and reviews in the field for further possible titles

Handsearching: Trial and research registers will be searched for ongoing studies and reviews including:

- Clinicaltrials.gov
- metaRegister of Controlled Trials and ISRCTN Register
- WHO International Clinical Trials Registry Platform
- Prospero systematic review register
- Epistemonikos

The database will be managed in Endnote X7. After individual tests have been identified then a second search will be run for individual test costs and where possible source the acquisition costs for the various tools.

6.2 Study Selection

The citations identified will be assessed for inclusion through two stages using Covidence software package.[56] Firstly, two reviewers scan all the titles and abstracts identified by the searching exercise to identify the potentially relevant articles to be retrieved. Full text copies of the selected studies will subsequently be obtained and assessed by a reviewer for inclusion using the inclusion and exclusion criteria outlined below, and a second reviewer will check this independently. Disagreements will be resolved by consensus or arbitration by a third reviewer.

The eligibility criteria for the diagnostic accuracy studies (Table 6) and monitoring studies (Table 7) are listed below.

Table 6 Eligibility criteria – diagnostic accuracy

Criteria	Included	Excluded
Study design	Index test and reference tests are evaluated in the same study population which are fully paired (all study participants receive the index test, and the reference standard).	Any case studies, qualitative studies, studies with samples < 10
Patient population	Adults (aged over 18 years) with suspected MCI or early dementia	Patients diagnosed with neurological damage caused by stroke or head injury, learning disabilities, and brain tumours. Studies which report on both late and early stages of dementia will be included, only if both the populations are reported separately
Setting	Primary care, secondary care, memory clinics, acute care settings, care homes, tertiary or community based setting	
Index test	Any commercial or non-commercial computer-based cognitive diagnostic tool with automated interpretation, addressing one or more domains of cognitive impairment	Automated cognitive diagnostic tool in a non-English language
Outcomes	Diagnostic accuracy (e.g. specificity, sensitivity, likelihood ratios, diagnostic odds ratio, intra-patient variability) Acceptability (any studies recording a measure of acceptability)	Studies need to report on at least one outcome to be included.

Table 7 Eligibility criteria - monitoring

Criteria	Included	Excluded
Study design	Index test and reference tests are evaluated in the same study population which are fully paired (all study participants receive the index test, and the reference standard).	Any case studies, qualitative studies, studies with samples < 10
Patient population	Adults (aged over 18 years) with diagnosed MCI and early dementia.	Patients diagnosed with neurological damage caused by stroke or head injury, learning disabilities, and brain tumours. Studies which report on both late and early stages of dementia will be included, only if both the populations are reported separately.
Setting	Primary care, secondary care, memory clinics, acute care settings, care homes, tertiary or community based setting.	
Index test	Any commercial and non-commercial computer-based cognitive monitoring tool with automated interpretation, addressing one or more domains of cognitive impairment used for monitoring disease progression and treatment	Automated cognitive diagnostic tool in a non-English language
Outcomes	Monitoring accuracy (e.g. specificity, sensitivity, likelihood ratios, diagnostic odds ratio, intra-patient variability) Acceptability (any studies recording a measure of acceptability)	Studies need to report on at least one outcome to be included.

6.3 Data extraction strategy

A data extraction form will be developed, piloted and standardised. One reviewer will extract details of study design, participants, index and reference standard tests, outcome data and other relevant data, and a second reviewer will check the data extraction. Disagreements will be resolved by consensus or arbitration by a third reviewer.

6.4 Assessment of methodological quality

The quality assessment of studies meeting the inclusion criteria will be assessed by one reviewer, and independently checked for accuracy by a second reviewer. The methodological quality of the included studies will be assessed using the QUADAS-2 tool.[57] This tool is designed evaluate the risk of bias and applicability of primary diagnostic accuracy studies. As per the tools guidelines the tool will be tailored for this review with any irrelevant signalling questions being omitted and any additional review relevant questions added. The results of the quality assessment will be presented in summary tables and a narrative synthesis.

6.5 Method of analysis/synthesis

6.5.1 Statistical analysis and data synthesis

Individual study results: The results of the individual diagnostic studies will be tabulated, and sensitivity, specificity, predictive values, likelihood ratios and diagnostic odds ratios will be calculated for the index test for each study.

Meta-analysis: If at least two diagnostic studies report sufficient data, we will produce summary receiver operating characteristic (SROC) curves. If it is considered to be appropriate to pool data from these studies, meta-analysis will be performed using the hierarchal summary receiver operating characteristic (HSROC) model in SAS version 9.3. Where studies report 2x2 data for various cut-off values (thresholds) to indicate test positivity, the most frequently used threshold (across all studies) will be selected to be included in the analysis. Summary sensitivity, specificity, positive and negative likelihood ratios, and diagnostics odds ratios (DORs) for each model will be reported as the point estimate and the corresponding 95% confidence interval (CI).

If numerical difficulties are encountered with the HSROC model, or if it is more appropriate to summarise sensitivity and specificity as single point estimates (i.e. there is no threshold effect), then the data will be pooled using the bivariate model. If studies do report data for a variety of different thresholds, pooled estimates will be provided for different thresholds. In this case, data for more than one threshold from any given study may be incorporated (although pooled under separate analyses). These analyses will be carried out using SAS version 9.3. Summary sensitivity, specificity, positive and negative likelihood ratios, and diagnostics odds ratios (DORs) for each model will be reported as the point estimate and the corresponding 95% confidence interval (CI).

If it is not appropriate or possible to perform a meta-analysis, the results of the included studies will be synthesised narratively. The possible effects of study quality (based on the assessment of risk of bias) on the effectiveness data and review findings will be considered.

Comparator tests: If there are studies which report data for the index test and a comparator test, we will produce SROC plots and summarise specificity and sensitivity as described above for both the index test and the comparator test. We will use HSROC methods to compare test accuracy. We will introduce a binary covariate to identify the test, allowing us to assess whether the test type is associated with the shape and position of the summary ROC curve. If the Bivariate model was used for data synthesis, and studies have used a consistent threshold on a continuous or ordinal scale to define test positivity for both the index and the comparator test, then we will use the bivariate model in order to investigate whether the expected sensitivity and/or specificity differs between the tests. If results for

other thresholds are reported, we will use the available data to investigate the relative diagnostic accuracy of the tests at the alternative thresholds.

6.5.2 Investigations of heterogeneity

There are likely to be high levels of heterogeneity between studies based on several factors. The demographics of the participant group may vary particularly in relation to age, the setting where the assessment is being made and who is completing the assessment. Studies may also vary in what indicators they use to complete an assessment.

We will investigate heterogeneity through visual examination of forest plots of sensitivity and specificity, and by considering the degree to which observed study results lie close to the SROC. If sufficient studies are available, we will explore the possible influence of the covariates which may be sources of heterogeneity, by adding covariate terms to the meta-analysis models described above. The significance of the difference in test accuracy will be assessed by a likelihood ratio test comparing models with and without covariate terms.

6.5.3 Sensitivity analyses

If appropriate and data allow, we will conduct sensitivity analyses in order to provide estimates of test accuracy for the sub-groups of MCI and early stage dementia. We may also perform sensitivity analyses in order to exclude studies which have methodological shortcomings, or if we are uncertain about the appropriateness of including them in the primary meta-analysis.

6.6 PPI involvement

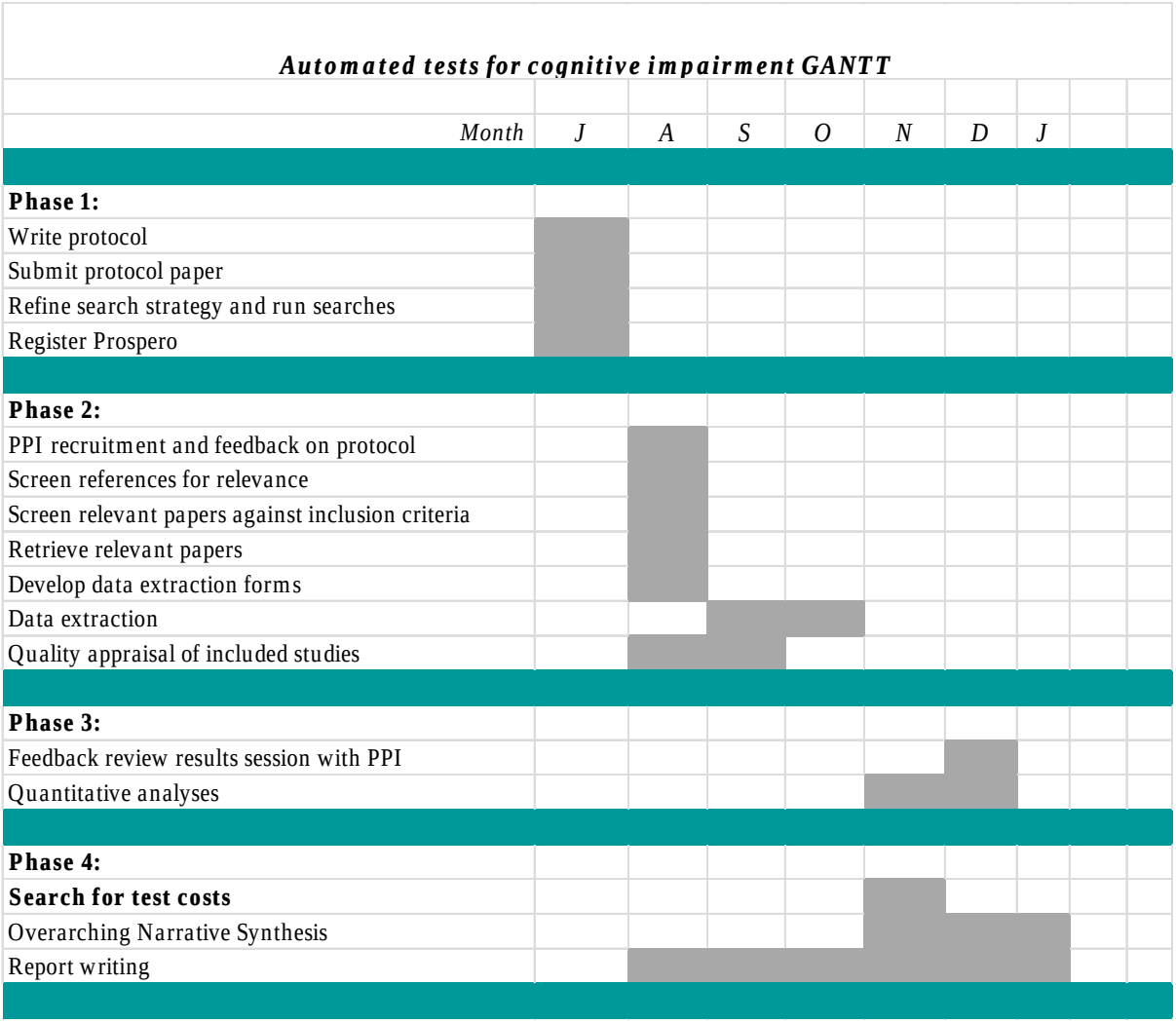
The review team will be guided during the review by an advisory group comprising of service users and carers. Building trusted contacts with service users lead us to judge that the most effective way of obtaining engagement with service users will be through frontline agencies, like Alzheimer's Society and Dementia UK already working with people with MCI and early dementia. We will send out a call through these frontline groups for people interested in giving feedback on the protocol, results of the review and the final report. We will prioritise the ease and comfort of the participants and their carers, and will take guidance in structuring and facilitation of these meetings from these agencies and the briefing notes from INVOLVE.[58]

The advisory group will meet with the research team twice during the course of the project, and its members will also be available for consultation by email between meetings.

7 PROJECT TIMELINES

The proposed timelines for this project are summarised in Figure 2.

Figure 2 Project timelines



8 EXPERTISE IN THIS TAR TEAM AND COMPETING INTERESTS

The Liverpool Reviews and Implementation Group (LR*i*G) was established at the University of Liverpool in April 2001. It is a multi-disciplinary research group whose purpose, in the first instance, is to conduct Technology Assessment Reviews commissioned by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme. The team has substantial expertise in systematic reviewing, literature searching and assessing clinical outcomes and is well practised in applying this expertise to health technology evaluations. In addition, for the specific purposes of this review, LRiG has approached clinical experts with research experience and a specific interest in the diagnosis of dementia. They have agreed to contribute to all aspects of the review process. This TAR team will be made up of the individuals listed in Table 8.

Table 8 TAR team for this project

Role	**Person**
Team lead / systematic reviewer	Rabeea'h Waseem Aslam, LR*i*G
Systematic reviewer	Vickie Bates, LR*i*G
Systematic reviewer	Juliet Hounsome, LR*i*G
Systematic reviewer/ Information specialist	Yenal Dundar, LR*i*G
Information specialist	Eleanor Kotas, LR*i*G
Medical statisticians	Marty Richardson, LR*i*G Ashma Krishan, LR*i*G
Director/systematic reviewer	Rumona Dickson, LR*i*G
Clinical advisor	Dr Sudip Sikdar FRCPsych, MD Consultant Old Age Psychiatrist Associate Medical Director, PMH and Outcomes Honorary Research Fellow, University of Liverpool We have also identified the need for a General Practitioner with a specific interest in the diagnosis of dementia and are in the process of establishing contact

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10 APPENDICES

Appendix 1 Proposed search strategy

# ▲	Searches
1	exp mild cognitive impairment/
2	((early* or onset* or initial* or young*) adj2 (dementia* or Alzheimer* or AD)).tw.
3	((Mild* or early* or onset* or initial* or progress* or minor or young* or moderat* or suspect*) adj2 Cognit* adj1 (impair* or disord* or diseas* or declin* or deteriorat* or fail* or complain* or dysfunct* or degenerat* or deficit*)).tw.
4	MCI.tw.
5	("preclinical alzheimer*" or "pre-clinical alzheimer*").tw.
6	(prodrom* adj2 dement*).tw.
7	*dementia/ or *alzheimer disease/ or *dementia, vascular/ or *dementia, multi-infarct/ or *frontotemporal dementia/
8	or/1-7
9	((computer* or automate*) adj2 (test* or assess* or evaluat* or screen* or battery or monitor* or identif* or assess* or evaluat* or interpret*)).tw.
10	(automat* adj2 (interpretat* or test*)).tw.
11	*Neuropsychological Tests/
12	((neuropsychological or neuro-psychological) adj5 (computer* or automate*) adj5 (test* or assess* or evaluat* or screen* or battery or monitor* or identif* or assess* or evaluat* or interpret*)).tw.
13	or/9-12
14	8 and 13
15	Diagnosis, Computer-Assisted/
16	((computer* or automate*) adj4 (diagnos* or detect*)).tw.
17	or/15-16
18	8 and 17
19	disease progression/
20	((test* or assess* or evaluat* or screen* or battery or monitor* or identif* or assess* or evaluat* or interpret*) adj3 diseas* adj3 (progress* or exacerbat*)).tw.
21	or/19-20
22	14 and 21
23	"cambridge Neuropsychology Test*".tw.
24	Computerized Neuropsychological Test Battery.tw.
25	Six Item Cognitive Impairment Test.tw.

26	"Computer Assessment of Mild Cognitive Impairment".tw.
27	MindStream*.tw.
28	"Mild Cognitive Impairment Screen*".tw.
29	Computer Administered Neuropsychological Screen for Mild Cognitive Impairment.tw.
30	Automated Neuropsychological Assessment Metrics.tw.
31	CANS-MCI.tw.
32	"CNS Vital Signs".tw.
33	Cognitive Drug Research Computerized Assessment System for Dementia.tw.
34	CogState.tw.
35	"Cognitive Stability Index*".tw.
36	"Cognitive Screening Test*".tw.
37	Microcog.tw.
38	(COGDRAS-D or COGDRASD or COGDRAS).tw.
39	MCIS.tw.
40	(CAMCI or CNTB).tw.
41	6CIT.tw.
42	(CANTAB-A or CANTABA or CANTAB).tw.
43	ANAM.tw.
44	or/23-43
45	14 or 18 or 22 or 44
46	animals/ not humans/
47	45 not 46
48	comment/ or editorial/ or letter/
49	case reports/
50	(comment or editorial or letter or journal correspondence or opinion).pt.
51	or/48-50
52	47 not 51
53	**limit 52 to yr="2005 -Current"**