

# Topic proposal

I understand that this proposal will be retained by the SIGN Programme Lead and be made available on the SIGN website for time period that the proposal is being considered. **Only proposals with a completed Declaration of Interests for the principal proposer will be considered**

<b>1.</b>	<p><b>What is the problem/need for a guideline/clinical scenario?</b></p> <p>Dementia is an irreversible, progressive neurodegenerative disease with a variety of subtypes (ICD 10). People living with dementia have fluid, complex needs depending on the range and severity of cognitive and non-cognitive symptoms experienced. Across Scotland and its care settings, wide variations exist in the methods utilised for assessment, diagnosis, treatment and support for dementia. Such variations may contribute to poorer health and quality of life outcomes for people living with dementia and their carers, along with higher health and social costs.</p> <p>With an ever-increasing body of research on all aspects of dementia, the impetus to develop a new guideline is increasingly apparent. The proposed guideline would offer the potential to reduce variation in standards and to enhance patient outcomes, whilst increasing equality and reducing costs. Rather than providing a medical guideline or duplication, this guideline would offer added value for all members of the multidisciplinary team.</p> <p>Scotland's national and healthcare policies underline key priorities and aspirations for integrated health and social services in dementia care. These highlight equality-based, human rights based approach throughout a person's experience of living with dementia. With timely diagnosis, along with appropriate care and support at all stages of the disease, people living with dementia and their carers could benefit from enhanced health and quality of life outcomes, which could in turn minimise health and social costs. The growing emphasis on self-directed utilisation of community resources may build resilience in both the person with dementia and their carer. This in turn may lead to reductions in the costs from hospital and care home services.</p> <p>The National Dementia Strategy recognises the importance of equality of access to services for early diagnosis. Variations in access to these services, along with variations in the form these take, are evident throughout Scotland and its care settings. The proposed guideline would offer an evidence based set of recommendations on early diagnosis and management in dementia and its subtypes that would inform and provide added value to all stakeholders, ensuring timely, person-centred interventions and efficient utilisation of resources.</p> <p>A further area of variation is the treatment of cognitive and non-cognitive symptoms in dementia, including co-morbid emotional disorders. Stress and distress behaviours are common in dementia, particularly as the condition advances. A wide range of pharmacological and psychological interventions are available, reflecting individualised complex needs and the changing pattern of symptoms during the illness. Psychological approaches are recommended for first line management but variance and uncertainty exist across Scotland in terms of availability of resources and differences in staff training. The proposed guideline would provide evidence based guidance for stakeholders to facilitate consistency, equality and improved person-centred outcomes.</p>
<b>2.</b>	<p><b>Burden of the condition</b></p> <p>Mortality</p> <p>In the UK, dementia is the only disease in the top 10 causes of death that does not have a cure or treatment to slow its progression (<a href="https://www.dementiastatistics.org/statistics/deaths-due-to-dementia/">https://www.dementiastatistics.org/statistics/deaths-due-to-dementia/</a>).</p>

	<p>Mortality rates for Alzheimer’s disease and other dementias have increased over the last decade. In contrast, the other top four leading causes of death in 2015 – ischemic heart disease, cerebro-vascular disease, chronic lower respiratory disease and lung cancer – have all seen falling mortality rates in the last 15 years.</p> <p>In the UK, dementia was the leading cause of death in women and second most common cause of death for men in 2015 (Source: England and Wales; Mortality Statistics: Deaths Registered in England and Wales (Series DR). Scotland: National Records of Scotland Vital Events Reference Tables. Northern Ireland; Northern Ireland Statistic &amp; Research Agency Registrar General Annual Report 2015).</p>
	<p>Incidence</p> <p>More than 93,000 people in Scotland have a dementia diagnosis; some 3200 are aged under 65 (<a href="http://www.alzscot.org/campaigning/statistics">http://www.alzscot.org/campaigning/statistics</a>, downloaded 7.9.17).</p>
	<p>Prevalence</p> <p>Prevalence increases with age. Women are slightly more affected than men from age 70 onwards. Prevalence rates rise from 1.8% for those aged 65-69, to 7.0 -7.6% for those aged 75-79 and 14.5-16.4% for ages 80-84. A sharp increase in prevalence occurs from age 85 onwards with female prevalence at age 90-94 reported as 44.4% (males 29.2%; (<a href="http://www.alzscot.org/campaigning/statistics">http://www.alzscot.org/campaigning/statistics</a>; downloaded 7.9.17).</p>
<b>3.</b>	<b>Variations</b>
	<p>In practice in Scotland</p> <p>Variations exist across Scotland in the standard and consistency of diagnosis, assessment, care and support in dementia care, treatment and management.</p>
	<p>In health outcomes in Scotland</p> <p>The above-mentioned variations may contribute to poorer health and quality of life outcomes for people with dementia and their carers, along with higher health and social costs. Currently, these costs are estimated at £24 billion per annum in the UK and expected to rise to £32.5 billion by 2025 (Alzheimer’s Research 2016).</p>
<b>4.</b>	<b>Areas of uncertainty to be covered</b>
	<p>Key question 1</p> <p>From the evidence base, which aspects of dementia assessment and diagnosis for people living with dementia could be standardised to promote improved patient outcomes throughout Scotland’s care settings?</p>
	<p>Key question 2</p> <p>What is the evidence base for the pharmacological and non-pharmacological risk reduction and treatment for cognitive and non-cognitive symptoms, including co-morbid emotional disorders in dementia?</p>
<b>5.</b>	<b>Areas that will not be covered</b>
	<p>Head Injury, Alcohol related brain damage</p>
<b>6.</b>	<b>Aspects of the proposed clinical topic that are key areas of concern for patients, carers and/or the organisations that represent them</b>
	<p>Variance and uncertainty in approaches to diagnosis, treatment and management of dementia which leads to missed opportunities in early diagnosis, treatment and support that align with person-centred, human rights based approach.</p>

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<b>7.</b>	<b>Population</b>
	Included People with dementia and their primary carers
	Not included nil
<b>8.</b>	<b>Healthcare setting</b>
	Included Primary, Secondary and Tertiary care in the community
	Not included
<b>9.</b>	<b>Potential</b>
	Potential to improve current practice  Reduction of variance and uncertainty across practice in diagnosis, treatment and management of dementia aligning practice across multidisciplinary teams to Scottish Government policies and aspirations.
	Potential impact on important health outcomes (name measureable indicators) 1. Diagnosis Rates 2. Quality of Life Indicators 3. Functioning indicators e.g. Activities of Daily Living
	Potential impact on resources (name measureable indicators)  1.Acute hospital admission rates for people with dementia 2.Prescription of antipsychotic and anxiolytic medications 3.Post diagnostic engagement
<b>10.</b>	<b>What evidence based guidance is currently available?</b>
	None
	Out-of-date (list) SIGN 86 – Management of patients with dementia
	Current (list)  NICE CG42 (2006): Supporting people with dementia and their carers in health and social care British Association of Psychopharmacology (2017) - <b>Clinical practice with anti-dementia drugs: A revised (third) consensus statement from the British Association for Psychopharmacology</b>
<b>11.</b>	<b>Relevance to current Scottish Government policies</b>
	The Scottish Government: Scotland's National Dementia Strategy 2017-2020 Scottish Government, <i>Strategic Framework for Action on Palliative and End of Life Care</i> (Edinburgh, 2015)  Scottish Government, <i>Self-directed Support Strategy 2010-2020, Implementation Plan 2016-2018</i> (Edinburgh, 2016)  Scottish Government, <i>Promoting Excellence: A framework for all health and social services staff working with people with dementia, their families and carers</i> (Edinburgh, 2011)

	<p>The Scottish Government (2011): The Standards of Care of Dementia in Scotland</p> <p>Scottish Government <i>Technology Charter for People Living with Dementia in Scotland</i> (2015)</p> <p>Mental Welfare Commission for Scotland, <i>Dignity and respect: dementia continuing care visits</i> (Edinburgh, 2014)</p> <p>Health Improvement Scotland: Care of Older People in Hospital Standards  Health Improvement Scotland: Older People in Acute Care Improvement Programme  Health Improvement Scotland: Focus on Dementia Programme</p> <p>NHS Health Scotland, <i>Dementia and Equality - Meeting the challenge in Scotland</i> (Edinburgh, 2016)</p> <p>Equality and Human Rights Commission, Scotland: Equality Act 2010</p>
<b>12.</b>	<b>Who is this guidance for?</b>
	Multidisciplinary team including doctors, nurses, key workers in primary, secondary and social care settings
<b>13.</b>	<b>Implementation</b>
	<p>Links with existing audit programmes  National and Local Quality Improvement programmes: Health Improvement Scotland  Alzheimer Scotland</p> <p>Existing educational initiatives  Learn Pro  NES – Promoting Excellence  The Scottish Patient Safety Programme  Local training and educational initiatives</p> <p>Strategies for monitoring implementation  Local clinical governance and self-inspection processes  HIS Targets  National and local quality improvement initiatives and audits</p>
<b>14.</b>	<b>Primary contact for topic proposal</b>
	<p>Dr Ajay Macharouthu, NHS Ayrshire &amp; Arran  Dr Carol Quinn, , NHS Tayside  Dr Adam Daly, NHS Lanarkshire  Janice McAlister, Dementia Nurse Consultant  Andy Shewan, Alzheimer Scotland Dementia Nurse Consultant</p>
<b>15.</b>	<b>Group(s) or institution(s) supporting the proposal</b>
	<p>The Royal College of Psychiatrists, Scotland</p> <p>Alzheimer’s Scotland</p>

## Declaration of Interests

*Please complete all sections and if you have nothing to declare please put 'N/A'*

Having read the [SIGN Policy on Declaration of Competing Interests](#) I declare the following competing interests for the previous year, and the following year. I understand that this declaration will be retained by the SIGN Programme Lead and be made available on the SIGN website for time period that the proposal is being considered.

<b>Signature:</b>	
<b>Name:</b>	Dr Ajay Macharouthu
<b>Relationship to SIGN:</b>	Topic proposal primary contact
<b>Date:</b>	01/02/2018
<b>Date received at SIGN:</b>	

### Personal Interests

#### Remuneration from employment

	Name of Employer and Post held	Nature of Business	Self or partner/relative	Specific?
<b>Details of employment held which may be significant to, or relevant to, or bear upon the work of SIGN</b>			N/a	n/a

#### Remuneration from self employment

	Name of Business	Nature of Business	Self or partner/relative	Specific?
<b>Details of self employment held which may be significant to, or relevant to, or bear upon the work of SIGN</b>	N/A			

#### Remuneration as holder of paid office

	Nature of Office held	Organisation	Self or partner/relative	Specific?
<b>Details of office held which may be significant to, or relevant to, or bear upon the work of SIGN</b>	N/A			

**Remuneration as a director of an undertaking**

	<b>Name of Undertaking</b>	<b>Nature of Business</b>	<b>Self or partner/ relative</b>	<b>Specific?</b>
<b>Details of directorship held which may be significant to, or relevant to, or bear upon the work of SIGN</b>	N/A			

**Remuneration as a partner in a firm**

	<b>Name of Partnership</b>	<b>Nature of Business</b>	<b>Self or partner/ relative</b>	<b>Specific?</b>
<b>Details of Partnership held which may be significant to, or relevant to, or bear upon the work of SIGN</b>	N/A			

**Shares and securities**

	<b>Description of organisation</b>	<b>Description of nature of holding (value need not be disclosed)</b>	<b>Self or partner/ relative</b>	<b>Specific?</b>
<b>Details of interests in shares and securities in commercial healthcare companies, organisations and undertakings</b>	N/A			

**Remuneration from consultancy or other fee paid work commissioned by, or gifts from, commercial healthcare companies, organisations and undertakings**

	<b>Nature of work</b>	<b>For whom undertaken and frequency</b>	<b>Self or partner/ relative</b>	<b>Specific?</b>
<b>Details of consultancy or other fee paid work which may be significant of to, or relevant to, or bear upon the work of SIGN</b>	N/A			


Details of gifts which may be significant to, or relevant to, or bear upon the work of SIGN				
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**Non-financial interests**

	Description of interest	Self or partner/ relative	Specific?
Details of non-financial interests which may be significant to, or relevant to, or bear upon the work of SIGN	N/A		

**Non-personal interests**

	Name of company, organisation or undertaking	Nature of interest
Details of non-personal support from commercial healthcare companies, organisations or undertakings	N/A	

Signature  \_\_\_\_\_

Date: 01/02/18

*Thank you for completing this form.*

**Please return to  
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**Data Protection**

Your details will be stored on a database for the purposes of managing this guideline topic proposal. We may retain your details so that we can contact you about future Healthcare Improvement Scotland activities. We will not pass these details on to any third parties. Please indicate if you do not want your details to be stored after the proposal is published.



## Initial screen

**Purpose:** initial screening by SIGN Senior Management Team to exclude proposals that are neither clinical, nor multi-professional, nor appropriate for the SIGN process.

1.	<b>Is this an appropriate clinical topic for a SIGN guideline?</b> Is it a clinical topic, what is the breadth of the topic and is there a need for the guideline as identified in the proposal?	
	Yes, but not in current form. Clinicians know how to assess people but the key thing is getting the correct people into clinics. Need to focus on the areas that will have the biggest impact on patient care, eg strategies of care and support.	
2.	<b>Is there a suitable alternative product which would address this topic?</b> Would another Healthcare Improvement Scotland product better address the topic?	
	No, however some aspects may be covered in other HIS outputs eg Older People in Acute Care work stream.	
3.	<b>Has this topic been considered before and rejected?</b> What were the reasons for rejection and are they still applicable	
	No, SIGN 86 recently withdrawn as over 10 years old.	
4.	<b>Outcome</b>	
	Go forward to the next stage of topic selection	<b>YES</b> <b>07/12/2016</b>
	Reject	

## Scope of recent evidence

### Summary:

Twenty five **guidelines** were identified with publication dates ranging from 2006–2016. The guidelines were from the UK, USA, Canada and Europe and 10 of which were guidelines/pathways/quality standards from NICE. The following topics were covered in the guidelines:

- diagnosis, radiology appropriateness criteria and neuroimaging
- cognitive assessment
- disability and fragility
- behavioural disturbances
- independence and well being
- health and social care support
- long term care and nursing
- pharmacological interventions.

There is evidence from 22 **health technology assessments** from the UK and north America on:

- novel diagnostic methods
- non-pharmacological and pharmacological interventions
- psychiatric care
- management of behaviour and psychological symptoms
- long-term care
- managing comorbidities and complications (eg incontinence)

A further fifty five **Cochrane reviews** provide evidence on:

- diagnosis, and assessment
- neuroimaging
- pharmacological and non- pharmacological interventions for cognitive and behavioural disturbance
- comorbidities.

Patient groups include those with mild-moderate, and severe dementia and those requiring palliative care. Settings include primary care, home support and community care, long term care and nursing home care.

A further **504** systematic reviews and **1998** randomised controlled trials (published between 2012 and 2017) were identified.

See Annex 1 for further details

## Suitability screen

**Purpose:** screening by the Guideline Programme Advisory Board to select applications suitable for inclusion in the SIGN topic selection process.

<b>1.</b>	<b>Is there an owner for the project?</b> (preferably an individual)
	Yes, with multidisciplinary and geographically representative support.
<b>2.</b>	<b>Is this a clinical priority area for NHSScotland?</b>
	This is a clinical priority for Scotland. The Scottish Government's National Dementia Strategy published in 2017. Health and social care cost for managing people with dementia are high and rising. The previous SIGN guideline has been withdrawn due to being over 10 years old.
<b>3.</b>	<b>Is there a gap between current and optimal practice? OR Is there wide variation in current practice?</b> (is this an area of clinical uncertainty)
	Variations exist across Scotland in the standard and consistency of diagnosis, assessment, care and support in dementia care, treatment and management. Variations may contribute to poorer health and quality of life outcomes for people with dementia and their carers, along with higher health and social costs.
<b>4.</b>	<b>Is there a suitable guideline already available that could be adapted?</b> (not necessarily by SIGN)
	Ten guidelines/pathways/quality standards are available from NICE, as well as guidelines from other organisations and countries.
<b>5.</b>	<b>Is there adequate literature to make an evidence-based decision about appropriate practice?</b> (is effective intervention proven and would it reduce mortality or morbidity)
	Yes, there is a body of evidence from systematic reviews and HTAs covering many aspect of managing people with dementia and their carers.
<b>6.</b>	<b>Would the proposed practice change result in sufficient change in outcomes</b> (health status, provider and consumer satisfaction and cost) <b>to justify the effort?</b>
	There is potential to improve diagnosis, post diagnosis interventions and patient outcomes of quality of life and activities of daily living.
	How big is the gap?
	Not sure
	How much effort will it take to close the gap?
	Not sure
<b>7.</b>	<b>Is there a perceived need for the guideline, as indicated by a network of relevant stakeholders?</b>
	There is a need as described by the Royal College of Psychiatrists, Scotland and Alzheimer's Scotland.
<b>8.</b>	<b>Is there a reasonable likelihood that NHSScotland could implement the change?</b>
	Strategies and standards from Scottish Government and the Focus on Dementia work stream from Healthcare Improvement Scotland may aid implementation.
<b>9.</b>	<b>Does the proposer have any conflicts of interest? If so how will these be managed?</b>

	None	
<b>10.</b>	<b>Outcome</b>	
	Go forward to the next stage of topic selection <b>The scope of the proposal does not fit with current requirement for focused guideline remits in areas of uncertainty. While acknowledging a need for a guideline GPAG remains uncertain over the focus of this guideline and seeks discussion at SIGN Council</b>	<b>YES</b> <b>14/02/2018</b>
	Reject	
<b>11.</b>	<b>Decision</b>	
	Accepted by SIGN Council for inclusion on the current SIGN guideline development programme	<b>Date</b>
	<i>Comment</i> Following further correspondence from interested parties about aspects of dementia care not covered by Focus on Dementia it was agreed that the proposal would go ahead with a focus on interventions and in cross collaboration with the Focus on dementia team.	<b>10/10/2018</b>
	Rejected by SIGN Council for inclusion on the current SIGN guideline development programme	<b>Date</b>
	<i>Comment</i> After discussion with Michelle Miller, Portfolio Lead: Focus on Dementia in Healthcare Improvement Scotland who provided an overview of EU Joint Action-Act on Dementia, it was agreed that this proposal would go on hold until findings from these studies emerge and we can develop a guideline to add value rather than duplicate effort ( <a href="http://www.actondementia.eu">www.actondementia.eu</a> ). Rona Tatler, lead at Scottish Government agreed to meet when appropriate.	<b>13/06/2018</b>

## Annex 1 Scope of recent evidence

### Resources searched:

[GIN](#) 10 guidelines

[National Guidelines Clearinghouse](#) 5 guidelines. [NICE](#) 10 guidelines/pathways/quality standards

[Cochrane Library](#) 55 Cochrane reviews

It is worth noting that there are 28 protocols for new reviews that have not been included. This is quite a large number. Similarly there are a lot of HTAs in progress.

[CRD databases](#)

DARE (only up to 2014) - 188

[UKHTA](#) – 22 results

Medline – Searched for Reviews from 2015-2017 to top up DARE - 351

Embase - Searched for Reviews from 2015-2017 to top up DARE(Medline journals excl) – 128

Sifted down to 316

CENTRAL searched from numbers of RCTs alone 2012-2017 – 1998 results

### **Dates searched: Searched from 2012 (last scoping search) to September 2017**

Notes:-

I have only looked for guidelines that are focused on dementia. Widening it out to older people generally would produce many more results.

I have also not included guidelines on Parkinson's unless it mentions dementia specifically. I have not included guidelines on Huntington's although that also has dementia symptoms associated with it. This is a rare disease. I have also only included reviews that are focused on dementia to keep it manageable (!).

### **Guidelines**

NICE. Dementia CG42. 2006; Available from: <https://www.nice.org.uk/guidance/cg42#>.

NICE. Dementia, disability and frailty in later life: mid-life approaches to delay or prevent onset overview - Pathway. 2015 Available from: <https://pathways.nice.org.uk/pathways/dementia-disability-and-frailty-in-later-life-mid-life-approaches-to-delay-or-prevent-onset>.

NICE. Dementia - Pathway. 2011; Available from: <https://pathways.nice.org.uk/pathways/dementia>.

NICE. Dementia, disability and frailty in later life – mid-life approaches to delay or prevent onset NG16. 2015; Available from: <https://www.nice.org.uk/guidance/ng16#>.

NICE. Management of aggression, agitation and behavioural disturbances in dementia: carbamazepine ESUOM40. 2015; Available from: <https://www.nice.org.uk/advice/esuom40/chapter/Key-points-from-the-evidence#>.

NICE. Management of aggression, agitation and behavioural disturbances in dementia: valproate preparations ESUOM41. 2015; Available from: <https://www.nice.org.uk/advice/esuom41/chapter/Key-points-from-the-evidence#>.

NICE. Low-dose antipsychotics in people with dementia KTT7. 2015; Available from: <https://www.nice.org.uk/advice/ktt7#>.

NICE. Dementia: independence and wellbeing QS30. 2013 ; Available from: <https://www.nice.org.uk/guidance/qs30#>.

NICE. Dementia: support in health and social care QS1. 2010 ; Available from: <https://www.nice.org.uk/guidance/qs1#>.

NICE. Dementia resource for carers and care providers. 2012 ; Available from: <https://www.nice.org.uk/About/NICE-Communities/Social-care/Tailored-resources/Dementia>.

Ontario RNAo. Delirium, Dementia, and Depression in Older Adults: Assessment and Care, Second Edition. 2016 ; Available from: [http://rناo.ca/sites/rناo-ca/files/bpg/RNAO\\_Delirium\\_Dementia\\_Depression\\_Older\\_Adults\\_Assessment\\_and\\_Care.pdf](http://rناo.ca/sites/rناo-ca/files/bpg/RNAO_Delirium_Dementia_Depression_Older_Adults_Assessment_and_Care.pdf).

Association AMD. Dementia in the long term care setting. 2012 ; Available from: <https://www.guideline.gov/summaries/downloadcontent/ngc-9847?contentType=pdf>.

Nursing HfG. Evidence-based geriatric nursing protocols for best practice. 2012 ; Available from: <https://www.guideline.gov/summaries/downloadcontent/ngc-9709?contentType=pdf>.

Radiology ACo. ACR Appropriateness Criteria® dementia and movement disorders. 2014 ; Available from: <https://www.guideline.gov/summaries/downloadcontent/ngc-10450?contentType=pdf>.

European Academy of Neurology. EFNS-ENS guidelines on the diagnosis and management of disorders associated with dementia. 2012 ; Available from: <https://www.guideline.gov/summaries/downloadcontent/ngc-9359?contentType=pdf>.

European Academy of Neurology. EFNS task force: the use of neuroimaging in the diagnosis of dementia. 2012 ; Available from: <https://www.guideline.gov/summaries/downloadcontent/ngc-9695?contentType=pdf>.

University of Iowa College of Nursing. Bathing persons with dementia. . 2013 ; Available from: <https://www.guideline.gov/summaries/downloadcontent/ngc-9791?contentType=pdf>.

Association As. Appropriate use criteria for amyloid PET: a report of the Amyloid Imaging Task Force, the Society of Nuclear Medicine and Molecular Imaging, and the Alzheimer's Association. 2013 ; Available from: <https://www.guideline.gov/summaries/downloadcontent/ngc-10095?contentType=pdf>.

Hartford Institute for Geriatric Nursing. Assessing cognitive functioning. In: Evidence-based geriatric nursing protocols for best practice. Developer. 2012 ; Available from: <https://www.guideline.gov/summaries/downloadcontent/ngc-9705?contentType=pdf>.

Association As. Alzheimer's Association recommendations for operationalizing the detection of cognitive impairment during the Medicare Annual Wellness Visit in a primary care setting. 2013 ; Available from: <https://www.guideline.gov/summaries/downloadcontent/ngc-9977?contentType=pdf>.

Association AP. The American Psychiatric Association practice guideline on the use of antipsychotics to treat agitation or psychosis in patients with dementia. 2016 ; Available from: <https://www.guideline.gov/summaries/downloadcontent/ngc-10994?contentType=pdf>.

Hartford Institute for Geriatric Nursing. Recognition and management of dementia. In: Evidence-based geriatric nursing protocols for best practice. 2012 ; Available from: <https://www.guideline.gov/summaries/downloadcontent/ngc-9709?contentType=pdf>.

Neurology AAo. Practice parameter update: evaluation and management of driving risk in dementia. Report of the Quality Standards Subcommittee of the American Academy of Neurology. 2013 ; Available from: <https://www.guideline.gov/summaries/downloadcontent/ngc-7824?contentType=pdf>.

Force UPSt. Screening for cognitive impairment in older adults: U.S. Preventive Services Task Force recommendation statement. 2014 ; Available from: <https://www.guideline.gov/summaries/downloadcontent/ngc-10364?contentType=pdf>.

Care CTFoPH. Recommendations on screening for cognitive impairment in older adults. 2016 ; Available from: <https://www.guideline.gov/summaries/downloadcontent/ngc-10869?contentType=pdf>.

## **Health Technology Assessments**

Evidence briefing on non-pharmacological interventions for dementia in care home settings (Structured abstract). Health Technology Assessment Database. 2013; 4. [cited: url: <https://www.york.ac.uk/media/crd/Evidence%20briefing%20on%20non-pharmacological%20interventions%20for%20dementia%20in%20care%20home%20settings.pdf>

- Inappropriate prescribing of antipsychotic drugs has a negative impact on the quality of care and quality of life experienced by people with dementia in care home settings.
- Leeds and York Partnership NHS Foundation Trust (LYPFT) has begun implementing a multidisciplinary team approach to reduce inappropriate prescribing of antipsychotic drugs for people with dementia in care homes.
- There is reasonable evidence for a range of non-pharmacological interventions including structured activity, caregiver education and training, and individual assessment and care planning.
- As the LYPFT team have noted, there is a need to identify and initially target those homes with the highest levels of antipsychotic use and to engage with managers of homes to understand context and to encourage support/ involvement for the training delivered by the team.

- A recent systematic review of qualitative studies provides support for this strategy and also emphasises the need to collaborate with staff at all levels and to involve family members for successful implementation of nonpharmacological interventions.
- Barriers to implementation can be considerable, especially at a time of pressure on resources, and need to be identified and addressed at an early stage. The review of qualitative studies provides guidance as to the likely barriers and suggests selecting interventions that allow residents meaningful interactions with others and that can be integrated easily into routine care.
- Given limited resources, the LYPFT team could consider prioritising staff training over individual assessment as less input from specialist staff is required and more residents could potentially benefit more quickly.

Best practices in the management of behavioural and psychological symptoms of dementia in residents of long-term care facilities in Alberta (Structured abstract). Health Technology Assessment Database. 2014; 4. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/hta.32015000511/frame.html>]

## 2. POLICY QUESTION

What is/are the best clinical practice(s) alternatives to antipsychotic use for the management of behavioural and psychological symptoms in dementia in long-term care facilities in Alberta?

## 3. RESEARCH OBJECTIVE

To summarize the clinical and cost-effectiveness evidence for pharmacological and nonpharmacological alternatives to antipsychotics to support the development of a clinical practice guideline and provincial policy development for the best clinical practice(s) alternatives to antipsychotics use for the management of behavioural and psychological symptoms of dementia in long-term care facilities in Alberta.

Dementia carers. Effective information, support and services to meet their needs (Structured abstract). Health Technology Assessment Database. 2014; 4. [cited: url: <https://www.york.ac.uk/crd/publications/effectiveness-matters/dementia-carers-em/>]

Carers are the mainstay of dementia care in the UK and the Alzheimer's Society estimate that at least 670,000 people are acting as a primary carer.

As dementia is on the increase, carers will be essential in helping health and social services meet the demand for care.

Carers are known to experience high rates of depression and anxiety. Their need for practical and emotional support to relieve the stress of caring is equally high.

Psychosocial therapy can improve carers' health and well-being; combining two or more psychosocial interventions is likely to be more effective than a single intervention.

Developing carers' coping skills can improve their psychological health and well-being.

Carers indicate they need staged access to clear and understandable information about dementia generally and on the availability of advice and support services.

Locked units to limit access for dementia patients in long-term care facilities: clinical evidence (Structured abstract). Health Technology Assessment Database. 2014; 4. [cited: url: <https://www.cadth.ca/sites/default/files/pdf/htis/nov-2014/RB0744%20Lock-Down%20Final.pdf>]

## RESEARCH QUESTION

What is the clinical evidence regarding the use of locked units to limit access for dementia patients residing in long-term care facilities?

## KEY FINDINGS

No relevant health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, or non-randomized studies were identified regarding locked units to limit access for dementia patients in long-term care facilities.

Managing Faecal Incontinence in people with advanced dementia resident in Care Homes, a realist synthesis of the evidence (FINCH study) (Project record). Health Technology Assessment Database. 2015; 4. [cited: url: <https://njl-admin.nihr.ac.uk/document/download/2010815>]

Background: Eighty per cent of care home residents in the UK are living with dementia. The prevalence of faecal incontinence (FI) in care homes is estimated to range from 30% to 50%. There is limited evidence of what is effective in the reduction and management of FI in care homes.

Objective: To provide a theory-driven explanation of the effectiveness of programmes that aim to improve FI in people with advanced dementia in care homes.

Design: A realist synthesis. This was an iterative approach that involved scoping of the literature and consultation with five stakeholder groups, a systematic search and analysis of published and unpublished evidence, and a validation of programme theories with relevant stakeholders.

Data sources: The databases searched included PubMed, Cumulative Index to Nursing and Allied Health

Literature, The Cochrane Library, Scopus, SocAbs, Applied Social Sciences Index and Abstracts, BiblioMap, Sirius, OpenGrey, Social Care Online and the National Research Register.

Results: The scoping identified six programme theories with related context–mechanism–outcome configurations for testing. These addressed (1) clinician-led support, assessment and review, (2) the contribution of teaching and support for care home staff on how to reduce and manage FI, (3) the causes and prevention of constipation, (4) how the cognitive and physical capacity of the resident affect outcomes, (5) how the potential for recovery, reduction and management of FI is understood by those involved and (6) how the care of people living with dementia and FI is integral to the work patterns of the care home and its staff. Data extraction was completed on 62 core papers with iterative searches of linked literature. Dementia was a known risk factor for FI, but its affect on the uptake of different interventions and the dementia-specific continence and toileting skills staff required was not addressed. Most care home residents with FI will be doubly incontinent and, therefore, there is limited value in focusing solely on FI or on single causes of FI such as constipation. Clinical assessment, knowledge of the causes of FI and strategies that recognise the individuals' preferences are necessary contextual factors. Valuing the intimate and personal care work that care home staff provide to people living with dementia and addressing the dementia-related challenges when providing continence care within the daily work routines are key to helping to reduce and manage FI in this population.

Limitations: The synthesis was constrained by limited evidence specific to FI and people with dementia in care homes and by the lack of dementia-specific evidence on continence aids.

Conclusions: This realist synthesis provides a theory-driven understanding of the conditions under which improvement in care for care home residents living with dementia and FI is likely to be successful.

Future work: Future multicomponent interventions need to take account of how the presence of dementia affects the behaviours and choices of those delivering and receiving continence care within a care home environment.

Study registration: This study is registered as PROSPERO CRD42014009902.

Funding: The National Institute for Health Research Health Technology Assessment programme

Banerjee S, Hellier J, Romeo R, Dewey M, Knapp M, Ballard C, et al. Study of the use of antidepressants for depression in dementia: the HTA -SADD trial - a multicentre, randomised, double-blind, placebo-controlled trial of the clinical effectiveness and cost-effectiveness of sertraline and mirtazapine (Structured abstract). Health Technology Assessment Database. 2013; 4. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1111/hta.12111>]

#### BACKGROUND:

Depression is common in dementia but the evidence base for appropriate drug treatment is sparse and equivocal. We aimed to assess efficacy and safety of two of the most commonly prescribed drugs, sertraline and mirtazapine, compared with placebo.

#### METHODS:

We undertook the parallel-group, double-blind, placebo-controlled, Health Technology Assessment Study of the Use of Antidepressants for Depression in Dementia (HTA-SADD) trial in participants from old-age psychiatry services in nine centres in England. Participants were eligible if they had probable or possible Alzheimer's disease, depression (lasting  $\geq 4$  weeks), and a Cornell scale for depression in dementia (CSDD) score of 8 or more. Participants were ineligible if they were clinically critical (eg, suicide risk), contraindicated to study drugs, on antidepressants, in another trial, or had no carer. The clinical trials unit at King's College London (UK) randomly allocated participants with a computer-generated block randomisation sequence, stratified by centre, with varying block sizes, in a 1:1:1 ratio to receive sertraline (target dose 150 mg per day), mirtazapine (45 mg), or placebo (control group), all with standard care. The primary outcome was reduction in depression (CSDD score) at 13 weeks (outcomes to 39 weeks were also assessed), assessed with a mixed linear-regression model adjusted for baseline CSDD, time, and treatment centre. This study is registered, number ISRCTN88882979 and EudraCT 2006-000105-38.

#### FINDINGS:

Decreases in depression scores at 13 weeks did not differ between 111 controls and 107 participants allocated to receive sertraline (mean difference 1.17, 95% CI -0.23 to 2.58;  $p=0.10$ ) or mirtazapine (0.01, -1.37 to 1.38;  $p=0.99$ ), or between participants in the mirtazapine and sertraline groups (1.16, -0.25 to 2.57;  $p=0.11$ ); these findings persisted to 39 weeks. Fewer controls had adverse reactions (29 of 111 [26%]) than did participants in the sertraline group (46 of 107, 43%;  $p=0.010$ ) or mirtazapine group (44 of 108, 41%;  $p=0.031$ ), and fewer serious adverse events rated as severe ( $p=0.003$ ). Five patients in every group died by week 39.

#### INTERPRETATION:

Because of the absence of benefit compared with placebo and increased risk of adverse events, the present practice of use of these antidepressants, with usual care, for first-line treatment of depression in Alzheimer's disease should be reconsidered.

Bond M, Rogers G, Peters J, Anderson R, Hoyle M, Miners A, et al. The effectiveness and cost-effectiveness of donepezil, galantamine, rivastigmine and memantine for the treatment of Alzheimer's disease (review of TA111): a systematic review and economic model (Structured abstract). Health Technology Assessment Database. 2012; 4. [cited: url: <https://www.ncbi.nlm.nih.gov/books/NBK98910/>]



The three acetylcholinesterase inhibitors donepezil, galantamine and rivastigmine are recommended as options in the management of patients with Alzheimer's disease of moderate severity only (that is, subject to section 1.2 below, those with a Mini Mental State Examination [MMSE] score of between 10 and 20 points), and under specified conditions .

Memantine is not recommended as a treatment option for patients with moderately severe to severe Alzheimer's disease except as part of well-designed clinical studies.

Brasure M, Jutkowitz E, Fuchs E, Nelson VA, Kane RA, Shippee T, et al. Nonpharmacologic interventions for agitation and aggression in dementia (Structured abstract). Health Technology Assessment Database. 2016; 4. [cited: url: <https://effectivehealthcare.ahrq.gov/topics/dementia-agitation-aggression/research/>]

#### Objective

To assess the efficacy, comparative effectiveness, and adverse effects of nonpharmacologic interventions for agitation and aggression in individuals with dementia.

#### Data sources

Ovid MEDLINE®, Ovid Embase®, and the Cochrane Central Register of Controlled Trials bibliographic databases; hand searches of references of relevant studies.

#### Review methods

Two investigators screened abstracts and full-text articles of identified references for eligibility. Eligible studies included randomized controlled trials evaluating nonpharmacologic interventions to manage agitation/aggression in individuals with dementia in nursing home, assisted living, or community settings. We analyzed outcomes of agitation/aggression, general behavior, patient quality of life, admission to long-term care, and staff and caregiver outcomes related to patient behavior and care burden. We assessed risk of bias, extracted data, and evaluated strength of evidence for each comparison and outcome. We analyzed pooled estimates to assess efficacy and comparative effectiveness. We conducted a qualitative analysis when data could not be pooled.

#### Results

We identified 126 unique randomized controlled trials as of July 2015. Patient-level interventions involving music, aromatherapy with lavender, and bright light were similar to usual treatment or attention control at managing agitation/aggression in people with dementia (low-strength evidence); interventions tailored to recipients' skills, interests, or both were similar to usual care in managing agitation/aggression in people with dementia (low-strength evidence). Care delivery–level interventions (dementia care mapping and person-centered care) were similar to usual care in managing agitation/aggression in people with dementia (low-strength evidence). Evidence was insufficient to draw conclusions on the effectiveness of most caregiver-level interventions in managing agitation/aggression in people with dementia; caregiver interventions targeting caregiver skills and behavior were similar to attention control in managing agitation/aggression (low-strength evidence). However, these interventions show benefits in caregiver confidence in caregiving and caregiver distress. Adverse effects were rarely reported.

#### Conclusions

Although many trials have been conducted to determine effective nonpharmacologic interventions for agitation/aggression in dementia, which is a critical topic, the evidence base is weak because of the variety of comparisons, measurement issues, and other methodological limitations. When evidence was sufficient to draw conclusions about effectiveness for a group of interventions, agitation/aggression outcomes were typically similar to those of control groups. Future research is needed to guide providers and informal caregivers toward effective interventions for agitation/aggression in dementia.

Bunn F, Burn AM, Goodman C, Robinson L, Rait G, Norton S, et al. Comorbidity and dementia: a mixed-method study on improving health care for people with dementia (CoDem) (Structured abstract). Health Technology Assessment Database. 2016; 4. [cited: url: <https://www.ncbi.nlm.nih.gov/books/NBK344389/>]

#### Background:

Among people living with dementia (PLWD) there is a high prevalence of comorbid medical conditions but little is known about the effects of comorbidity on processes and quality of care and patient needs or how services are adapting to address the particular needs of this population.

#### Objectives:

To explore the impact of dementia on access to non-dementia services and identify ways of improving the integration of services for this population.

#### Design:

We undertook a scoping review, cross-sectional analysis of a population cohort database, interviews with PLWD and comorbidity and their family carers and focus groups or interviews with health-care professionals (HCPs). We focused specifically on three conditions: diabetes, stroke and vision impairment (VI). The analysis was informed by theories of continuity of care and access to care.

#### Participants:

The study included 28 community-dwelling PLWD with one of our target comorbidities, 33 family carers and 56 HCPs specialising in diabetes, stroke, VI or primary care.

#### Results:

The scoping review (n = 76 studies or reports) found a lack of continuity in health-care systems for PLWD and comorbidity, with little integration or communication between different teams and specialities. PLWD had poorer access to services than those without dementia. Analysis of a population cohort database found that 17% of PLWD had diabetes, 18% had had a stroke and 17% had some form of VI. There has been an increase in the use of unpaid care for PLWD and comorbidity over the last decade. Our qualitative data supported the findings of the scoping review: communication was often poor, with an absence of a standardised approach to sharing information about a person's dementia and how it might affect the management of other conditions. Although HCPs acknowledged the vital role that family carers play in managing health-care conditions of PLWD and facilitating continuity and access to care, this recognition did not translate into their routine involvement in appointments or decision-making about their family member. Although we found examples of good practice, these tended to be about the behaviour of individual practitioners rather than system-based approaches; current systems may unintentionally block access to care for PLWD. Pathways and guidelines for our three target conditions do not address the possibility of a dementia diagnosis or provide decision-making support for practitioners trying to weigh up the risks and benefits of treatment for PLWD.

#### Conclusions:

Significant numbers of PLWD have comorbid conditions such as stroke, diabetes and VI. The presence of dementia complicates the delivery of health and social care and magnifies the difficulties that people with long-term conditions experience. Key elements of good care for PLWD and comorbidity include having the PLWD and family carer at the centre, flexibility around processes and good communication which ensures that all services are aware when someone has a diagnosis of dementia. The impact of a diagnosis of dementia on pre-existing conditions should be incorporated into guidelines and care planning. Future work needs to focus on the development and evaluation of interventions to improve continuity of care and access to services for PLWD with comorbidity.

Cadth. Tools and devices for the management of dementia in older adults: review of evidence-based guidelines (Structured abstract). Health Technology Assessment Database. 2013; 4. [cited: url: <https://www.cadth.ca/media/pdf/htis/apr-2013/RC0444%20Tools%20for%20Dementia%20Final.pdf>

#### RESEARCH QUESTION

What are the evidence-based guidelines for the use of tools or devices for the management of dementia in older adults?

#### KEY FINDINGS

A limited volume of lower quality evidence from one guideline suggests that safety locks, alarm systems, and mobile locator devices are likely useful for the management of wandering in patients with dementia.

Cadth. Psychiatrist-led care of patients with dementia and psychiatric disorders in long-term care settings: clinical evidence and guidelines (Structured abstract). Health Technology Assessment Database. 2014; 4. [cited: url: <https://www.cadth.ca/sites/default/files/pdf/htis/nov-2014/RB0753%20Psychiatric%20Coverage%20Final.pdf>

#### RESEARCH QUESTIONS

1. What is the clinical evidence regarding the need for psychiatrist-led care for patients under age 65 with dementia and a psychiatric diagnosis in long-term care settings?
2. What are the evidence-based guidelines regarding the management of patients under age 65 with dementia and a psychiatric diagnosis in long-term care settings?

#### KEY FINDINGS

No health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, or evidence-based guidelines were identified regarding psychiatrist-led care of patients with dementia and psychiatric disorders in long-term care settings.

Cadth. Screening tools to identify adults with cognitive impairment associated with dementia: diagnostic accuracy (Structured abstract). Health Technology Assessment Database. 2014; 4. [cited: url: <https://www.cadth.ca/sites/default/files/pdf/htis/nov-2014/RB0752%20Cognitive%20Assessments%20for%20Dementia%20Final.pdf>

## RESEARCH QUESTION

What is the diagnostic accuracy of screening tools to identify adults with cognitive impairment associated with dementia?

## KEY FINDINGS

Nine systematic reviews and meta-analyses, and 43 non-randomized studies were identified regarding the diagnostic accuracy of screening tools to identify adults with cognitive impairment associated with dementia. No relevant randomized controlled trials were identified.

Gridley K, Brooks J, Birks Y, Baxter K, Parker G. Improving care for people with dementia: development and initial feasibility study for evaluation of life story work in dementia care (Structured abstract). Health Technology Assessment Database. 2016; 4. [cited: url: <https://www.ncbi.nlm.nih.gov/books/NBK379598/>]

## Abstract

### Background:

Improving dementia care quality is an urgent priority nationally and internationally. Life story work (LSW) is an intervention that aims to improve individual outcomes and care for people with dementia and their carers. LSW gathers information and artefacts about the person, their history and interests, and produces a tangible output: the 'life story'.

### Objective:

To establish whether or not full evaluation of LSW was feasible.

### Design:

Mixed-methods feasibility study.

### Methods:

In-depth interviews and focus groups explored experiences of LSW and best practice with people with dementia, family members and dementia care staff. A systematic review explored best practice and theories of change for LSW. These stages helped to identify the outcomes and resources to explore in the feasibility study. A representative sample survey of health and social care dementia care providers in England established LSW practice in different settings. A survey of a self-selected sample of family members of people with dementia explored how LSW is experienced. Two small outcome studies (stepped-wedge study in six care homes and pre-test post-test study in inpatient specialist dementia care wards) explored the feasibility of full evaluation of LSW in these settings.

### Settings:

Survey: generalist and specialist care homes; NHS dementia care settings; and community dementia services.

Feasibility study: care homes and NHS inpatient dementia care wards.

### Participants:

NHS and social care services, people with dementia, family carers, care home staff and NHS staff.

### Interventions:

LSW.

### Main outcome measures:

Spread of LSW and good practice, quality of life (QoL) for the person with dementia and carers, relationships between people with dementia and family carers, staff attitudes about dementia, staff burnout, resource use and costs.

### Review methods:

Narrative review and synthesis, following Centre for Review and Dissemination guidelines.

### Results:

Good practice in LSW is identifiable, as are theories of change about how it might affect given outcomes. Indicators of best practice were produced. LSW is spreading but practice and use vary between care settings and are not always in line with identified good practice. Two different models of LSW are evident; these are likely to be appropriate at different stages of the dementia journey. The feasibility study showed some positive changes in staff attitudes towards dementia and, for some people with dementia, improvements in QoL. These may be attributable to LSW but these potential benefits require full evaluation. The feasibility work established the likely costs of LSW and highlighted the challenges of future evaluation in care homes and inpatient dementia care settings.

### Limitations:

There was insufficient evidence in the literature to allow estimation of outcome size. We did not carry out planned Markov chain modelling to inform decisions about carrying out future evaluation because of the dearth of outcome data in the literature; low levels of data return for people with dementia in the hospital settings; lack of detected effect for most people with dementia; and questions about implementation in the research settings.

### Conclusions:

LSW is used across different health and social care settings in England, but in different ways, not all of which reflect 'good practice'. This large, complex study identified a wide range of challenges for future research, but also the possibility that LSW may help to improve care staff attitudes towards dementia and QoL for some people with dementia.

### Future work:

Full evaluation of LSW as an intervention to improve staff attitudes and care is feasible with researchers based in

or very close to care settings to ensure high-quality data collection.

Livingston G, Barber J, Rapaport P, Knapp M, Griffin M, Romeo R, et al. START (STrAtegies for RelaTives) study: a pragmatic randomised controlled trial to determine the clinical effectiveness and cost-effectiveness of a manual-based coping strategy programme in promoting the mental health of carers of people with dementia (Structured abstract). Health Technology Assessment Database. 2014; 4. [cited: url: <https://www.ncbi.nlm.nih.gov/books/NBK262901/>]

#### Abstract

##### Background:

Two-thirds of people with dementia live at home, receiving most care from family carers, about 40% of whom have clinically significant depression or anxiety. This impacts on the person with dementia, families and society, predicting care breakdown. There are currently no clinically effective and cost-effective NHS family carer interventions.

##### Objectives:

To assess the STrAtegies for RelaTives (START) intervention in the short (4 and 8 months) and long term (1 and 2 years) compared with treatment as usual (TAU).

##### Design:

Randomised, parallel-group, superiority trial with blinded assessment recruiting participants 2 : 1 (intervention to TAU) to allow for therapist clustering.

##### Setting:

Three UK mental health services and one neurological service.

##### Participants:

Family carers of people with dementia.

##### Intervention:

Eight-session manual-based coping intervention delivered by supervised psychology graduates to individuals.

##### Main outcome measures:

Affective symptoms [Hospital Anxiety and Depression Scale-total (HADS-T)] and cost-effectiveness. Secondary measures: anxiety and depression symptoms and caseness, quality of life (QoL), abusive behaviour and long-term care home admission.

##### Results:

Two hundred and sixty participants were randomised (173 intervention, 87 TAU). We used intention-to-treat analysis in the short term (152 intervention, 77 TAU) and in the long term (140 intervention, 69 TAU).

In the short term, the intervention group had lower HADS-T [mean difference  $-1.80$ , 95% confidence interval (CI)  $-3.29$  to  $-0.31$ ;  $p = 0.02$ ] and higher quality-adjusted life-years (QALYs) (mean difference  $0.03$ , 95% CI  $-0.01$  to  $0.08$ ). Costs were no different between groups [mean  $\pounds 252$  (95% CI  $-\pounds 28$  to  $\pounds 565$ ) for intervention group]. The cost-effectiveness acceptability curve showed a greater than 99% chance of being cost-effective at a  $\pounds 30,000$ /QALY willingness-to-pay threshold and a high probability of cost-effectiveness based on the HADS-T score. Carers in the intervention group had less case-level depression [odds ratio (OR)  $0.24$ , 95% CI  $0.07$  to  $0.76$ ], a trend towards reduced case-level anxiety (OR  $0.30$ , 95% CI  $0.08$  to  $1.05$ ), lower Hospital Anxiety and Depression Scale-anxiety (HADS-A) ( $-0.91$ , 95% CI  $-1.76$  to  $-0.07$ ;  $p = 0.03$ ) and Hospital Anxiety and Depression Scale-depression (HADS-D) ( $-0.91$ , 95% CI  $-1.71$  to  $-0.10$ ;  $p = 0.03$ ) and higher Health Status Questionnaire (HSQ) QoL (mean difference  $4.09$ , 95% CI  $0.34$  to  $7.83$ ). Group differences in abusive behaviour (OR  $0.48$ , 95% CI  $0.18$  to  $1.27$ ) and the person with dementia's quality of life-Alzheimer's disease (QoL-AD) (mean increase  $0.59$ , 95% CI  $-0.72$  to  $1.89$ ) were not significant.

In the long term, the intervention group had lower HADS-T (mean difference  $-2.58$ , 95% CI  $-4.26$  to  $-0.90$ ;  $p = 0.03$ ) and higher QALYs (mean difference  $0.03$ , 95% CI  $-0.01$  to  $0.06$ ). Carers in the intervention group had less case-level depression (OR  $0.14$ , 95% CI  $0.04$  to  $0.53$ ), a trend towards reduced case-level anxiety (OR  $0.57$ , 95% CI  $0.26$  to  $1.24$ ), lower HADS-A ( $-1.16$ , 95% CI  $-2.15$  to  $-0.18$ ) and HADS-D ( $1.45$ , 95% CI  $-2.32$  to  $-0.57$ ), and higher HSQ (mean difference  $7.47$ , 95% CI  $2.87$  to  $12.08$ ). Thirty-two (18.7%) people with dementia in the intervention group and 17 (20.2%) in TAU were admitted to a care home (hazard ratio  $0.83$ , 95% CI  $0.44$  to  $1.56$ ;  $p = 0.56$ ). There were no significant differences between groups in abusive behaviour (OR  $0.83$ , 95% CI  $0.36$  to  $1.94$ ), the person with dementia's QoL-AD ( $0.17$ , 95% CI  $-1.37$  to  $1.70$ ) or costs ( $\pounds 336$ , 95% CI  $-\pounds 223$  to  $\pounds 895$ ) for intervention group. The probability that the intervention would be seen as cost-effective at  $\pounds 30,000$ /QALY threshold and cost-effectiveness on the HADS-T remained high.

##### Conclusions:

The START intervention was clinically effective and cost-effective in the short and longer term. The results are robust to the sensitivity analyses performed. Future work is needed to consider mechanism of action; the effects on people with dementia in clinical terms (cognition, neuropsychiatric symptoms, longer-term care home admission); and on health and social care costs. In addition, we will explore the effects of carer abusive behaviour on the care recipient's care home admission and if this then reduces abusive behaviour. We would also like to implement START and evaluate this implementation in clinical practice.

Livingston G, Kelly L, Lewis-Holmes E, Baio G, Morris S, Patel N, et al. A systematic review of the clinical



effectiveness and cost-effectiveness of sensory, psychological and behavioural interventions for managing agitation in older adults with dementia (Structured abstract). Health Technology Assessment Database. 2014; 4. [cited: url: <https://www.ncbi.nlm.nih.gov/books/NBK262105/>]

## Abstract

### Background:

Agitation is common, persistent and distressing in dementia and is linked with care breakdown. Psychotropic medication is often ineffective or harmful, but the evidence regarding non-pharmacological interventions is unclear.

### Objectives:

We systematically reviewed and synthesised the evidence for clinical effectiveness and cost-effectiveness of non-pharmacological interventions for reducing agitation in dementia, considering dementia severity, the setting, the person with whom the intervention is implemented, whether the effects are immediate or longer term, and cost-effectiveness.

### Data sources:

We searched twice using relevant search terms (9 August 2011 and 12 June 2012) in Web of Knowledge (incorporating MEDLINE); EMBASE; British Nursing Index; the Health Technology Assessment programme database; PsycINFO; NHS Evidence; System for Information on Grey Literature; The Stationery Office Official Documents website; The Stationery National Technical Information Service; Cumulative Index to Nursing and Allied Health Literature; and The Cochrane Library. We also searched Cochrane reviews of interventions for behaviour in dementia, included papers' references, and contacted authors about 'missed' studies. We included quantitative studies, evaluating non-pharmacological interventions for agitation in dementia, in all settings.

### Review method:

We rated quality, prioritising higher-quality studies. We separated results by intervention type and agitation level. As we were unable to meta-analyse results except for light therapy, we present a qualitative evidence synthesis. In addition, we calculated standardised effect sizes (SESs) with available data, to compare heterogeneous interventions. In the health economic analysis, we reviewed economic studies, calculated the cost of effective interventions from the effectiveness review, calculated the incremental cost per unit improvement in agitation, used data from a cohort study to evaluate the relationship between health and social care costs and health-related quality of life (DEMQOL-Proxy-U scores) and developed a new cost-effectiveness model.

### Results:

We included 160 out of 1916 papers screened. Supervised person-centred care, communication skills (SES = -1.8 to -0.3) or modified dementia care mapping (DCM) with implementing plans (SES = -1.4 to -0.6) were all efficacious at reducing clinically significant agitation in care home residents, both immediately and up to 6 months afterwards. In care home residents, during interventions but not at follow-up, activities (SES = -0.8 to -0.6) and music therapy (SES = -0.8 to -0.5) by protocol reduced mean levels of agitation; sensory intervention (SES = -1.3 to -0.6) reduced mean and clinically significant symptoms. Advantages were not demonstrated with 'therapeutic touch' or individualised activity. Aromatherapy and light therapy did not show clinical effectiveness. Training family carers in behavioural or cognitive interventions did not decrease severe agitation. The few studies reporting activities of daily living or quality-of-life outcomes found no improvement, even when agitation had improved. We identified two health economic studies. Costs of interventions which significantly impacted on agitation were activities, £80–696; music therapy, £13–27; sensory interventions, £3–527; and training paid caregivers in person-centred care or communication skills with or without behavioural management training and DCM, £31–339. Among the 11 interventions that were evaluated using the Cohen-Mansfield Agitation Inventory (CMAI), the incremental cost per unit reduction in CMAI score ranged from £162 to £3480 for activities, £4 for music therapy, £24 to £143 for sensory interventions, and £6 to £62 for training paid caregivers in person-centred care or communication skills with or without behavioural management training and DCM. Health and social care costs ranged from around £7000 over 3 months in people without clinically significant agitation symptoms to around £15,000 at the most severe agitation levels. There is some evidence that DEMQOL-Proxy-U scores decline with Neuropsychiatric Inventory agitation scores. A multicomponent intervention in participants with mild to moderate dementia had a positive monetary net benefit and a 82.2% probability of being cost-effective at a maximum willingness to pay for a quality-adjusted life-year of £20,000 and a 83.18% probability at a value of £30,000.

### Limitations:

Although there were some high-quality studies, there were only 33 reasonably sized (> 45 participants) randomised controlled trials, and lack of evidence means that we cannot comment on many interventions' effectiveness. There were no hospital studies and few studies in people's homes. More health economic data are needed.

### Conclusions:

Person-centred care, communication skills and DCM (all with supervision), sensory therapy activities, and structured music therapies reduce agitation in care-home dementia residents. Future interventions should change care home culture through staff training and permanently implement evidence-based treatments and evaluate health economics. There is a need for further work on interventions for agitation in people with dementia living in their own homes.

Nihr HSC. COGNISION? for neurological disorders, including dementia (Structured abstract). Health Technology Assessment Database. 2013; 4. [cited: url: <http://www.io.nihr.ac.uk/topics/cognision-for-neurological-disorders->]

[including-dementia/](#)

COGNISION™ is a new system developed by Neuronetrix to assist clinicians in the diagnosis and evaluation of Alzheimer's disease, related dementias and other neurological disorders. The system is intended to non-invasively detect differences in the neural processing of auditory stimuli in people with neurological disorders.

Nihr HSC. Leuco-methylthionium (LMTX) for behavioural variant frontotemporal dementia ? first line (Structured abstract). Health Technology Assessment Database. 2013; 4. [cited: url: <http://www.io.nihr.ac.uk/topics/leuco-methylthionium-lmtx-for-behavioural-variant-frontotemporal-dementia-first-line/>]

Leuco-methylthionium is a tau protein aggregation inhibitor. It acts by preventing the formation and spread of neurofibrillary tangles, which consist of aberrant tau protein clusters that aggregate within neurons causing toxicity and neuronal cell death in the brain of patients with certain forms of dementia. Leuco-methylthionium is a stabilised, reduced form of charged methylthionium chloride, which requires the low pH of the stomach to allow enzyme conversion to uncharged leuco-methylthionium prior to absorption. In a phase III clinical trial, leuco-methylthionium was administered at 100mg twice a day.

Dementia is a chronic progressive mental disorder which is largely irreversible and is characterised by a widespread impairment of mental function. Frontotemporal dementia (FTD) is a heterogeneous group of dementias that cause frontotemporal lobe degeneration. There are three main clinical syndromes of FTD. The most common type is bvFTD, which is characterised by early progressive personality changes, emotional blunting and loss of empathy. Patients may also experience difficulty in ameliorating their behaviour, often causing socially inappropriate actions. Patients often lose insight into their own behaviour. Language impairment can also occur after behavioural changes and there is sometimes overlap of clinical symptoms of the different syndromes of FTD. As with most forms of FTD, patients' personal hygiene often suffers, mood changes are frequent and abrupt and patients can become apathetic.

The number of patients with dementia in the UK is estimated to be over 821,000 representing 1.3% of the UK population. Around 3-10% of degenerative dementia is FTD; the prevalence of FTD is approximately 10 per 100,000. The prevalence of bvFTD is 1.1-18 cases per 100,000 but could be higher due to under-diagnosis. There are currently no effective disease modifying agents available to this patient group. Leuco-methylthionium is currently undergoing a phase III trial comparing its effectiveness against placebo as assessed by the change from baseline measurements on a number of dementia specific composite endpoints.

Nihr HSC. Leuco-methylthionium for alzheimer's disease (Structured abstract). Health Technology Assessment Database. 2013; 4. [cited: url: <http://www.io.nihr.ac.uk/topics/leuco-methylthionium-for-alzheimers-disease/>]

Leuco-methylthionium is intended for the treatment of mild to moderate Alzheimer's disease (AD). It is a first-in-class tau aggregation inhibitor and if licensed, it will offer a wholly new treatment option for patients with mild-moderate AD who currently have few effective therapies available. Leuco-methylthionium is a tau protein aggregation inhibitor that acts by preventing the formation and spread of neurofibrillary tangles. It is a stabilised, reduced form of charged methylthionium chloride, which requires the low pH of the stomach to allow enzyme conversion to uncharged leuco-methylthionium prior to absorption. It is administered orally at 150mg or 250mg twice daily.

The number of patients with dementia in the UK is estimated to be over 821,000 representing 1.3% of the UK population. AD is the most common form of dementia, accounting for around 60% of all dementia cases. The UK incidence of AD in people over the age of 65 years is estimated to be 4.9 per 1,000 person-years. Between 50 and 64% of people with AD are estimated to have mild to moderately severe disease. In 2011-12, there were 5,512 hospital admissions with a primary diagnosis of AD in England, resulting in 373,085 bed days and 9,083 finished consultant episodes.

The aims of treatment for AD are to promote independence, maintain function and treat symptoms including cognitive, non-cognitive, behavioural and psychological symptoms. Pharmacological options include donepezil, galantamine, rivastigmine, and memantine. Leuco-methylthionium is currently in two phase III clinical trials comparing its effect on AD assessment scale—cognitive subscale scores against treatment with placebo. These trials are expected to be completed in 2015.

Nihr HSC. NeuroAD? for mild and moderate Alzheimer's Disease (Structured abstract). Health Technology Assessment Database. 2013; 4. [cited: url: <http://www.io.nihr.ac.uk/topics/neuroad-for-mild-and-moderate-alzheimers-disease/>]

The NeuroAD™ system, developed by Neuronix, is a new non-invasive treatment for patients with mild and moderate Alzheimer's disease. The NeuroAD™ is the first system to combine focused transcranial magnetic stimulation of the brain with cognitive training to simultaneously target specific brain regions affected by Alzheimer's disease.

Orgeta V, Leung P, Yates L, Kang S, Hoare Z, Henderson C, et al. Individual cognitive stimulation therapy for

dementia: a clinical effectiveness and cost-effectiveness pragmatic, multicentre, randomised controlled trial (Structured abstract). Health Technology Assessment Database. 2015; 4. [cited: url: <https://www.ncbi.nlm.nih.gov/books/NBK311123/>]

#### Abstract

##### Background:

Group cognitive stimulation therapy programmes can benefit cognition and quality of life for people with dementia. Evidence for home-based, carer-led cognitive stimulation interventions is limited.

##### Objectives:

To evaluate the clinical effectiveness and cost-effectiveness of carer-delivered individual cognitive stimulation therapy (iCST) for people with dementia and their family carers, compared with treatment as usual (TAU).

##### Design:

A multicentre, single-blind, randomised controlled trial assessing clinical effectiveness and cost-effectiveness. Assessments were at baseline, 13 weeks and 26 weeks (primary end point).

##### Setting:

Participants were recruited through Memory Clinics and Community Mental Health Teams for older people.

##### Participants:

A total of 356 caregiving dyads were recruited and 273 completed the trial.

##### Intervention:

iCST consisted of structured cognitive stimulation sessions for people with dementia, completed up to three times weekly over 25 weeks. Family carers were supported to deliver the sessions at home.

##### Main outcome measures:

Primary outcomes for the person with dementia were cognition and quality of life. Secondary outcomes included behavioural and psychological symptoms, activities of daily living, depressive symptoms and relationship quality. The primary outcome for the family carers was mental/physical health (Short Form questionnaire-12 items). Health-related quality of life (European Quality of Life-5 Dimensions), mood symptoms, resilience and relationship quality comprised the secondary outcomes. Costs were estimated from health and social care and societal perspectives.

##### Results:

There were no differences in any of the primary outcomes for people with dementia between intervention and TAU [cognition: mean difference  $-0.55$ , 95% confidence interval (CI)  $-2.00$  to  $0.90$ ;  $p$ -value =  $0.45$ ; self-reported quality of life: mean difference  $-0.02$ , 95% CI  $-1.22$  to  $0.82$ ;  $p$ -value =  $0.97$  at the 6-month follow-up]. iCST did not improve mental/physical health for carers. People with dementia in the iCST group experienced better relationship quality with their carer, but there was no evidence that iCST improved their activities of daily living, depression or behavioural and psychological symptoms. iCST seemed to improve health-related quality of life for carers but did not benefit carers' resilience or their relationship quality with their relative. Carers conducting more sessions had fewer depressive symptoms. Qualitative data suggested that people with dementia and their carers experienced better communication owing to iCST. Adjusted mean costs were not significantly different between the groups. From the societal perspective, both health gains and cost savings were observed.

##### Conclusions:

iCST did not improve cognition or quality of life for people with dementia, or carers' physical and mental health. Costs of the intervention were offset by some reductions in social care and other services. Although there was some evidence of improvement in terms of the caregiving relationship and carers' health-related quality of life, iCST does not appear to deliver clinical benefits for cognition and quality of life for people with dementia. Most people received fewer than the recommended number of iCST sessions. Further research is needed to ascertain the clinical effectiveness of carer-led cognitive stimulation interventions for people with dementia.

Woods RT, Bruce E, Edwards RT, Elvish R, Hoare Z, Hounsborne B, et al. REMCARE: reminiscence groups for people with dementia and their family caregivers - effectiveness and cost-effectiveness pragmatic multicentre randomised trial (Structured abstract). Health Technology Assessment Database. 2012; 4. [cited: url: <https://www.ncbi.nlm.nih.gov/books/NBK115063/>]

The objectives of this trial were twofold: first, to explore the effectiveness of joint reminiscence groups for both people with dementia and their carers compared with usual care; and, secondly, to explore the cost-effectiveness of this intervention, paying particular attention to the pattern of health care, social care and voluntary sector service use and associated costs, by people with dementia and their carers.

This trial does not provide support for the effectiveness or cost-effectiveness of joint reminiscence groups for people with dementia and their carers. Although there may perhaps be some beneficial effects for people with dementia who attend sessions as planned, this must be viewed in the context of raised anxiety and stress in their carers. The reasons for these discrepant outcomes need to be explored further, and may necessitate reappraisal of the movement towards joint interventions.

Zimmerman S, Anderson W, Brode S, Jonas D, Lux L, Beeber A, et al. Comparison of characteristics of nursing homes and other residential long-term care settings for people with dementia (Structured abstract). Health

Technology Assessment Database. 2012; 4. [cited: url: <https://effectivehealthcare.ahrq.gov/topics/dementia-nursing-home-characteristics/research/Structured Abstract>

### Objectives

To compare characteristics and related outcomes of nursing homes (NHs) and other residential long-term care settings for people with dementia so as to reduce uncertainty when choosing a setting of care for someone with dementia.

### Data Sources

We searched MEDLINE®, Embase®, the Cochrane Library, the Cumulative Index to Nursing and Allied Health Literature (CINAHL®), AgeLine®, and PsycINFO® from 1990 through March 23, 2012. We identified additional studies from reference lists and experts.

### Review methods

Two people independently selected, abstracted data from, and rated the quality of relevant studies. Given that quantitative analyses were inappropriate because of clinical heterogeneity, insufficient numbers of similar studies, or insufficient or variation in outcome reporting, we synthesized the data qualitatively. Two reviewers graded the strength of evidence (SOE) using established criteria.

### Results

We identified 14 studies meeting our inclusion criteria. Generally, studies examined characteristics, structures, and process of care for populations with mild to severe dementia. Ten studies addressed health outcomes (Key Question [KQ] 1), and 10 examined psychosocial outcomes (KQ 2) for people with dementia. No eligible studies examined health or psychosocial outcomes for informal caregivers (KQ 3 and KQ 4, respectively). The studies included four prospective cohort studies, nine randomized controlled trials (RCTs), and one non-RCT. Two studies showed that the use of pleasant sensory stimulation reduces agitation. We found limited evidence on a number of interventions, including protocols for individualized care to reduce pain/discomfort and agitation/aggression and functional skill training to improve function. We found largely no differences across outcomes including function, cognition, depressive symptoms, pain, morbidity, behavioral symptoms, engagement, and quality of life based on residence in an NH or residential care/assisted living (RC/AL), other than increased hospitalization for people with mild dementia in RC/AL compared with NHs and increased restraint use in NHs compared with RC/AL for imminently dying residents.

### Conclusions

Overall, we found low or insufficient SOE regarding the effect of organizational characteristics, structures, and processes of care on health and psychosocial outcomes for people with dementia and no evidence for informal caregivers. Findings of moderate SOE indicate that pleasant sensory stimulation reduces agitation. Also, although the SOE is low, protocols for individualized care and to improve function result in better outcomes. Finally, outcomes do not differ between NHs and RC/AL except when medical care is indicated. Additional research is needed to develop a sufficient evidence base to support decisionmaking.

## **Cochrane reviews**

Abraham I, Rimland Joseph M, Lozano-Montoya I, Dell'Aquila G, Vélez-Díaz-Pallarés M, Trotta Fabiana M, et al. Simulated presence therapy for dementia. Cochrane Database of Systematic Reviews. 2017; 4. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011882.pub2/abstract>

Background: Dementia is a common and serious neuropsychiatric syndrome, characterised by progressive cognitive and functional decline. The majority of people with dementia develop behavioural disturbances, also known as behavioural and psychological symptoms of dementia (BPSD). Several non-pharmacological interventions have been evaluated to treat BPSD in people with dementia. Simulated presence therapy (SPT), an intervention that uses video or audiotape recordings of family members played to the person with dementia, is a possible approach to treat BPSD. Objectives: To assess the effects of SPT on behavioural and psychological symptoms and quality of life in people with dementia. Search methods: We searched ALOIS (the Specialised Register of the Cochrane Dementia and Cognitive Improvement Group), CENTRAL (The Cochrane Library) (9 February 2016), MEDLINE Ovid SP (1946 to 6 January 2017), Embase Ovid SP (1972 to 6 January 2017), PsycINFO Ovid SP (1806 to 6 January 2017), CINAHL via EBSCOhost (1980 to 6 January 2017), LILACS via BIREME (all dates to 6 January 2017), ClinicalTrials.gov (ClinicalTrials.gov) (all dates to 6 January 2017), and the World Health Organization (WHO) Portal ([apps.who.int/trialsearch](http://apps.who.int/trialsearch)) (all dates to 6 January 2017). We also checked the reference lists of relevant articles to identify any additional studies. Selection criteria: Randomised and quasi-randomised controlled trials, including cross-over studies, that evaluated the efficacy of SPT, consisting of personalised audio or videotape recordings of family members, in people with any form of dementia. Data collection and analysis: Two authors independently selected studies, assessed risk of bias and extracted data. No meta-analyses were conducted because of substantial heterogeneity among the included studies. Main results: Three trials with 144 participants met the inclusion criteria. Two of the trials had a randomised cross-over design, one was a cross-over trial which we classified as quasi-randomised. Participants in the included studies were people with



dementia living in nursing homes. They were predominantly women and had a mean age of over 80 years. SPT was performed using an audio or video recording prepared by family members or surrogates. It varied in its content, frequency of administration and duration. All the studies compared multiple treatments. In one study, SPT was compared with two other interventions; in the other two studies, it was compared with three other interventions. Specifically, SPT was compared to usual care, personalised music (two studies), a 'placebo' audiotape containing the voice of a person (two studies), and one-to-one social interaction performed by trained research assistants (one study). In terms of outcomes evaluated, one study considered agitation and withdrawn behaviour (both assessed with three methods); the second study evaluated verbal disruptive behaviour (assessed with three methods); and the third study evaluated physically agitated behaviour and verbally agitated behaviour (the method used was not clearly described). According to the GRADE criteria, the overall quality of the evidence was very low due to very small numbers of participants and risk of bias in the included studies; (none of the trials was at low risk of selection bias; all the trials were at high risk of performance bias; one trial was at high risk of attrition bias; and all had unclear selective reporting). Because of variation in the participants, the format of SPT, the comparison interventions, and the measures used to assess outcomes, we judged the results unsuitable for a meta-analysis. Within each trial, the effect of SPT on behaviour, compared to usual care, was mixed and depended on the measure used. Two trials which included a personalised music intervention reported no significant differences between simulated presence and music on behavioural outcomes. Because the overall quality of the evidence was very low, we were very uncertain regarding all the results. None of the studies evaluated quality of life or any of our secondary outcome measures (performance of activities of daily living, dropout and carer burden). Authors' conclusions: We were unable to draw any conclusions about the efficacy of SPT for treating behavioural and psychological symptoms and improving quality of life of people with dementia. New high-quality studies are needed to investigate the effect of SPT.

Archer Hilary A, Smailagic N, John C, Holmes Robin B, Takwoingi Y, Coulthard Elizabeth J, et al. Regional Cerebral Blood Flow Single Photon Emission Computed Tomography for detection of Frontotemporal dementia in people with suspected dementia. *Cochrane Database of Systematic Reviews*. 2015; 6. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010896.pub2/abstract>

**Background:** In the UK, dementia affects 5% of the population aged over 65 years and 25% of those over 85 years. Frontotemporal dementia (FTD) represents one subtype and is thought to account for up to 16% of all degenerative dementias. Although the core of the diagnostic process in dementia rests firmly on clinical and cognitive assessments, a wide range of investigations are available to aid diagnosis. Regional cerebral blood flow (rCBF) single-photon emission computed tomography (SPECT) is an established clinical tool that uses an intravenously injected radiolabelled tracer to map blood flow in the brain. In FTD the characteristic pattern seen is hypoperfusion of the frontal and anterior temporal lobes. This pattern of blood flow is different to patterns seen in other subtypes of dementia and so can be used to differentiate FTD. It has been proposed that a diagnosis of FTD, (particularly early stage), should be made not only on the basis of clinical criteria but using a combination of other diagnostic findings, including rCBF SPECT. However, more extensive testing comes at a financial cost, and with a potential risk to patient safety and comfort. **Objectives:** To determine the diagnostic accuracy of rCBF SPECT for diagnosing FTD in populations with suspected dementia in secondary/tertiary healthcare settings and in the differential diagnosis of FTD from other dementia subtypes. **Search methods:** Our search strategy used two concepts: (a) the index test and (b) the condition of interest. We searched citation databases, including MEDLINE (Ovid SP), EMBASE (Ovid SP), BIOSIS (Ovid SP), Web of Science Core Collection (ISI Web of Science), PsycINFO (Ovid SP), CINAHL (EBSCOhost) and LILACS (Bireme), using structured search strategies appropriate for each database. In addition we searched specialised sources of diagnostic test accuracy studies and reviews including: MEDION (Universities of Maastricht and Leuven), DARE (Database of Abstracts of Reviews of Effects) and HTA (Health Technology Assessment) database. We requested a search of the Cochrane Register of Diagnostic Test Accuracy Studies and used the related articles feature in PubMed to search for additional studies. We tracked key studies in citation databases such as Science Citation Index and Scopus to ascertain any further relevant studies. We identified grey literature, mainly in the form of conference abstracts, through the Web of Science Core Collection, including Conference Proceedings Citation Index and Embase. The most recent search for this review was run on the 1 June 2013. **Following title and abstract screening of the search results, full-text papers were obtained for each potentially eligible study. These papers were then independently evaluated for inclusion or exclusion. Selection criteria:** We included both case-control and cohort (delayed verification of diagnosis) studies. Where studies used a case-control design we included all participants who had a clinical diagnosis of FTD or other dementia subtype using standard clinical diagnostic criteria. For cohort studies, we included studies where all participants with suspected dementia were administered rCBF SPECT at baseline. We excluded studies of participants from selected populations (e.g. post-stroke) and studies of participants with a secondary cause of cognitive impairment. **Data collection and analysis:** Two review authors extracted information on study characteristics and data for the assessment of methodological quality and the investigation of heterogeneity. We assessed the methodological quality of each study using the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) tool. We produced a narrative summary describing numbers of studies that were found to have high/low/unclear risk of bias as well as concerns regarding applicability. To produce 2 x 2 tables, we dichotomised the rCBF SPECT results (scan positive or negative for FTD) and cross-tabulated them against the results for the reference standard. These tables were then used to calculate the sensitivity and specificity of the

index test. eta-analysis was not performed due to the considerable between-study variation in clinical and methodological characteristics. Main results: Eleven studies (1117 participants) met our inclusion criteria. These consisted of six case-control studies, two retrospective cohort studies and three prospective cohort studies. Three studies used single-headed camera SPECT while the remaining eight used multiple-headed camera SPECT. Study design and methods varied widely. Overall, participant selection was not well described and the studies were judged as having either high or unclear risk of bias. Often the threshold used to define a positive SPECT result was not predefined and the results were reported with knowledge of the reference standard. Concerns regarding applicability of the studies to the review question were generally low across all three domains (participant selection, index test and reference standard). Sensitivities and specificities for differentiating FTD from non-FTD ranged from 0.73 to 1.00 and from 0.80 to 1.00, respectively, for the three multiple-headed camera studies. Sensitivities were lower for the two single-headed camera studies; one reported a sensitivity and specificity of 0.40 (95% confidence interval (CI) 0.05 to 0.85) and 0.95 (95% CI 0.90 to 0.98), respectively, and the other a sensitivity and specificity of 0.36 (95% CI 0.24 to 0.50) and 0.92 (95% CI 0.88 to 0.95), respectively. Eight of the 11 studies which used SPECT to differentiate FTD from Alzheimer's disease used multiple-headed camera SPECT. Of these studies, five used a case-control design and reported sensitivities of between 0.52 and 1.00, and specificities of between 0.41 and 0.86. The remaining three studies used a cohort design and reported sensitivities of between 0.73 and 1.00, and specificities of between 0.94 and 1.00. The three studies that used single-headed camera SPECT reported sensitivities of between 0.40 and 0.80, and specificities of between 0.61 and 0.97. Authors' conclusions: At present, we would not recommend the routine use of rCBF SPECT in clinical practice because there is insufficient evidence from the available literature to support this. Further research into the use of rCBF SPECT for differentiating FTD from other dementias is required. In particular, protocols should be standardised, study populations should be well described, the threshold for 'abnormal' scans predefined and clear details given on how scans are analysed. More prospective cohort studies that verify the presence or absence of FTD during a period of follow up should be undertaken.

Areosa Sastre A, Vernooij Robin WM, González-Colaço Harmand M, Martínez G. Effect of the treatment of Type 2 diabetes mellitus on the development of cognitive impairment and dementia. *Cochrane Database of Systematic Reviews*. 2017; 6. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003804.pub2/abstract>

Background: Prevention of cognitive impairment and dementia is an important public health goal. Epidemiological evidence shows a relationship between cognitive impairment and Type 2 diabetes mellitus. The risk of dementia increases with duration of disease. This updated systematic review investigated the effect on cognitive function of the type of treatment and level of metabolic control in people with Type 2 diabetes. Objectives: To assess the effects of different strategies for managing Type 2 diabetes mellitus on cognitive function and the incidence of dementia. Search methods: We searched ALOIS (the Specialized Register of the Cochrane Dementia and Cognitive Improvement Group (CDCIG)), the Cochrane Library, MEDLINE, Embase, PsycINFO, CINAHL and LILACS on 15 October 2016. ALOIS contains records from all major health care databases, (CENTRAL, MEDLINE, Embase, PsycINFO, CINAHL, LILACS), as well as from many trials' registers and grey literature sources. Selection criteria: We included randomised controlled trials (RCTs) which compared two or more different treatments for Type 2 diabetes mellitus and in which cognitive function was measured at baseline and after treatment. Data collection and analysis: Two review authors independently extracted data and assessed the quality of the included RCTs. We pooled data for comparable trials and estimated the effects of treatment by using risk ratios (RRs) and mean differences (MDs), according to the nature of the outcome. We assessed the quality of the evidence using GRADE methods. Main results: We identified seven eligible studies but only four provided data we could include in efficacy analyses. Two of these studies compared intensive versus standard glycaemic control and two compared different pharmacological treatments. All studies were at unclear risk of bias in at least two domains and one large study was at high risk of performance and detection bias. (a) Two studies with 13,934 participants at high cardiovascular risk provided efficacy data on intensive versus standard glycaemic control. A third study with 1791 participants provided additional data on hypoglycaemic episodes and mortality. There is probably no difference between treatment groups in the number of participants who decline by at least 3 points on the Mini-Mental State Examination (MMSE) over five years (RR 0.98, 95% CI 0.88 to 1.08; 1 study; n = 11,140; moderate-quality evidence); and there may also be little or no difference in the incidence of dementia (RR 1.27, 95% CI 0.87 to 1.85; 1 study; n = 11,140; low-quality evidence). From another study, there was probably little or no difference in MMSE score after 40 months (MD 0.01, 95% CI -0.18 to 0.16; 1 study; n = 2794; moderate quality evidence). Participants exposed to the intensive glycaemic control strategy probably experience more episodes of severe hypoglycaemia than those who have standard treatment (RR 2.18, 95% CI 1.52 to 3.14; 2 studies; n = 12,827; moderate-quality evidence). The evidence from these trials suggests that the intensity of glycaemic control may have little or no effect on all-cause mortality (RR 0.99, 95% CI 0.87 to 1.13; 3 studies; n = 15,888; low-quality evidence). (b) One study with 156 participants compared glibenclamide (glyburide) with repaglinide. There may be a small advantage of glibenclamide on global cognitive function measured with the MMSE after 12 months (MD 0.90, 95% CI -1.68 to 0.12; low-quality evidence). No data were reported on the incidence of dementia, hypoglycaemic events or all-cause mortality. (c) One study with 145 participants compared rosiglitazone plus metformin to glibenclamide (glyburide) plus metformin over 24 weeks. It reported only on cognitive subdomains and not on global cognitive function, incidence of MCI or dementia, hypoglycaemic events or all causes of mortality. Authors' conclusions: We found no good evidence that any specific treatment or treatment strategy for

Type 2 diabetes can prevent or delay cognitive impairment. The best available evidence related to the comparison of intensive with standard glycaemic control strategies. Here there was moderate-quality evidence that the strategies do not differ in their effect on global cognitive functioning over 40 to 60 months.

Arevalo-Rodriguez I, Smailagic N, Roqué i Figuls M, Ciapponi A, Sanchez-Perez E, Giannakou A, et al. Mini-Mental State Examination (MMSE) for the detection of Alzheimer's disease and other dementias in people with mild cognitive impairment (MCI). *Cochrane Database of Systematic Reviews*. 2015; 3. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010783.pub2/abstract>

**Background:** Dementia is a progressive global cognitive impairment syndrome. In 2010, more than 35 million people worldwide were estimated to be living with dementia. Some people with mild cognitive impairment (MCI) will progress to dementia but others remain stable or recover full function. There is great interest in finding good predictors of dementia in people with MCI. The Mini-Mental State Examination (MMSE) is the best-known and the most often used short screening tool for providing an overall measure of cognitive impairment in clinical, research and community settings. **Objectives:** To determine the diagnostic accuracy of the MMSE at various thresholds for detecting individuals with baseline MCI who would clinically convert to dementia in general, Alzheimer's disease dementia or other forms of dementia at follow-up. **Search methods:** We searched ALOIS (Cochrane Dementia and Cognitive Improvement Specialized Register of diagnostic and intervention studies (inception to May 2014); MEDLINE (OvidSP) (1946 to May 2014); EMBASE (OvidSP) (1980 to May 2014); BIOSIS (Web of Science) (inception to May 2014); Web of Science Core Collection, including the Conference Proceedings Citation Index (ISI Web of Science) (inception to May 2014); PsycINFO (OvidSP) (inception to May 2014), and LILACS (BIREME) (1982 to May 2014). We also searched specialized sources of diagnostic test accuracy studies and reviews, most recently in May 2014: MEDION (Universities of Maastricht and Leuven, [www.mediondatabase.nl](http://www.mediondatabase.nl)), DARE (Database of Abstracts of Reviews of Effects, via the Cochrane Library), HTA Database (Health Technology Assessment Database, via the Cochrane Library), and ARIF (University of Birmingham, UK, [www.arif.bham.ac.uk](http://www.arif.bham.ac.uk)). No language or date restrictions were applied to the electronic searches and methodological filters were not used as a method to restrict the search overall so as to maximize sensitivity. We also checked reference lists of relevant studies and reviews, tracked citations in Scopus and Science Citation Index, used searches of known relevant studies in PubMed to track related articles, and contacted research groups conducting work on MMSE for dementia diagnosis to try to locate possibly relevant but unpublished data. **Selection criteria:** We considered longitudinal studies in which results of the MMSE administered to MCI participants at baseline were obtained and the reference standard was obtained by follow-up over time. We included participants recruited and clinically classified as individuals with MCI under Petersen and revised Petersen criteria, Matthews criteria, or a Clinical Dementia Rating = 0.5. We used acceptable and commonly used reference standards for dementia in general, Alzheimer's dementia, Lewy body dementia, vascular dementia and frontotemporal dementia. **Data collection and analysis:** We screened all titles generated by the electronic database searches. Two review authors independently assessed the abstracts of all potentially relevant studies. We assessed the identified full papers for eligibility and extracted data to create two by two tables for dementia in general and other dementias. Two authors independently performed quality assessment using the QUADAS-2 tool. Due to high heterogeneity and scarcity of data, we derived estimates of sensitivity at fixed values of specificity from the model we fitted to produce the summary receiver operating characteristic curve. **Main results:** In this review, we included 11 heterogeneous studies with a total number of 1569 MCI patients followed for conversion to dementia. Four studies assessed the role of baseline scores of the MMSE in conversion from MCI to all-cause dementia and eight studies assessed this test in conversion from MCI to Alzheimer's disease dementia. Only one study provided information about the MMSE and conversion from MCI to vascular dementia. For conversion from MCI to dementia in general, the accuracy of baseline MMSE scores ranged from sensitivities of 23% to 76% and specificities from 40% to 94%. In relationship to conversion from MCI to Alzheimer's disease dementia, the accuracy of baseline MMSE scores ranged from sensitivities of 27% to 89% and specificities from 32% to 90%. Only one study provided information about conversion from MCI to vascular dementia, presenting a sensitivity of 36% and a specificity of 80% with an incidence of vascular dementia of 6.2%. Although we had planned to explore possible sources of heterogeneity, this was not undertaken due to the scarcity of studies included in our analysis. **Authors' conclusions:** Our review did not find evidence supporting a substantial role of MMSE as a stand-alone single-administration test in the identification of MCI patients who could develop dementia. Clinicians could prefer to request additional and extensive tests to be sure about the management of these patients. An important aspect to assess in future updates is if conversion to dementia from MCI stages could be predicted better by MMSE changes over time instead of single measurements. It is also important to assess if a set of tests, rather than an isolated one, may be more successful in predicting conversion from MCI to dementia.

Bahar-Fuchs A, Clare L, Woods B. Cognitive training and cognitive rehabilitation for mild to moderate Alzheimer's disease and vascular dementia. *Cochrane Database of Systematic Reviews*. 2013; 6. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003260.pub2/abstract>

**Background:** Cognitive impairments, particularly memory problems, are a defining feature of the early stages of Alzheimer's disease (AD) and vascular dementia. Cognitive training and cognitive rehabilitation are specific interventional approaches designed to address difficulties with memory and other aspects of cognitive functioning. The present review is an update of previous versions of this review. **Objectives:** The main aim of the

current review was to evaluate the effectiveness and impact of cognitive training and cognitive rehabilitation for people with mild Alzheimer's disease or vascular dementia in relation to important cognitive and non-cognitive outcomes for the person with dementia and the primary caregiver in the short, medium and long term. Search methods: The CDCIG Specialized Register, ALOIS, which contains records from MEDLINE, EMBASE, CINAHL, PsycINFO, LILACS and many other clinical trial databases and grey literature sources, was most recently searched on 2 November 2012. Selection criteria: Randomised controlled trials (RCTs), published in English, comparing cognitive rehabilitation or cognitive training interventions with control conditions, and reporting relevant outcomes for the person with dementia and/or the family caregiver, were considered for inclusion. Data collection and analysis: Eleven RCTs reporting cognitive training interventions were included in the review. A large number of measures were used in the different studies, and meta-analysis could be conducted for 11 of the primary and secondary outcomes of interest. Several outcomes were not measured in any of the studies. The unit of analysis in the meta-analysis was the change from baseline score. Overall estimates of treatment effect were calculated using a fixed-effect model, and statistical heterogeneity was measured using a standard Chi<sup>2</sup> statistic. One RCT of cognitive rehabilitation was identified, allowing examination of effect sizes, but no meta-analysis could be conducted. Main results: Cognitive training was not associated with positive or negative effects in relation to any reported outcomes. The overall quality of the trials was low to moderate. The single RCT of cognitive rehabilitation found promising results in relation to a number of participant and caregiver outcomes, and was generally of high quality. Authors' conclusions: Available evidence regarding cognitive training remains limited, and the quality of the evidence needs to improve. However, there is still no indication of any significant benefit derived from cognitive training. Trial reports indicate that some gains resulting from intervention may not be captured adequately by available standardised outcome measures. The results of the single RCT of cognitive rehabilitation show promise but are preliminary in nature. Further, well-designed studies of cognitive training and cognitive rehabilitation are required to obtain more definitive evidence. Researchers should describe and classify their interventions appropriately using available terminology.

Birks J, McGuinness B, Craig D. Rivastigmine for vascular cognitive impairment. Cochrane Database of Systematic Reviews. 2013; 5. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004744.pub3/abstract>

Background: Vascular dementia represents the second most common type of dementia after Alzheimer's disease. In older patients, in particular, the combination of vascular dementia and Alzheimer's disease is common, and is referred to as mixed dementia. The classification of vascular dementia broadly follows three clinico-pathological processes: multi-infarct dementia, single strategic infarct dementia and subcortical dementia. Not all victims fulfil strict criteria for dementia and may be significantly cognitively impaired without memory loss, when the term vascular cognitive impairment (VCI) is more useful. Currently, no established standard treatment for VCI exists. Reductions in acetylcholine and acetyltransferase activity are common to both Alzheimer's disease and VCI, raising the possibility that cholinesterase inhibitors - such as rivastigmine - which are beneficial in Alzheimer's disease, may also be beneficial for VCI. Objectives: To assess the efficacy of rivastigmine compared with placebo in the treatment of people with vascular cognitive impairment (VCI), vascular dementia or mixed dementia. Search methods: We searched ALOIS (the Cochrane Dementia and Cognitive Improvement Group's Specialized Register) on 12 February 2013 using the terms: rivastigmine, exelon, "SDZ ENA 713". ALOIS contains records of clinical trials identified from monthly searches of a number of major healthcare databases (The Cochrane Library, MEDLINE, EMBASE, CINAHL, PsycINFO, LILACS), numerous trial registries and grey literature sources. Selection criteria: All unconfounded randomized double-blind trials comparing rivastigmine with placebo in the treatment of people with VCI, vascular dementia or mixed dementia were eligible for inclusion. Data collection and analysis: Two reviewers extracted and assessed data independently, and agreement was reached after discussion. They noted results concerning adverse effects. Main results: Three trials, with a total of 800 participants, were identified for inclusion. The participants in one trial did not have dementia, while the other two studies included participants with dementia of different severities. The dose of rivastigmine was different in each study. No pooling of study results was attempted because of these differences between the studies. One trial included 40 participants with subcortical vascular dementia (age range 40 to 90 years) with a mean mini-mental state examination (MMSE) score of 13.0 and 13.4 in the rivastigmine and placebo arms, respectively. Treatment over 26 weeks was limited to 3 mg rivastigmine twice daily, or placebo. No significant difference was found on any outcome measure relevant to cognition, neuropsychiatric symptoms, function or global rating, or in the number of withdrawals before the end of treatment. Another trial included 710 participants with vascular dementia, including subcortical and cortical forms (age range 50 to 85 years). Over 24 weeks, a mean dose of rivastigmine of 9.4 mg/day was achieved versus placebo. Baseline MMSE was identical for both groups, at 19.1. Statistically significant advantage in cognitive response (but not with global impression of change or non-cognitive measures) was seen with rivastigmine treatment at 24 weeks (MMSE change from baseline MD 0.6, 95% CI 0.11 to 1.09, P value 0.02; Vascular Dementia Assessment Scale (VaDAS) change from baseline MD -1.3, 95% CI -2.62 to 0.02, P value 0.05). Significantly higher rates of vomiting, nausea, diarrhoea and anorexia and withdrawals from treatment were noted in the participants randomized to rivastigmine compared with placebo (withdrawals rivastigmine 90/365, placebo 48/345, OR 2.02, 95% CI 1.38 to 2.98) (withdrawals due to an adverse event rivastigmine 49/365, placebo 19/345, OR 2.66, 95% CI 1.53 to 4.62, P value 0.0005). The third study included 50 participants (age range 48 to 84 years) with mean MMSE scores of 23.7 and 23.9 in the rivastigmine and placebo arms, respectively. Over a 24-week period, participants labelled as having cognitive impairment but no dementia (CIND) following ischaemic stroke were

given up to 4.5 mg rivastigmine twice daily, or placebo. Primary and secondary outcome measures showed no statistically significant difference when considering neurocognitive abilities, function, neuropsychiatric symptoms and global performance. One participant in the rivastigmine group and two in the placebo group discontinued their medication because of an adverse effect. Authors' conclusions: There is some evidence of benefit of rivastigmine in VCI from trial data from three studies. However, this conclusion is based on one large study. Rivastigmine is capable of inducing side effects that lead to withdrawal in a significant proportion of patients.

Birks Jacqueline S, Chong Lee Y, Grimley Evans J. Rivastigmine for Alzheimer's disease. Cochrane Database of Systematic Reviews. 2015; 9. [cited: url:

<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001191.pub4/abstract>

Background: Alzheimer's disease is the commonest cause of dementia affecting older people. One of the therapeutic strategies aimed at ameliorating the clinical manifestations of Alzheimer's disease is to enhance cholinergic neurotransmission in the brain by the use of cholinesterase inhibitors to delay the breakdown of acetylcholine released into synaptic clefts. Tacrine, the first of the cholinesterase inhibitors to undergo extensive trials for this purpose, was associated with significant adverse effects including hepatotoxicity. Other cholinesterase inhibitors, including rivastigmine, with superior properties in terms of specificity of action and lower risk of adverse effects have since been introduced. Rivastigmine has received approval for use in 60 countries including all member states of the European Union and the USA. Objectives: To determine the clinical efficacy and safety of rivastigmine for patients with dementia of Alzheimer's type. Search methods: We searched ALOIS, the Cochrane Dementia and Cognitive Improvement Group Specialized Register, on 2 March 2015 using the terms: Rivastigmine OR exelon OR ENA OR "SDZ ENA 713". ALOIS contains records of clinical trials identified from monthly searches of a number of major healthcare databases (Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL, LILACS), numerous trial registries and grey literature sources. Selection criteria: We included all unconfounded, double-blind, randomised, controlled trials in which treatment with rivastigmine was administered to patients with dementia of the Alzheimer's type for 12 weeks or more and its effects compared with those of placebo in a parallel group of patients, or where two formulations of rivastigmine were compared. Data collection and analysis: One review author (JSB) applied the study selection criteria, assessed the quality of studies and extracted data. Main results: A total of 13 trials met the inclusion criteria of the review. The trials had a duration of between 12 and 52 weeks. The older trials tested a capsule form with a dose of up to 12 mg/day. Trials reported since 2007 have tested continuous dose transdermal patch formulations delivering 4.6, 9.5 and 17.7 mg/day. Our main analysis compared the safety and efficacy of rivastigmine 6 to 12 mg/day orally or 9.5 mg/day transdermally with placebo. Seven trials contributed data from 3450 patients to this analysis. Data from another two studies were not included because of a lack of information and methodological concerns. All the included trials were multicentre trials and recruited patients with mild to moderate Alzheimer's disease with a mean age of about 75 years. All had low risk of bias for randomisation and allocation but the risk of bias due to attrition was unclear in four studies, low in one study and high in two studies. After 26 weeks of treatment rivastigmine compared to placebo was associated with better outcomes for cognitive function measured with the Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog) score (mean difference (MD) -1.79; 95% confidence interval (CI) -2.21 to -1.37, n = 3232, 6 studies) and the Mini-Mental State Examination (MMSE) score (MD 0.74; 95% CI 0.52 to 0.97, n = 3205, 6 studies), activities of daily living (SMD 0.20; 95% CI 0.13 to 0.27, n = 3230, 6 studies) and clinician rated global impression of changes, with a smaller proportion of patients treated with rivastigmine experiencing no change or a deterioration (OR 0.68; 95% CI 0.58 to 0.80, n = 3338, 7 studies). Three studies reported behavioural change, and there were no differences compared to placebo (standardised mean difference (SMD) -0.04; 95% CI -0.14 to 0.06, n = 1529, 3 studies). Only one study measured the impact on caregivers using the Neuropsychiatric Inventory-Caregiver Distress (NPI-D) scale and this found no difference between the groups (MD 0.10; 95% CI -0.91 to 1.11, n = 529, 1 study). Overall, participants who received rivastigmine were about twice as likely to withdraw from the trials (odds ratio (OR) 2.01, 95% CI 1.71 to 2.37, n = 3569, 7 studies) or to experience an adverse event during the trials (OR 2.16, 95% CI 1.82 to 2.57, n = 3587, 7 studies). Authors' conclusions: Rivastigmine (6 to 12 mg daily orally or 9.5 mg daily transdermally) appears to be beneficial for people with mild to moderate Alzheimer's disease. In comparisons with placebo, better outcomes were observed for rate of decline of cognitive function and activities of daily living, although the effects were small and of uncertain clinical importance. There was also a benefit from rivastigmine on the outcome of clinician's global assessment. There were no differences between the rivastigmine group and placebo group in behavioural change or impact on carers. At these doses the transdermal patch may have fewer side effects than the capsules but has comparable efficacy. The quality of evidence is only moderate for all of the outcomes reviewed because of a risk of bias due to dropouts. All the studies with usable data were industry funded or sponsored. This review has not examined economic data.

Brown R, Howard R, Candy B, Sampson Elizabeth L. Opioids for agitation in dementia. Cochrane Database of Systematic Reviews. 2015; 5. [cited: url:

<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009705.pub2/abstract>

Background: Agitation is a common experience for people living with dementia, particularly as day-to-day function and cognition start to decline more. At the present time there are limited pharmacological options for relieving agitation and little is known about the safety and efficacy of opioid drugs in this setting. Objectives: To determine the clinical efficacy and safety of opioids for agitation in people with dementia. Search methods: We

searched ALOIS, the Cochrane Dementia and Cognitive Improvement Group Specialized Register, on 13 June 2014 using the terms: narcotic OR opioid OR opium OR morphine OR buprenorphine OR codeine OR dextromoramide OR diphenoxylate OR dipipanone OR dextropropoxyphene OR propoxyphene OR diamorphine OR dihydrocodeine OR alfentanil OR fentanyl OR remifentanyl OR meptazinol OR methadone OR nalbuphine OR oxycodone OR papaveretum OR pentazocine OR meperidine OR pethidine OR phenazocine OR hydrocodone OR hydromorphone OR levorphanol OR oxymorphone OR butorphanol OR dezocine OR sufentanil OR ketobemidone. ALOIS contains records of clinical trials identified from monthly searches of a number of major healthcare databases such as MEDLINE, EMBASE and PsycINFO, as well as numerous trial registries and grey literature sources. Selection criteria: Randomised, controlled trials of opioids compared to placebo for agitation in people with dementia. Data collection and analysis: Two authors independently assessed the studies identified by the search against the inclusion criteria. Main results: There are currently no completed randomised, placebo controlled trials of opioids for agitation in dementia. There are two potentially relevant trials still in progress. Authors' conclusions: We found insufficient evidence to establish the clinical efficacy and safety of opioids for agitation in people with dementia. There remains a lack of data to determine if or when opioids either relieve or exacerbate agitation. More evidence is needed to guide the effective, appropriate and safe use of opioids in dementia.

Burckhardt M, Herke M, Wustmann T, Watzke S, Langer G, Fink A. Omega-3 fatty acids for the treatment of dementia. *Cochrane Database of Systematic Reviews*. 2016; 4. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009002.pub3/abstract>

Background: Omega-3 polyunsaturated fatty acids (omega-3 PUFAs) from fish and plant sources are commonly considered as a promising non-medical alternative to improve brain functions and slow down the progression of dementia. This assumption is mostly based on findings of preclinical studies and epidemiological research. Resulting explanatory models aim at the role omega-3 PUFAs play in the development and integrity of the brain's neurons, their protective antioxidative effect on cell membranes and potential neurochemical mechanisms directly related to Alzheimer-specific pathology. Epidemiological research also found evidence of malnutrition in people with dementia. Considering this and the fact that omega-3 PUFA cannot be synthesised by humans, omega-3 PUFAs might be a promising treatment option for dementia. Objectives: To assess the efficacy and safety of omega-3 polyunsaturated fatty acid (PUFA) supplementation for the treatment of people with dementia. Search methods: We searched the Specialized Register of the Cochrane Dementia and Cognitive Improvement Group (ALOIS), MEDLINE, EMBASE, PsycINFO, CINAHL, ClinicalTrials.gov and the World Health Organization (WHO) portal/ICTRP on 10 December 2015. We contacted manufacturers of omega-3 supplements and scanned reference lists of landmark papers and included articles. Selection criteria: We included randomised controlled trials (RCTs) in which omega-3 PUFA in the form of supplements or enriched diets were administered to people with Alzheimer's disease (AD), vascular dementia (VaD), dementia with Lewy bodies (DLB), Parkinson's disease dementia (PDD) or frontotemporal dementia (FTD). Data collection and analysis: The primary outcome measures of interest were changes in global and specific cognitive functions, functional performance, dementia severity and adverse effects. Two review authors independently selected studies, extracted data and assessed the quality of trials according to the Cochrane Handbook for Systematic Reviews of Interventions. We rated the quality of the evidence using the GRADE approach. We received unpublished data from the trial authors and collected adverse effects information from the published articles. We conducted meta-analyses for available outcome measures at six months. Main results: We included three comparable randomised, placebo-controlled trials investigating omega-3 PUFA supplements in 632 participants with mild to moderate AD over six, 12 and 18 months. We found no studies investigating other types of dementia. All trials were of high methodological quality. The overall quality of evidence for most of the outcomes was high. There was no evidence of a benefit from omega-3 PUFAs on cognitive function when measured at six months with the Alzheimer's Disease Assessment Scale - Cognitive subscale (standardised mean difference (SMD) -0.02, 95% confidence interval (CI) -0.19 to 0.15; 566 participants; 3 studies; high quality evidence) or Mini-Mental State Examination (mean difference (MD) 0.18, 95% CI -1.05 to 1.41; 202 participants; 2 studies; high quality evidence) or on activities of daily living (SMD -0.02, 95% CI -0.19 to 0.16; 544 participants; 2 studies; high quality evidence). There was also no effect at six months of treatment on severity of dementia measured with the Clinical Dementia Rating - Sum of Boxes (MD -0.00, 95% CI -0.58 to 0.57; 542 participants; 2 studies; high quality evidence) or on quality of life measured with the Quality of Life Alzheimer's Disease scale (MD -0.10, 95% CI -1.28 to 1.08; 322 participants; 1 study; high quality evidence). There was no difference at six months on mental health measured with the Montgomery-Åsberg Depression Rating Scale (MD -0.10, 95% CI -0.74 to 0.54; 178 participants; 1 study; high quality of evidence) or the Neuropsychiatric Inventory (SMD 0.10, 95% CI -0.07 to 0.27; 543 participants; 2 studies; high quality of evidence). One very small study showed a benefit for omega-3 PUFAs in instrumental activities of daily living after 12 months of treatment (MD -3.50, 95% CI -4.30 to -2.70; 22 participants; moderate quality evidence). The included studies did not measure specific cognitive function. The studies did not report adverse events well. Two studies stated that all adverse events were mild and that they did not differ in overall frequency between omega-3 PUFA and placebo groups. Data from one study showed no difference between groups in frequency of any adverse event (risk ratio (RR) 1.02, 95% CI 0.95 to 1.10; 402 participants; 1 study; moderate quality evidence) or any serious adverse event (RR 1.05, 95% CI 0.78 to 1.41; 402 participants; 1 study; high quality evidence) at 18 months of treatment. Authors' conclusions: We found no convincing evidence for the efficacy of omega-3 PUFA supplements in the treatment of mild to moderate AD. This result was consistent for all outcomes relevant for people with dementia. Adverse effects

of omega-3 PUFAs seemed to be low, but based on the evidence synthesised in this review, we cannot make a final statement on tolerability. The effects on other populations remain unclear.

Chau S, Herrmann N, Ruthirakuhan Myuri T, Chen Jinghan J, Lanctôt Krista L. Latrepirdine for Alzheimer's disease. Cochrane Database of Systematic Reviews. 2015; 4. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009524.pub2/abstract>

**Background:** Current treatments for Alzheimer's disease (AD) provide modest symptomatic relief but do not slow the progression of the disease. Latrepirdine may modulate several targets involved in AD pathology, including lipid peroxidation, mitochondrial permeability, voltage-gated calcium ion channels as well as neurotransmitter receptor activity, and thus potentially represents both a symptomatic and disease-modifying intervention. Several randomized, placebo-controlled trials have sought to evaluate the effect of latrepirdine on cognition, function and behaviour in patients with AD. **Objectives:** To evaluate the efficacy and safety of latrepirdine for the treatment of AD. **Search methods:** We searched the Specialized Register of the Cochrane Dementia and Cognitive Improvement Group on 4 June 2014 using the terms: latrepirdine OR dimebon OR dimebolin OR 2,3,4,5-tetrahydro-2,8-dimethyl-5-(2-(6-methyl-3-pyridyl)ethyl)-1H-pyrido(4,3-b)indole. **Selection criteria:** We included all randomized, double-blind, placebo-controlled trials where latrepirdine was administered to patients with mild, moderate or severe AD. **Data collection and analysis:** We assessed the quality of studies and two authors extracted data. We calculated mean difference (MD), risk ratio (RR) and 95% confidence interval (CI) on an intention-to-treat (ITT) basis for all relevant outcome measures. **Main results:** Seven trials involving a total of 1697 participants were found and six were included in the quantitative analyses. No data were available from the seventh trial. Three trials involving 1243 patients were included in analyses of efficacy outcomes, and four trials involving 1034 patients were included in analyses of safety and tolerability outcomes. We judged five trials to be at high risk of bias due to selective outcome reporting and three to be at high risk of attrition bias. There was low quality evidence favouring latrepirdine on the Clinician's Interview - Based Impression of Change Plus Caregiver Input after 26 weeks (CIBIC-Plus) (MD -0.60, 95% CI -0.89 to -0.31, 1 study,  $P < 0.001$ ). Due to imprecision in the results, it was not possible to determine whether latrepirdine had any effect on cognition measured with the Alzheimer's Disease Assessment Scale cognitive subscale (ADAS-Cog) (MD -1.49, 95% CI -3.47 to 0.49, 3 studies,  $P = 0.14$ ) or the Mini-Mental State Examination (MMSE) (MD 0.59, 95% CI -0.94 to 2.11, 3 studies,  $P = 0.45$ ), or on function measured with the Alzheimer's Disease Co-operative Study - Activities of Daily Living scale (ADCS-ADL) (MD 1.00, 95% CI -1.15 to 3.15, 3 studies,  $P = 0.36$ ) at study endpoint (26 or 52 weeks). We considered the evidence provided on these outcomes to be of overall low quality. However, there was some high quality evidence showing a very small benefit of latrepirdine on the Neuropsychiatric Inventory (NPI) (MD -1.77, 95% CI -3.09 to -0.45, 3 studies,  $P = 0.009$ ) at study endpoint (26 or 52 weeks). Additionally, moderate quality evidence suggested that latrepirdine and placebo were comparable in adverse events (RR 1.03, 95% CI 0.93 to 1.14,  $P = 0.51$ ), serious adverse events (RR 0.86, 95% CI 0.55 to 1.35,  $P = 0.52$ ), dropouts (RR 0.91, 95% CI 0.65 to 1.27,  $P = 0.57$ ) and dropouts due to adverse events (RR 0.98, 95% CI 0.57 to 1.67,  $P = 0.93$ ). **Authors' conclusions:** Our meta-analysis is limited by the small number of studies, imprecision, inconsistencies between studies and likelihood of bias. Nevertheless, the evidence to date suggests that while not associated with an increased risk of adverse events compared with placebo, there is no effect of latrepirdine on cognition and function in mild-to-moderate AD patients, though there appears to be a modest benefit for behaviour. Further studies should investigate the potential benefit of latrepirdine on neuropsychiatric symptoms in AD.

Chen N, Yang M, Guo J, Zhou M, Zhu C, He L. Cerebrolysin for vascular dementia. Cochrane Database of Systematic Reviews. 2013; 1. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008900.pub2/abstract>

**Background:** Vascular dementia is a common disorder without definitive treatments. Cerebrolysin seems to be a promising intervention based on its potential neurotrophic and pro-cognitive effects, but studies of its efficacy have yielded inconsistent results. **Objectives:** To assess the efficacy and safety of Cerebrolysin for vascular dementia. **Search methods:** We searched ALOIS - the Cochrane Dementia and Cognitive Improvement Group's Specialized Register on 4 November 2012 using the terms: Cerebrolysin, Cere, FPF1070, FPF-1070. ALOIS contains records of clinical trials identified from monthly searches of a number of major healthcare databases, numerous trial registries and grey literature sources. **Selection criteria:** All randomized controlled trials of Cerebrolysin for treating vascular dementia without language restriction. **Data collection and analysis:** Two authors independently selected trials and evaluated the methodological quality, then extracted and analysed data from the included trials. **Main results:** Six randomized controlled trials with a total of 597 participants were eligible. The meta-analyses revealed a beneficial effect of Cerebrolysin on general cognitive function measured by mini-mental state examination (MMSE) (weighted mean difference (WMD) 1.10; 95% confidence interval (CI) 0.37 to 1.82) or Alzheimer's Disease Assessment Scale Cognitive Subpart, extended version (ADAS-cog+) (WMD -4.01; 95% CI -5.36 to -2.66). It also improved patients' global clinical function evaluated by the response rates (relative risk (RR) 2.71, 95% CI 1.83 to 4.00). Only non-serious adverse events were observed in the included trials, and there was no significant difference in occurrence of non-serious side effects between groups (RR 0.97, 95% CI 0.49 to 1.94). **Authors' conclusions:** Cerebrolysin may have positive effects on cognitive function and global function in elderly patients with vascular dementia of mild to moderate severity, but there is still insufficient evidence to recommend Cerebrolysin as a routine treatment for vascular dementia due to the limited number of included trials,



wide variety of treatment durations and short-term follow-up in most of the trials.

Creavin Sam T, Wisniewski S, Noel-Storr Anna H, Trevelyan Clare M, Hampton T, Rayment D, et al. Mini-Mental State Examination (MMSE) for the detection of dementia in clinically unevaluated people aged 65 and over in community and primary care populations. *Cochrane Database of Systematic Reviews*. 2016; 1. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011145.pub2/abstract>

**Background:** The Mini Mental State Examination (MMSE) is a cognitive test that is commonly used as part of the evaluation for possible dementia. **Objectives:** To determine the diagnostic accuracy of the Mini-Mental State Examination (MMSE) at various cut points for dementia in people aged 65 years and over in community and primary care settings who had not undergone prior testing for dementia. **Search methods:** We searched the specialised register of the Cochrane Dementia and Cognitive Improvement Group, MEDLINE (OvidSP), EMBASE (OvidSP), PsycINFO (OvidSP), LILACS (BIREME), ALOIS, BIOSIS previews (Thomson Reuters Web of Science), and Web of Science Core Collection, including the Science Citation Index and the Conference Proceedings Citation Index (Thomson Reuters Web of Science). We also searched specialised sources of diagnostic test accuracy studies and reviews: MEDION (Universities of Maastricht and Leuven, [www.mediondatabase.nl](http://www.mediondatabase.nl)), DARE (Database of Abstracts of Reviews of Effects, via the Cochrane Library), HTA Database (Health Technology Assessment Database, via the Cochrane Library), and ARIF (University of Birmingham, UK, [www.arif.bham.ac.uk](http://www.arif.bham.ac.uk)). We attempted to locate possibly relevant but unpublished data by contacting researchers in this field. We first performed the searches in November 2012 and then fully updated them in May 2014. We did not apply any language or date restrictions to the electronic searches, and we did not use any methodological filters as a method to restrict the search overall. **Selection criteria:** We included studies that compared the 11-item (maximum score 30) MMSE test (at any cut point) in people who had not undergone prior testing versus a commonly accepted clinical reference standard for all-cause dementia and subtypes (Alzheimer disease dementia, Lewy body dementia, vascular dementia, frontotemporal dementia). Clinical diagnosis included all-cause (unspecified) dementia, as defined by any version of the Diagnostic and Statistical Manual of Mental Disorders (DSM); International Classification of Diseases (ICD) and the Clinical Dementia Rating. **Data collection and analysis:** At least three authors screened all citations. Two authors handled data extraction and quality assessment. We performed meta-analysis using the hierarchical summary receiver-operator curves (HSROC) method and the bivariate method. **Main results:** We retrieved 24,310 citations after removal of duplicates. We reviewed the full text of 317 full-text articles and finally included 70 records, referring to 48 studies, in our synthesis. We were able to perform meta-analysis on 28 studies in the community setting (44 articles) and on 6 studies in primary care (8 articles), but we could not extract usable 2 x 2 data for the remaining 14 community studies, which we did not include in the meta-analysis. All of the studies in the community were in asymptomatic people, whereas two of the six studies in primary care were conducted in people who had symptoms of possible dementia. We judged two studies to be at high risk of bias in the patient selection domain, three studies to be at high risk of bias in the index test domain and nine studies to be at high risk of bias regarding flow and timing. We assessed most studies as being applicable to the review question though we had concerns about selection of participants in six studies and target condition in one study. The accuracy of the MMSE for diagnosing dementia was reported at 18 cut points in the community (MMSE score 10, 14-30 inclusive) and 10 cut points in primary care (MMSE score 17-26 inclusive). The total number of participants in studies included in the meta-analyses ranged from 37 to 2727, median 314 (interquartile range (IQR) 160 to 647). In the community, the pooled accuracy at a cut point of 24 (15 studies) was sensitivity 0.85 (95% confidence interval (CI) 0.74 to 0.92), specificity 0.90 (95% CI 0.82 to 0.95); at a cut point of 25 (10 studies), sensitivity 0.87 (95% CI 0.78 to 0.93), specificity 0.82 (95% CI 0.65 to 0.92); and in seven studies that adjusted accuracy estimates for level of education, sensitivity 0.97 (95% CI 0.83 to 1.00), specificity 0.70 (95% CI 0.50 to 0.85). There was insufficient data to evaluate the accuracy of the MMSE for diagnosing dementia subtypes. We could not estimate summary diagnostic accuracy in primary care due to insufficient data. **Authors' conclusions:** The MMSE contributes to a diagnosis of dementia in low prevalence settings, but should not be used in isolation to confirm or exclude disease. We recommend that future work evaluates the diagnostic accuracy of tests in the context of the diagnostic pathway experienced by the patient and that investigators report how undergoing the MMSE changes patient-relevant outcomes.

Davis Daniel HJ, Creavin Sam T, Yip Jennifer LY, Noel-Storr Anna H, Brayne C, Cullum S. Montreal Cognitive Assessment for the diagnosis of Alzheimer's disease and other dementias. *Cochrane Database of Systematic Reviews*. 2015; 10. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010775.pub2/abstract>

**Background:** Dementia is a progressive syndrome of global cognitive impairment with significant health and social care costs. Global prevalence is projected to increase, particularly in resource-limited settings. Recent policy changes in Western countries to increase detection mandates a careful examination of the diagnostic accuracy of neuropsychological tests for dementia. **Objectives:** To determine the diagnostic accuracy of the Montreal Cognitive Assessment (MoCA) at various thresholds for dementia and its subtypes. **Search methods:** We searched MEDLINE, EMBASE, BIOSIS Previews, Science Citation Index, PsycINFO and LILACS databases to August 2012. In addition, we searched specialised sources containing diagnostic studies and reviews, including MEDION (Meta-analyses van Diagnostisch Onderzoek), DARE (Database of Abstracts of Reviews of Effects), HTA (Health Technology Assessment Database), ARIF (Aggressive Research Intelligence Facility) and C-EBLM (International Federation of Clinical Chemistry and Laboratory Medicine Committee for Evidence-based Laboratory Medicine)



databases. We also searched ALOIS (Cochrane Dementia and Cognitive Improvement Group specialized register of diagnostic and intervention studies). We identified further relevant studies from the PubMed related articles? feature and by tracking key studies in Science Citation Index and Scopus. We also searched for relevant grey literature from the Web of Science Core Collection, including Science Citation Index and Conference Proceedings Citation Index (Thomson Reuters Web of Science), PhD theses and contacted researchers with potential relevant data. Selection criteria: Cross-sectional designs where all participants were recruited from the same sample were sought; case-control studies were excluded due to high chance of bias. We searched for studies from memory clinics, hospital clinics, primary care and community populations. We excluded studies of early onset dementia, dementia from a secondary cause, or studies where participants were selected on the basis of a specific disease type such as Parkinson's disease or specific settings such as nursing homes. Data collection and analysis: We extracted dementia study prevalence and dichotomised test positive/test negative results with thresholds used to diagnose dementia. This allowed calculation of sensitivity and specificity if not already reported in the study. Study authors were contacted where there was insufficient information to complete the 2x2 tables. We performed quality assessment according to the QUADAS-2 criteria. Methodological variation in selected studies precluded quantitative meta-analysis, therefore results from individual studies were presented with a narrative synthesis. Main results: Seven studies were selected: three in memory clinics, two in hospital clinics, none in primary care and two in population-derived samples. There were 9422 participants in total, but most of studies recruited only small samples, with only one having more than 350 participants. The prevalence of dementia was 22% to 54% in the clinic-based studies, and 5% to 10% in population samples. In the four studies that used the recommended threshold score of 26 or over indicating normal cognition, the MoCA had high sensitivity of 0.94 or more but low specificity of 0.60 or less. Authors' conclusions: The overall quality and quantity of information is insufficient to make recommendations on the clinical utility of MoCA for detecting dementia in different settings. Further studies that do not recruit participants based on diagnoses already present (case-control design) but apply diagnostic tests and reference standards prospectively are required. Methodological clarity could be improved in subsequent DTA studies of MoCA by reporting findings using recommended guidelines (e.g. STARDdem). Thresholds lower than 26 are likely to be more useful for optimal diagnostic accuracy of MoCA in dementia, but this requires confirmation in further studies.

Declercq T, Petrovic M, Azermai M, Vander Stichele R, De Sutter An IM, van Driel Mieke L, et al. Withdrawal versus continuation of chronic antipsychotic drugs for behavioural and psychological symptoms in older people with dementia. *Cochrane Database of Systematic Reviews*. 2013; 3. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD007726.pub2/abstract>

Background: Antipsychotic agents are often used to treat neuropsychiatric symptoms (NPS) in dementia, although the literature is sceptical about their long-term use for this indication. Their effectiveness is limited and there is concern about adverse effects, including higher mortality with long-term use. When behavioural strategies have failed and drug therapy is instituted, regular attempts to withdraw these drugs are recommended. Physicians, nurses and families of older people with dementia are often reluctant to try to stop antipsychotics, fearing deterioration of NPS. Strategies to reduce antipsychotic use have been proposed, but a systematic review of interventions aimed at withdrawal of antipsychotic agents in older people with dementia has not yet been performed. Objectives: To evaluate whether withdrawal of antipsychotic agents is successful in older people with dementia in community or nursing home settings, to list the different strategies for withdrawal of antipsychotic agents in older people with dementia and NPS, and to measure the effects of withdrawal of antipsychotic agents on behaviour. Search methods: ALOIS, the Specialized Register of the Cochrane Dementia and Cognitive Improvement Group (CDCIG), The Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL, LILACS, clinical trials registries and grey literature sources were searched on 23 November 2012. The search included the following terms: antipsychotic\* or neuroleptic\* or phenothiazines or butyrophenones or risperidone or olanzapine or haloperidol or prothipendyl or methotrimeprazine or clopenthixol or flupenthixol or clothiapine or metylperon or droperidol or pipamperone or benperidol or bromperidol or fluspirilene or pimozide or penfluridol or sulpiride or veralipride or levosulpiride or sultopride or aripiprazole or clozapine or quetiapine or thioridazine combined with terms such as discontinu\* or withdraw\* or cessat\* or reduce\* or reducing or reduct\* or taper\* or stop\*. ALOIS contains records from all major healthcare databases (The Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL, LILACS), as well as from many clinical trials registries and grey literature sources. Selection criteria: Randomised, placebo-controlled trials comparing an antipsychotic withdrawal strategy to continuation of antipsychotics in people with dementia. Data collection and analysis: Review authors independently assessed trials for inclusion, rated their risk of bias and extracted data. Main results: We included nine trials with 606 randomised participants. Seven trials were conducted in nursing homes, one trial in an outpatient setting and one in both settings. In these trials, different types of antipsychotics prescribed at different doses were withdrawn. Both abrupt and gradual withdrawal schedules were used. The risk of bias of the included studies was generally low regarding blinding and outcome reporting and unclear for randomisation procedures and recruitment of participants. There was a wide variety of outcome measures. Our primary efficacy outcomes were success of withdrawal (i.e. remaining in study off antipsychotics) and NPS. Eight of nine trials reported no overall significant difference between groups on the primary outcomes, although in one pilot study of people with psychosis and agitation that had responded to haloperidol, time to relapse was significantly shorter in the discontinuation group (Chi<sup>2</sup> = 4.1, P value = 0.04). The ninth trial included people with psychosis or agitation who had responded well to risperidone

therapy for four to eight months and reported that discontinuation led to an increased risk of relapse, that is, increase in the Neuropsychiatric Inventory (NPI)-core score of 30% or greater (P value = 0.004, hazard ratio (HR) 1.94, 95% confidence interval (CI) 1.09 to 3.45 at four months). The only outcome that could be pooled was the full NPI-score, used in two studies. For this outcome there was no significant difference between people withdrawn from and those continuing on antipsychotics at three months (mean difference (MD) -1.49, 95% CI - .39 to 2.40). These two studies reported subgroup analyses according to baseline NPI-score (14 or less versus > 14). In one study, those with milder symptoms at baseline were significantly less agitated at three months in the discontinuation group (NPI-agitation, Mann-Whitney U test  $z = 2.4$ , P value = 0.018). In both studies, there was evidence of significant behavioural deterioration in people with more severe baseline NPS who were withdrawn from antipsychotics (Chi2 = 6.8; P value = 0.009 for the marked symptom score in one study). Individual studies did not report significant differences between groups on any other outcome except one trial that found a significant difference in a measure of verbal fluency, favouring discontinuation. Most trials lacked power to detect clinically important differences between groups. Adverse events were not systematically assessed. In one trial there was a non-significant increase in mortality in people who continued antipsychotic treatment (5% to 8% greater than placebo, depending on the population analysed, measured at 12 months). This trend became significant three years after randomisation, but due to dropout and uncertainty about the use of antipsychotics in this follow-up period this result should be interpreted with caution. Authors' conclusions: Our findings suggest that many older people with Alzheimer's dementia and NPS can be withdrawn from chronic antipsychotic medication without detrimental effects on their behaviour. It remains uncertain whether withdrawal is beneficial for cognition or psychomotor status, but the results of this review suggest that discontinuation programmes could be incorporated into routine practice. However, two studies of people whose agitation or psychosis had previously responded well to antipsychotic treatment found an increased risk of relapse or shorter time to relapse after discontinuation. Two other studies suggest that people with more severe NPS at baseline could benefit from continuing their antipsychotic medication. In these people, withdrawal might not be recommended.

Fage Bruce A, Chan Calvin CH, Gill Sudeep S, Noel-Storr Anna H, Herrmann N, Smailagic N, et al. Mini-Cog for the diagnosis of Alzheimer's disease dementia and other dementias within a community setting. Cochrane Database of Systematic Reviews. 2015; 2. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010860.pub2/abstract>

Background: Alzheimer's disease and related forms of dementia are becoming increasingly prevalent with the aging of many populations. The diagnosis of Alzheimer's disease relies on tests to evaluate cognition and discriminate between individuals with dementia and those without dementia. The Mini-Cog is a brief, cognitive screening test that is frequently used to evaluate cognition in older adults in various settings. Objectives: The primary objective of this review was to determine the diagnostic accuracy of the Mini-Cog for detecting Alzheimer's disease dementia and related dementias in a community setting. Secondary objectives included investigations of the heterogeneity of test accuracy in the included studies and potential sources of heterogeneity. These potential sources of heterogeneity included the baseline prevalence of dementia in study samples, thresholds used to determine positive test results, the type of dementia (Alzheimer's disease dementia or all causes of dementia), and aspects of study design related to study quality. Overall, the goals of this review were to determine if the Mini-Cog is a cognitive screening test that could be recommended to screen for cognitive impairment in community settings. Search methods: We searched MEDLINE (OvidSP), EMBASE (OvidSP), PsycINFO (Ovid SP), Science Citation Index (Web of Science), BIOSIS previews (Web of Science), LILACS (BIREME), and the Cochrane Dementia Group's developing register of diagnostic test accuracy studies to March 2013. We used citation tracking (using the database's related articles feature, where available) as an additional search method and contacted authors of eligible studies for unpublished data. Selection criteria: We included all cross-sectional studies that utilized the Mini-Cog as an index test for the diagnosis of dementia when compared to a reference standard diagnosis of dementia using standardized dementia diagnostic criteria. For the current review we only included studies that were conducted on samples from community settings, and excluded studies that were conducted in primary care or secondary care settings. We considered studies to be conducted in a community setting where participants were sampled from the general population. Data collection and analysis: Information from studies meeting the inclusion criteria were extracted including information on the characteristics of participants in the studies. The quality of the studies was assessed using the QUADAS-2 criteria and summarized using risk of bias applicability and summary graphs. We extracted information on the diagnostic test accuracy of studies including the sensitivity, specificity, and 95% confidence intervals of these measures and summarized the findings using forest plots. Study specific sensitivities and specificities were also plotted in receiver operating curve space. Main results: Three studies met the inclusion criteria, with a total of 1620 participants. The sensitivities of the Mini-Cog in the individual studies were reported as 0.99, 0.76 and 0.99. The specificity of the Mini-Cog varied in the individual studies and was 0.93, 0.89 and 0.83. There was clinical and methodological heterogeneity between the studies which precluded a pooled meta-analysis of the results. Methodological limitations were present in all the studies introducing potential sources of bias, specifically with respect to the methods for participant selection. Authors' conclusions: There are currently few studies assessing the diagnostic test accuracy of the Mini-Cog in community settings. The limited number of studies and the methodological limitations that are present in the current studies make it difficult to provide recommendations for or against the use of the Mini-Cog as a cognitive screening test in community settings. Additional well-designed studies comparing the Mini-Cog to other brief cognitive screening

tests are required in order to determine the accuracy and utility of the Mini-Cog in community based settings.

Farina N, Llewellyn D, Isaac Mokhtar Gad El Kareem N, Tabet N. Vitamin E for Alzheimer's dementia and mild cognitive impairment. Cochrane Database of Systematic Reviews. 2017; 4. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002854.pub5/abstract>

Background: Vitamin E occurs naturally in the diet. It has several biological activities, including functioning as an antioxidant to scavenge toxic free radicals. Evidence that free radicals may contribute to the pathological processes behind cognitive impairment has led to interest in the use of vitamin E supplements to treat mild cognitive impairment (MCI) and Alzheimer's disease (AD). This is an update of a Cochrane Review first published in 2000, and previously updated in 2006 and 2012. Objectives: To assess the efficacy of vitamin E in the treatment of MCI and dementia due to AD. Search methods: We searched the Specialized Register of the Cochrane Dementia and Cognitive Improvement Group (ALOIS), the Cochrane Library, MEDLINE, Embase, PsycINFO, CINAHL, LILACS as well as many trials databases and grey literature sources on 22 April 2016 using the terms: "Vitamin E", vitamin-E, alpha-tocopherol. Selection criteria: We included all double-blind, randomised trials in which treatment with any dose of vitamin E was compared with placebo in people with AD or MCI. Data collection and analysis: We used standard methodological procedures according to the Cochrane Handbook for Systematic Reviews of Interventions. We rated the quality of the evidence using the GRADE approach. Where appropriate we attempted to contact authors to obtain missing information. Main results: Four trials met the inclusion criteria, but we could only extract outcome data in accordance with our protocol from two trials, one in an AD population (n = 304) and one in an MCI population (n = 516). Both trials had an overall low to unclear risk of bias. It was not possible to pool data across studies owing to a lack of comparable outcome measures. In people with AD, we found no evidence of any clinically important effect of vitamin E on cognition, measured with change from baseline in the Alzheimer's Disease Assessment Scale - Cognitive subscale (ADAS-Cog) over six to 48 months (mean difference (MD) -1.81, 95% confidence interval (CI) -3.75 to 0.13, P = 0.07, 1 study, n = 272; moderate quality evidence). There was no evidence of a difference between vitamin E and placebo groups in the risk of experiencing at least one serious adverse event over six to 48 months (risk ratio (RR) 0.86, 95% CI 0.71 to 1.05, P = 0.13, 1 study, n = 304; moderate quality evidence), or in the risk of death (RR 0.84, 95% CI 0.52 to 1.34, P = 0.46, 1 study, n = 304; moderate quality evidence). People with AD receiving vitamin E showed less functional decline on the Alzheimer's Disease Cooperative Study/Activities of Daily Living Inventory than people receiving placebo at six to 48 months (mean difference (MD) 3.15, 95% CI 0.07 to 6.23, P = 0.04, 1 study, n = 280; moderate quality evidence). There was no evidence of any clinically important effect on neuropsychiatric symptoms measured with the Neuropsychiatric Inventory (MD -1.47, 95% CI -4.26 to 1.32, P = 0.30, 1 study, n = 280; moderate quality evidence). We found no evidence that vitamin E affected the probability of progression from MCI to probable dementia due to AD over 36 months (RR 1.03, 95% CI 0.79 to 1.35, P = 0.81, 1 study, n = 516; moderate quality evidence). Five deaths occurred in each of the vitamin E and placebo groups over the 36 months (RR 1.01, 95% CI 0.30 to 3.44, P = 0.99, 1 study, n = 516; moderate quality evidence). We were unable to extract data in accordance with the review protocol for other outcomes. However, the study authors found no evidence that vitamin E differed from placebo in its effect on cognitive function, global severity or activities of daily living. There was also no evidence of a difference between groups in the more commonly reported adverse events. Authors' conclusions: We found no evidence that the alpha-tocopherol form of vitamin E given to people with MCI prevents progression to dementia, or that it improves cognitive function in people with MCI or dementia due to AD. However, there is moderate quality evidence from a single study that it may slow functional decline in AD. Vitamin E was not associated with an increased risk of serious adverse events or mortality in the trials in this review. These conclusions have changed since the previous update, however they are still based on small numbers of trials and participants and further research is quite likely to affect the results.

Forbes D, Blake Catherine M, Thiessen Emily J, Peacock S, Hawranik P. Light therapy for improving cognition, activities of daily living, sleep, challenging behaviour, and psychiatric disturbances in dementia. Cochrane Database of Systematic Reviews. 2014; 2. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003946.pub4/abstract>

Background: Rest-activity and sleep-wake cycles are controlled by the endogenous circadian rhythm generated by the suprachiasmatic nuclei (SCN) of the hypothalamus. Degenerative changes in the SCN appear to be a biological basis for circadian disturbances in people with dementia, and might be reversed by stimulation of the SCN by light. Objectives: The review examines the effectiveness of light therapy in improving cognition, activities of daily living (ADLs), sleep, challenging behaviour, and psychiatric symptoms associated with dementia. Search methods: ALOIS, the Specialized Register of the Cochrane Dementia and Cognitive Improvement Group (CDCIG), The Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL and LILACS were searched on 20 January 2014 using the terms: "bright light\*", "light box\*", "light visor\*", "dawn-dusk\*", phototherapy, "photo therapy", "light therapy" "light treatment", light\*. The CDCIG Specialized Register contains records from all major healthcare databases (The Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL, LILACS) as well as from many trials databases and grey literature sources. Selection criteria: All relevant, randomized controlled trials were included in which light therapy, at any intensity and duration, was compared with a control group for the effect of improving cognition, ADLs, sleep, challenging behaviour, and psychiatric symptoms associated with dementia (as well as institutionalization rates or cost of care). Included were people with dementia of any type and degree of

severity. Data collection and analysis: Two review authors independently assessed the retrieved articles for relevance, and four review authors independently assessed the selected studies for risk of bias and extracted the data. Statistically significant differences in outcomes between the treatment and control groups at the end of treatment and follow-up were examined. Each study was summarized using a measure of effect (for example mean difference). Main results: Eleven trials (13 articles) met the inclusion criteria. However, three of the studies could not be included in the analyses either because the reported data could not be used in the meta-analysis or we were unable to retrieve the required data from the authors. This updated review found no effect of light therapy on cognitive function, sleep, challenging behaviour (for example agitation), or psychiatric symptoms associated with dementia. Reduction in the development of ADL limitations was reported in one study, at three of five time points, and light therapy was found to have an effect after six weeks and two years but not after one year. Authors' conclusions: There is insufficient evidence to justify the use of bright light therapy in dementia. Further research should concentrate on replicating the suggested effect on ADLs, and establishing the biological mechanism for how light therapy improves these important outcomes.

Forbes D, Forbes Scott C, Blake Catherine M, Thiessen Emily J, Forbes S. Exercise programs for people with dementia. Cochrane Database of Systematic Reviews. 2015; 4. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006489.pub4/abstract>

Background: This is an update of our previous 2013 review. Several recent trials and systematic reviews of the impact of exercise on people with dementia are reporting promising findings. Objectives: Primary objective Do exercise programs for older people with dementia improve their cognition, activities of daily living (ADLs), neuropsychiatric symptoms, depression, and mortality? Secondary objectives Do exercise programs for older people with dementia have an indirect impact on family caregivers' burden, quality of life, and mortality? Do exercise programs for older people with dementia reduce the use of healthcare services (e.g. visits to the emergency department) by participants and their family caregivers? Search methods: We identified trials for inclusion in the review by searching ALOIS ([www.medicine.ox.ac.uk/alouis](http://www.medicine.ox.ac.uk/alouis)), the Cochrane Dementia and Cognitive Improvement Group's Specialised Register, on 4 September 2011, on 13 August 2012, and again on 3 October 2013. Selection criteria: In this review, we included randomized controlled trials in which older people, diagnosed with dementia, were allocated either to exercise programs or to control groups (usual care or social contact/activities) with the aim of improving cognition, ADLs, neuropsychiatric symptoms, depression, and mortality. Secondary outcomes related to the family caregiver(s) and included caregiver burden, quality of life, mortality, and use of healthcare services. Data collection and analysis: Independently, at least two authors assessed the retrieved articles for inclusion, assessed methodological quality, and extracted data. We analysed data for summary effects. We calculated mean differences or standardized mean difference (SMD) for continuous data, and synthesized data for each outcome using a fixed-effect model, unless there was substantial heterogeneity between studies, when we used a random-effects model. We planned to explore heterogeneity in relation to severity and type of dementia, and type, frequency, and duration of exercise program. We also evaluated adverse events. Main results: Seventeen trials with 1067 participants met the inclusion criteria. However, the required data from three included trials and some of the data from a fourth trial were not published and not made available. The included trials were highly heterogeneous in terms of subtype and severity of participants' dementia, and type, duration, and frequency of exercise. Only two trials included participants living at home. Our meta-analysis revealed that there was no clear evidence of benefit from exercise on cognitive functioning. The estimated standardized mean difference between exercise and control groups was 0.43 (95% CI -0.05 to 0.92, P value 0.08; 9 studies, 409 participants). There was very substantial heterogeneity in this analysis ( $I^2$  value 80%), most of which we were unable to explain, and we rated the quality of this evidence as very low. We found a benefit of exercise programs on the ability of people with dementia to perform ADLs in six trials with 289 participants. The estimated standardized mean difference between exercise and control groups was 0.68 (95% CI 0.08 to 1.27, P value 0.02). However, again we observed considerable unexplained heterogeneity ( $I^2$  value 77%) in this meta-analysis, and we rated the quality of this evidence as very low. This means that there is a need for caution in interpreting these findings. In further analyses, in one trial we found that the burden experienced by informal caregivers providing care in the home may be reduced when they supervise the participation of the family member with dementia in an exercise program. The mean difference between exercise and control groups was -15.30 (95% CI -24.73 to -5.87; 1 trial, 40 participants; P value 0.001). There was no apparent risk of bias in this study. In addition, there was no clear evidence of benefit from exercise on neuropsychiatric symptoms (MD -0.60, 95% CI -4.22 to 3.02; 1 trial, 110 participants; P value .0.75), or depression (SMD 0.14, 95% CI -0.07 to 0.36; 5 trials, 341 participants; P value 0.16). We could not examine the remaining outcomes, quality of life, mortality, and healthcare costs, as either the appropriate data were not reported, or we did not retrieve trials that examined these outcomes. Authors' conclusions: There is promising evidence that exercise programs may improve the ability to perform ADLs in people with dementia, although some caution is advised in interpreting these findings. The review revealed no evidence of benefit from exercise on cognition, neuropsychiatric symptoms, or depression. There was little or no evidence regarding the remaining outcomes of interest (i.e., mortality, caregiver burden, caregiver quality of life, caregiver mortality, and use of healthcare services).

Forrester Lene T, Maayan N, Orrell M, Spector Aimee E, Buchan Louise D, Soares-Weiser K. Aromatherapy for dementia. Cochrane Database of Systematic Reviews. 2014; 2. [cited: url:

<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003150.pub2/abstract>

Background: Complementary therapy has received great interest within the field of dementia treatment and the use of aromatherapy and essential oils is increasing. In a growing population where the majority of patients are treated by US Food and Drug Administration (FDA)-approved drugs, the efficacy of treatment is short term and accompanied by negative side effects. Utilisation of complimentary therapies in dementia care settings presents as one of few options that are attractive to practitioners and families as patients often have reduced insight and ability to verbally communicate adverse reactions. Amongst the most distressing features of dementia are the behavioural and psychological symptoms. Addressing this facet has received particular interest in aromatherapy trials, with a shift in focus from reducing cognitive dysfunction to the reduction of behavioural and psychological symptoms in dementia. Objectives: To assess the efficacy of aromatherapy as an intervention for people with dementia. Search methods: ALOIS, the Cochrane Dementia and Cognitive Improvement Group Specialized Register, was searched on 26 November 2012 and 20 January 2013 using the terms: aromatherapy, lemon, lavender, rose, aroma, alternative therapies, complementary therapies, essential oils. Selection criteria: All relevant randomised controlled trials were considered. A minimum length of a trial and requirements for follow-up were not included, and participants in included studies had a diagnosis of dementia of any type and severity. The review considered all trials using fragrance from plants defined as aromatherapy as an intervention with people with dementia and all relevant outcomes were considered. Data collection and analysis: Titles and abstracts extracted by the searches were screened for their eligibility for potential inclusion in the review. For Burns 2011, continuous outcomes were estimated as the mean difference between groups and its 95% confidence interval using a fixed-effect model. For Ballard 2002, analysis of co-variance was used for all outcomes, with the nursing home being treated as a random effect. Main results: Seven studies with 428 participants were included in this review; only two of these had published usable results. Individual patient data were obtained from one trial (Ballard 2002) and additional analyses performed. The additional analyses conducted using individual patient data from Ballard 2002 revealed a statistically significant treatment effect in favour of the aromatherapy intervention on measures of agitation (n = 71, MD -11.1, 95% CI -19.9 to -2.2) and behavioural symptoms (n = 71, MD -15.8, 95% CI -24.4 to -7.2). Burns 2011, however, found no difference in agitation (n = 63, MD 0.00, 95% CI -1.36 to 1.36), behavioural symptoms (n = 63, MD 2.80, 95% CI -5.84 to 11.44), activities of daily living (n = 63, MD -0.50, 95% CI -1.79 to 0.79) and quality of life (n = 63, MD 19.00, 95% CI -23.12 to 61.12). Burns 2011 and Fu 2013 found no difference in adverse effects (n = 124, RR 0.97, 95% CI 0.15 to 6.46) when aromatherapy was compared to placebo. Authors' conclusions: The benefits of aromatherapy for people with dementia are equivocal from the seven trials included in this review. It is important to note there were several methodological difficulties with the included studies. More well-designed, large-scale randomised controlled trials are needed before clear conclusions can be drawn regarding the effectiveness of aromatherapy for dementia. Additionally, several issues need to be addressed, such as whether different aromatherapy interventions are comparable and the possibility that outcomes may vary for different types of dementia.

Harrison Jennifer K, Fearon P, Noel-Storr Anna H, McShane R, Stott David J, Quinn Terry J. Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) for the diagnosis of dementia within a general practice (primary care) setting. Cochrane Database of Systematic Reviews. 2014; 7. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010771.pub2/abstract>

Background: The IQCODE (Informant Questionnaire for Cognitive Decline in the Elderly) is a commonly used questionnaire based tool that uses collateral information to assess for cognitive decline and dementia. Brief tools that can be used for dementia "screening" or "triage" may have particular utility in primary care / general practice healthcare settings but only if they have suitable test accuracy. A synthesis of the available data regarding IQCODE accuracy in a primary care setting should help inform cognitive assessment strategies for clinical practice; research and policy. Objectives: We sought to describe the accuracy of IQCODE (the index test) against a clinical diagnosis of dementia (the reference standard). In this review we focus on those studies conducted in a primary care (general practice) setting. Search methods: A search was performed in the following sources on the 28th of January 2013: ALOIS (Cochrane Dementia and Cognitive Improvement Group), MEDLINE (Ovid SP), EMBASE (Ovid SP), PsycINFO (Ovid SP), BIOSIS (Ovid SP), ISI Web of Science and Conference Proceedings (ISI Web of Knowledge), CINHALL (EBSCOhost) and LILACs (BIREME). We also searched sources specific to diagnostic test accuracy: MEDION (Universities of Maastricht and Leuven); DARE (York University); HTA Database (Health Technology Assessments Database via The Cochrane Library) and ARIF (Birmingham University). We developed a sensitive search strategy; search terms were designed to cover key concepts using several different approaches run in parallel and included terms relating to cognitive tests, cognitive screening and dementia. We used standardized database subject headings such as MeSH terms (in MEDLINE) and other standardized headings (controlled vocabulary) in other databases, as appropriate. Selection criteria: We selected those studies performed in primary care settings, which included (not necessarily exclusively) IQCODE to assess for the presence of dementia and where dementia diagnosis was confirmed with clinical assessment. For the "primary care" setting, we included those healthcare settings where unselected patients, present for initial, non-specialist assessment of memory or non-memory related symptoms; often with a view to onward referral for more definitive assessment. Data collection and analysis: We screened all titles generated by electronic database searches and abstracts of all potentially relevant studies were reviewed. Full papers were assessed for eligibility and data extracted by two independent assessors. Quality assessment (risk of bias and applicability) was determined using

the QUADAS-2 tool. Reporting quality was determined using the STARDdem extension to the STARD tool. Main results: From 71 papers describing IQCODE test accuracy, we included 1 paper, representing data from 230 individuals (n=16 [7%] with dementia). The paper described those patients consulting a primary care service who self-identified as Japanese-American. Dementia diagnosis was made using Benson & Cummings criteria and the IQCODE was recorded as part of a longer interview with the informant. IQCODE accuracy was assessed at various test thresholds, with a "trade-off" between sensitivity and specificity across these cutpoints. At an IQCODE threshold of 3.2 sensitivity: 100%, specificity: 76%; for IQCODE 3.7 sensitivity: 75%, specificity: 98%. Applying the QUADAS-2 assessments, the study was at high risk of bias in all categories. In particular degree of blinding was unclear and not all participants were included in the final analysis. Authors' conclusions: It is not possible to give definitive guidance on the test accuracy of IQCODE for the diagnosis of dementia in a primary care setting based on the single study identified. We are surprised by the lack of research using the IQCODE in primary care as this is, arguably, the most appropriate setting for targeted case finding of those with undiagnosed dementia in order to maximise opportunities to intervene and provide support for the individual and their carers.

Harrison Jennifer K, Fearon P, Noel-Storr Anna H, McShane R, Stott David J, Quinn Terry J. Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) for the diagnosis of dementia within a secondary care setting. *Cochrane Database of Systematic Reviews*. 2015; 3. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010772.pub2/abstract>

**Background:** The diagnosis of dementia relies on the presence of new-onset cognitive impairment affecting an individual's functioning and activities of daily living. The Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) is a questionnaire instrument, completed by a suitable 'informant' who knows the patient well, designed to assess change in functional performance secondary to cognitive change; it is used as a tool to identifying those who may have dementia. In secondary care there are two specific instances where patients may be assessed for the presence of dementia. These are in the general acute hospital setting, where opportunistic screening may be undertaken, or in specialist memory services where individuals have been referred due to perceived cognitive problems. To ensure an instrument is suitable for diagnostic use in these settings, its test accuracy must be established. **Objectives:** To determine the diagnostic accuracy of the informant-based questionnaire IQCODE, for detection of all-cause (undifferentiated) dementia in adults presenting to secondary-care services. **Search methods:** We searched the following sources on the 28th of January 2013: ALOIS (Cochrane Dementia and Cognitive Improvement Group), MEDLINE (Ovid SP), EMBASE (Ovid SP), PsycINFO (Ovid SP), BIOSIS Previews (Thomson Reuters Web of Science), Web of Science Core Collection (includes Conference Proceedings Citation Index) (Thomson Reuters Web of Science), CINAHL (EBSCOhost) and LILACS (BIREME). We also searched sources specific to diagnostic test accuracy: MEDION (Universities of Maastricht and Leuven); DARE (Database of Abstracts of Reviews of Effects - via the Cochrane Library); HTA Database (Health Technology Assessment Database via the Cochrane Library) and ARIF (Birmingham University). We also checked reference lists of relevant studies and reviews, used searches of known relevant studies in PubMed to track related articles, and contacted research groups conducting work on IQCODE for dementia diagnosis to try to find additional studies. We developed a sensitive search strategy; search terms were designed to cover key concepts using several different approaches run in parallel and included terms relating to cognitive tests, cognitive screening and dementia. We used standardised database subject headings such as MeSH terms (in MEDLINE) and other standardised headings (controlled vocabulary) in other databases, as appropriate. **Selection criteria:** We selected those studies performed in secondary-care settings, which included (not necessarily exclusively) IQCODE to assess for the presence of dementia and where dementia diagnosis was confirmed with clinical assessment. For the 'secondary care' setting we included all studies which assessed patients in hospital (e.g. acute unscheduled admissions, referrals to specialist geriatric assessment services etc.) and those referred for specialist 'memory' assessment, typically in psychogeriatric services. **Data collection and analysis:** We screened all titles generated by electronic database searches, and reviewed abstracts of all potentially relevant studies. Two independent assessors checked full papers for eligibility and extracted data. We determined quality assessment (risk of bias and applicability) using the QUADAS-2 tool, and reporting quality using the STARD tool. **Main results:** From 72 papers describing IQCODE test accuracy, we included 13 papers, representing data from 2745 individuals (n = 1413 (51%) with dementia). Pooled analysis of all studies using data presented closest to a cut-off of 3.3 indicated that sensitivity was 0.91 (95% CI 0.86 to 0.94); specificity 0.66 (95% CI 0.56 to 0.75); the positive likelihood ratio was 2.7 (95% CI 2.0 to 3.6) and the negative likelihood ratio was 0.14 (95% CI 0.09 to 0.22). There was a statistically significant difference in test accuracy between the general hospital setting and the specialist memory setting (P = 0.019), suggesting that IQCODE performs better in a 'general' setting. We found no significant differences in the test accuracy of the short (16-item) versus the 26-item IQCODE, or in the language of administration. There was significant heterogeneity in the included studies, including a highly varied prevalence of dementia (10.5% to 87.4%). Across the included papers there was substantial potential for bias, particularly around sampling of included participants and selection criteria, which may limit generalisability. There was also evidence of suboptimal reporting, particularly around disease severity and handling indeterminate results, which are important if considering use in clinical practice. **Authors' conclusions:** The IQCODE can be used to identify older adults in the general hospital setting who are at risk of dementia and require specialist assessment; it is useful specifically for ruling out those without evidence of cognitive decline. The language of administration did not affect test accuracy, which supports the cross-cultural use of the tool. These findings are qualified by the significant heterogeneity, the

potential for bias and suboptimal reporting found in the included studies.

Harrison Jennifer K, Stott David J, McShane R, Noel-Storr Anna H, Swann-Price Rhiannon S, Quinn Terry J. Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) for the early diagnosis of dementia across a variety of healthcare settings. *Cochrane Database of Systematic Reviews*. 2016; 11. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011333.pub2/abstract>

**Background:** The Informant Questionnaire for Cognitive Decline in the Elderly (IQCODE) is a structured interview based on informant responses that is used to assess for possible dementia. IQCODE has been used for retrospective or contemporaneous assessment of cognitive decline. There is considerable interest in tests that may identify those at future risk of developing dementia. Assessing a population free of dementia for the prospective development of dementia is an approach often used in studies of dementia biomarkers. In theory, questionnaire-based assessments, such as IQCODE, could be used in a similar way, assessing for dementia that is diagnosed on a later (delayed) assessment. **Objectives:** To determine the diagnostic accuracy of IQCODE in a population free from dementia for the delayed diagnosis of dementia (test accuracy with delayed verification study design). **Search methods:** We searched these sources on 16 January 2016: ALOIS (Cochrane Dementia and Cognitive Improvement Group), MEDLINE Ovid SP, Embase Ovid SP, PsycINFO Ovid SP, BIOSIS Previews on Thomson Reuters Web of Science, Web of Science Core Collection (includes Conference Proceedings Citation Index) on Thomson Reuters Web of Science, CINAHL EBSCOhost, and LILACS BIREME. We also searched sources specific to diagnostic test accuracy: MEDION (Universities of Maastricht and Leuven); DARE (Database of Abstracts of Reviews of Effects, in the Cochrane Library); HTA Database (Health Technology Assessment Database, in the Cochrane Library), and ARIF (Birmingham University). We checked reference lists of included studies and reviews, used searches of included studies in PubMed to track related articles, and contacted research groups conducting work on IQCODE for dementia diagnosis to try to find additional studies. We developed a sensitive search strategy; search terms were designed to cover key concepts using several different approaches run in parallel, and included terms relating to cognitive tests, cognitive screening, and dementia. We used standardised database subject headings, such as MeSH terms (in MEDLINE) and other standardised headings (controlled vocabulary) in other databases, as appropriate. **Selection criteria:** We selected studies that included a population free from dementia at baseline, who were assessed with the IQCODE and subsequently assessed for the development of dementia over time. The implication was that at the time of testing, the individual had a cognitive problem sufficient to result in an abnormal IQCODE score (defined by the study authors), but not yet meeting dementia diagnostic criteria. **Data collection and analysis:** We screened all titles generated by the electronic database searches, and reviewed abstracts of all potentially relevant studies. Two assessors independently checked the full papers for eligibility and extracted data. We determined quality assessment (risk of bias and applicability) using the QUADAS-2 tool, and reported quality using the STARDdem tool. **Main results:** From 85 papers describing IQCODE, we included three papers, representing data from 626 individuals. Of this total, 22% (N = 135/626) were excluded because of prevalent dementia. There was substantial attrition; 47% (N = 295) of the study population received reference standard assessment at first follow-up (three to six months) and 28% (N = 174) received reference standard assessment at final follow-up (one to three years). Prevalence of dementia ranged from 12% to 26% at first follow-up and 16% to 35% at final follow-up. The three studies were considered to be too heterogenous to combine, so we did not perform meta-analyses to describe summary estimates of interest. Included patients were poststroke (two papers) and hip fracture (one paper). The IQCODE was used at three thresholds of positivity (higher than 3.0, higher than 3.12 and higher than 3.3) to predict those at risk of a future diagnosis of dementia. Using a cut-off of 3.0, IQCODE had a sensitivity of 0.75 (95%CI 0.51 to 0.91) and a specificity of 0.46 (95%CI 0.34 to 0.59) at one year following stroke. Using a cut-off of 3.12, the IQCODE had a sensitivity of 0.80 (95%CI 0.44 to 0.97) and specificity of 0.53 (95%CI 0.41 to 0.65) for the clinical diagnosis of dementia at six months after hip fracture. Using a cut-off of 3.3, the IQCODE had a sensitivity of 0.84 (95%CI 0.68 to 0.94) and a specificity of 0.87 (95%CI 0.76 to 0.94) for the clinical diagnosis of dementia at one year after stroke. In general, the IQCODE was sensitive for identification of those who would develop dementia, but lacked specificity. Methods for both excluding prevalent dementia at baseline and assessing for the development of dementia were varied, and had the potential to introduce bias. **Authors' conclusions:** Included studies were heterogenous, recruited from specialist settings, and had potential biases. The studies identified did not allow us to make specific recommendations on the use of the IQCODE for the future diagnosis of dementia in clinical practice. The included studies highlighted the challenges of delayed verification dementia research, with issues around prevalent dementia assessment, loss to follow-up over time, and test non-completion potentially limiting the studies. Future research should recognise these issues and have explicit protocols for dealing with them.

Hilton Malcolm P, Zimmermann Eleanor F, Hunt William T. Ginkgo biloba for tinnitus. *Cochrane Database of Systematic Reviews*. 2013; 3. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003852.pub3/abstract>

**Background:** This is an update of a Cochrane review first published in *The Cochrane Library* in Issue 2, 2004 and previously updated in 2007 and 2009. Tinnitus can be described as the perception of sound in the absence of external acoustic stimulation. At present no specific therapy for tinnitus is acknowledged to be satisfactory in all patients. There are a number of reports in the literature suggesting that Ginkgo biloba may be effective in the management of tinnitus. However, there also appears to be a strong placebo effect in tinnitus



management. Objectives: To assess the effect of Ginkgo biloba in patients who are troubled by tinnitus. Search methods: We searched the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL); PubMed; EMBASE; AMED; Web of Science; BIOSIS Previews; Cambridge Scientific Abstracts; ICTRP and additional sources for published and unpublished trials. The date of the most recent search was 12 March 2012. Selection criteria: Adults (18 years and over) complaining of tinnitus or adults with a primary complaint of cerebral insufficiency, where tinnitus forms part of the syndrome. Data collection and analysis: Both original authors independently extracted data and assessed trials for quality. For the 2012 update two authors determined trial eligibility, extracted data, analysed data and updated the contents of the review. Main results: Four trials with a total of 1543 participants were included in the review; we assessed all the included studies as having a low risk of bias. Three trials (1143 participants) included patients with a primary complaint of tinnitus and one (400 participants) included patients with mild to moderate dementia, some of whom had tinnitus. There was no evidence that Ginkgo biloba was effective in patients with a primary complaint of tinnitus. In the study of patients with dementia, mean baseline levels of tinnitus were low (1.7 to 2.5 on a 10-point subjective symptom rating scale). A small but statistically significant reduction of 1.5 and 0.7 points was seen in patients taking Ginkgo biloba with vascular dementia and Alzheimer's disease respectively. The practical clinical significance of this is unclear. The incidence of side effects was low. Authors' conclusions: The limited evidence does not demonstrate that Ginkgo biloba is effective for tinnitus when this is the primary complaint.

Jaturapatporn D, Isaac Mokhtar Gad El Kareem N, McCleery J, Tabet N. Aspirin, steroidal and non-steroidal anti-inflammatory drugs for the treatment of Alzheimer's disease. Cochrane Database of Systematic Reviews. 2012; 2. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006378.pub2/abstract>

Background: Alzheimer's disease (AD) is the most common form of dementia. The incidence of AD rises exponentially with age and its prevalence will increase significantly worldwide in the next few decades. Inflammatory processes have been suspected in the pathogenesis of the disease. Objectives: To review the efficacy and side effects of aspirin, steroidal and non-steroidal anti-inflammatory drugs (NSAIDs) in the treatment of AD, compared to placebo. Search methods: We searched ALOIS: the Cochrane Dementia and Cognitive Improvement Group's Specialized Register on 12 April 2011 using the terms: aspirin OR "cyclooxygenase 2 inhibitor" OR aceclofenac OR acemetacin OR betamethasone OR celecoxib OR cortisone OR deflazacort OR dexamethasone OR dexibuprofen OR dexketoprofen OR diclofenac sodium OR diflunisal OR diflusal OR etodolac OR etoricoxib OR fenbufen OR fenoprofen OR flurbiprofen OR hydrocortisone OR ibuprofen OR indometacin OR indomethacin OR ketoprofen OR lumiracoxib OR mefenamic OR meloxicam OR methylprednisolone OR nabumetone OR naproxen OR nimesulide OR "anti-inflammatory" OR prednisone OR piroxicam OR sulindac OR tenoxicam OR tiaprofenic acid OR triamcinolone OR NSAIDS OR NSAID. ALOIS contains records of clinical trials identified from monthly searches of a number of major healthcare databases (including MEDLINE, EMBASE, PsycINFO, CINAHL, LILACS), numerous trial registries (including national, international and pharmaceutical registries) and grey literature sources. Selection criteria: All randomised controlled trials assessing the efficacy of aspirin, steroidal and non-steroidal anti-inflammatory drugs in AD. Data collection and analysis: One author assessed risk of bias of each study and extracted data. A second author verified data selection. Main results: Our search identified 604 potentially relevant studies. Of these, 14 studies (15 interventions) were RCTs and met our inclusion criteria. The numbers of participants were 352, 138 and 1745 for aspirin, steroid and NSAIDs groups, respectively. One selected study comprised two separate interventions. Interventions assessed in these studies were grouped into four categories: aspirin (three interventions), steroids (one intervention), traditional NSAIDs (six interventions), and selective cyclooxygenase-2 (COX-2) inhibitors (five interventions). All studies were evaluated for internal validity using a risk of bias assessment tool. The risk of bias was low for five studies, high for seven studies, and unclear for two studies. There was no significant improvement in cognitive decline for aspirin, steroid, traditional NSAIDs and selective COX-2 inhibitors. Compared to controls, patients receiving aspirin experienced more bleeding while patients receiving steroid experienced more hyperglycaemia, abnormal lab results and face edema. Patients receiving NSAIDs experienced nausea, vomiting, elevated creatinine, elevated LFT and hypertension. A trend towards higher death rates was observed among patients treated with NSAIDs compared with placebo and this was somewhat higher for selective COX-2 inhibitors than for traditional NSAIDs. Authors' conclusions: Based on the studies carried out so far, the efficacy of aspirin, steroid and NSAIDs (traditional NSAIDs and COX-2 inhibitors) is not proven. Therefore, these drugs cannot be recommended for the treatment of AD.

Jongstra S, Harrison Jennifer K, Quinn Terry J, Richard E. Antihypertensive withdrawal for the prevention of cognitive decline. Cochrane Database of Systematic Reviews. 2016; 11. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011971.pub2/abstract>

Background: Clinical trials and observational data have variously shown a protective, harmful or neutral effect of antihypertensives on cognitive function. In theory, withdrawal of antihypertensives could improve cerebral perfusion and reduce or delay cognitive decline. However, it is also plausible that withdrawal of antihypertensives may have a detrimental effect on cognition through increased incidence of stroke or other vascular events. Objectives: To assess the effects of complete withdrawal of at least one antihypertensive medication on incidence of dementia, cognitive function, blood pressure and other safety outcomes in cognitively intact and cognitively impaired adults. Search methods: We searched ALOIS, the specialised register of the Cochrane Dementia



and Cognitive Improvement Group, with additional searches conducted in MEDLINE, Embase, PsycINFO, CINAHL, LILACS, Web of Science Core Collection, ClinicalTrials.gov and the World Health Organization Portal/ICTRP on 12 December 2015. There were no language or date restrictions applied to the electronic searches, and no methodological filters were used to restrict the search. Selection criteria: We included randomised controlled trials (RCTs) and controlled clinical trials (CCTs) provided they compared withdrawal of antihypertensive medications with continuation of the medications and included an outcome measure assessing cognitive function or a clinical diagnosis of dementia. We included studies with healthy participants, but we also included studies with participants with all grades of severity of existing dementia or cognitive impairment. Data collection and analysis: Two review authors examined titles and abstracts of citations identified by the search for eligibility, retrieving full texts where needed to identify studies for inclusion, with any disagreement resolved by involvement of a third author. Data were extracted independently on primary and secondary outcomes. We used standard methodological procedures expected by Cochrane. The primary outcome measures of interest were changes in global and specific cognitive function and incidence of dementia; secondary outcomes included change in systolic and diastolic blood pressure, mortality, adverse events (including cardiovascular events, hospitalisation and falls) and adherence to withdrawal. The quality of the evidence was evaluated using the GRADE approach. Main results: We included two RCTs investigating withdrawal of antihypertensives in 2490 participants. There was substantial clinical heterogeneity between the included studies, therefore we did not combine data for our primary outcome. Overall, the quality of included studies was high and the risk of bias was low. Neither study investigated incident dementia. One study assessed withholding previously prescribed antihypertensive drugs for seven days following acute stroke. Cognition was assessed using telephone Mini-Mental State Examination (t-MMSE) and Telephone Interview for Cognitive Status (TICS-M) at 90 days as a secondary outcome. The t-MMSE score was a mean of 1.0 point higher in participants who withdrew antihypertensive medications compared to participants who continued them (95% confidence interval (CI) 0.35 to 1.65; 1784 participants) and the TICS-M was a mean of 2.10 points higher (95% CI 0.69 to 3.51; 1784 participants). However, in both cases the evidence was of very low quality downgraded due to risk of bias, indirectness and evidence from a single study. The other study was community based and included participants with mild cognitive impairment. Drug withdrawal was for 16 weeks. Cognitive performance was assessed using a composite of at least five out of six cognitive tests. There was no evidence of a difference comparing participants who withdrew antihypertensive medications and participants who continued (mean difference 0.02 points, 95% CI -0.19 to 0.21; 351 participants). This evidence was of low quality and was downgraded due to risk of bias and evidence from single study. In one study, the systolic blood pressure after seven days of withdrawal was 9.5 mmHg higher in the intervention compared to the control group (95% CI 7.43 to 11.57; 2095 participants) and diastolic blood pressure was 5.1 mmHg higher (95% CI 3.86 to 6.34; 2095 participants). This evidence was low quality, downgraded due to indirectness, because the data must be interpreted in the context of the wider study looking at glyceryl trinitrate administration or not, and evidence from a single study. In the other study, systolic blood pressure increased by 7.4 mmHg in the withdrawal group compared to the control group (95% CI 7.08 to 7.72; 356 participants) and diastolic blood pressure increased by 2.6 mmHg (95% CI 2.42 to 2.78; 356 participants). This was moderate quality evidence, downgraded as evidence was from a single study. We combined data for mortality and cardiovascular events. There was no clear evidence that antihypertensive medication withdrawal affected adverse events, although there was a possible trend to increased cardiovascular events in the large post-stroke study (pooled mortality risk ratio 0.88, 95% CI 0.72 to 1.08; 2485 participants; and cardiovascular events risk ratio 1.29, 95% CI 0.96 to 1.72). Certain prespecified outcomes of interest (falls, hospitalisation) were not reported. Authors' conclusions: The effects of withdrawing antihypertensive medications on cognition or prevention of dementia are uncertain. There was a signal of a positive effect in one study looking at withdrawal after acute stroke but these results are unlikely to be generalisable to non-stroke settings and were not a primary outcome of the study. Withdrawing antihypertensive drugs was associated with increased blood pressure. It is unlikely to increase mortality at three to four months' follow-up, although there was a signal from one large study looking at withdrawal after stroke that withdrawal was associated an increase in cardiovascular events.

Karkou V, Meekums B. Dance movement therapy for dementia. Cochrane Database of Systematic Reviews. 2017; 2. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011022.pub2/abstract>

Background: Dementia is a collective name for different degenerative brain syndromes which, according to Alzheimer's Disease International, affects approximately 35.6 million people worldwide. The latest NICE guideline for dementia highlights the value of diverse treatment options for the different stages and symptoms of dementia including non-pharmacological treatments. Relevant literature also argues for the value of interventions that acknowledge the complexity of the condition and address the person as a whole, including their physical, emotional, social and cognitive processes. At the same time, there is growing literature that highlights the capacity of the arts and embodied practices to address this complexity. Dance movement therapy is an embodied psychological intervention that can address complexity and thus, may be useful for people with dementia, but its effectiveness remains unclear. Objectives: To assess the effects of dance movement therapy on behavioural, social, cognitive and emotional symptoms of people with dementia in comparison to no treatment, standard care or any other treatment. Also, to compare different forms of dance movement therapy (e.g. Laban-based dance movement therapy, Chacian dance movement therapy or Authentic Movement). Search methods: Searches took place up to March 2016 through ALOIS, Cochrane Dementia and Cognitive Improvement's Specialized Register,

which covers CENTRAL, a number of major healthcare databases and trial registers, and grey literature sources. We checked bibliographies of relevant studies and reviews, and contacted professional associations, educational programmes and experts from around the world. Selection criteria: We considered randomised controlled trials (RCTs) in any language, including cross-over design and cluster-RCTs for inclusion. Studies considered had to include people with dementia, in any age group and in any setting, with interventions delivered by a dance movement therapy practitioner who (i) had received formal training (ii) was a dance movement therapist in training or (iii) was otherwise recognised as a dance movement therapist in the country in which the study was conducted. Data collection and analysis: The two review authors independently reviewed studies on an abstract/title level and again after reading the full paper, and we independently evaluated methodological quality. Main results: Of the 102 studies identified through electronic searches and personal communication, after de-duplication we screened 80 at title/abstract level. We then reviewed 19 full papers, none of which met the inclusion criteria. Although three studies mentioned dance movement therapy as their intervention, they were excluded because they were not delivered by a qualified dance movement therapy practitioner. As a result, no studies were included in this review. Authors' conclusions: Trials of high methodological quality, large sample sizes and clarity in the way the intervention is put together and delivered are needed to assess whether dance movement therapy is an effective intervention for dementia.

Li Y, Hai S, Zhou Y, Dong Bi R. Cholinesterase inhibitors for rarer dementias associated with neurological conditions. *Cochrane Database of Systematic Reviews*. 2015; 3. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009444.pub3/abstract>

Background: Rarer dementias include Huntington's disease (HD), cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), frontotemporal dementia (FTD), dementia in multiple sclerosis (MS) and progressive supranuclear palsy (PSP). Cholinesterase inhibitors, including donepezil, galantamine and rivastigmine, are considered to be the first-line medicines for Alzheimer's disease and some other dementias, such as dementia in Parkinson's disease. Cholinesterase inhibitors are hypothesised to work by inhibiting the enzyme acetylcholinesterase (AChE) which breaks down the neurotransmitter acetylcholine. Cholinesterase inhibitors may also lead to clinical improvement for rarer dementias associated with neurological conditions. Objectives: To assess the efficacy and safety of cholinesterase inhibitors for cognitive impairment or dementia associated with neurological conditions. Search methods: We searched the Cochrane Dementia and Cognitive Improvement Group's Specialised Register, CENTRAL, MEDLINE, EMBASE, PsycINFO, CINAHL, LILACS, several trial registries and grey literature sources in August 2013. Selection criteria: We included randomised, double-blind, controlled trials assessing the efficacy of treatment of rarer dementias associated with neurological conditions with currently marketed cholinesterase inhibitors. Data collection and analysis: Two review authors independently assessed eligibility and quality of trials, and extracted data. We used the standard methodological procedures of the Cochrane Collaboration. Main results: We included eight RCTs involving 567 participants. Six studies used a simple parallel-group design; the other two consisted of an open-label treatment period followed by a randomised phase. All trials were well concealed for allocation and double-blind, however the sample sizes of most trials were small. All trials used placebo as control. We performed meta-analyses for some outcomes in patients with MS. For all other conditions, results are presented narratively. Two trials included patients with HD; one found that cholinesterase inhibitor use in the short-term had no statistically significant impact on the cognitive portion of the Alzheimer Disease Assessment Scale (ADAS-Cog; 1 study, WMD 1.00, 95% CI -1.66 to 3.66,  $P = 0.46$ ; low quality evidence), Unified Huntington's Disease Rating Scale (UHDRS) Verbal Fluency Test (1 study, WMD -1.20, 95% CI -7.97 to 5.57,  $P = 0.73$ ; low quality evidence), UHDRS Symbol Digit Modalities Test (SDMT; 1 study, WMD 2.70, 95% CI -0.95 to 6.35,  $P = 0.15$ ; low quality evidence) and other psychometric tests. The other study found that cholinesterase inhibitor use in the medium-term improved the results of the verbal fluency test (1 study, WMD 6.43, 95% CI 0.66 to 12.20,  $P = 0.03$ ; moderate quality evidence) and California Verbal Learning Test - Second Edition (CVLT-II) Recognition Task (1 study, WMD 2.42, 95% CI 0.17 to 4.67,  $P = 0.04$ ; moderate quality evidence). There was no statistically significant difference between groups on the SDMT (1 study, WMD -0.31, 95% CI -7.77 to 7.15,  $P = 0.94$ ; moderate quality evidence), CVLT-II trials 1-5 (1 study, WMD -2.09, 95% CI -11.65 to 7.47,  $P = 0.67$ ; moderate quality evidence), short-delay recall (1 study, WMD 0.35, 95% CI -2.87 to 3.57,  $P = 0.83$ ; moderate quality evidence), or long-delay recall (1 study, WMD -0.14, 95% CI -3.08 to 2.80,  $P = 0.93$ ; moderate quality evidence), and other psychometric tests. Four trials included patients with MS; one found no differences between the cholinesterase inhibitors (short-term) and placebo groups on the Wechsler Memory Scales general memory score (1 study, WMD 0.90, 95% CI -0.52 to 2.32,  $P = 0.22$ ; low quality evidence). The three other trials found that, in the medium-term - cholinesterase inhibitors improved the clinician's impression of cognitive change (2 studies, OR 1.96, 95% CI 1.06 to 3.62,  $P = 0.03$ ; high quality evidence). However, the treatment effect on other aspects of cognitive change were unclear, measured by the Selective Reminding Test (3 studies, WMD 1.47, 95% CI -0.39 to 3.32,  $P = 0.12$ ; high quality evidence), patient's self-reported impression of memory change (2 studies, OR 1.67, 95% CI 0.93 to 3.00,  $P = 0.08$ ; high quality evidence) and cognitive change (1 study, OR 0.95, 95% CI 0.45 to 1.98,  $P = 0.89$ ; high quality evidence), clinician's impression of memory change (1 study, OR 1.50, 95% CI 0.59 to 3.84,  $P = 0.39$ ; moderate quality evidence), other psychometric tests, and activities of daily living - patient reported impact of multiple sclerosis activities (1 study, WMD -1.18, 95% CI -3.02 to 0.66,  $P = 0.21$ ; low quality evidence). One study on patients with CADASIL found a beneficial effect of cholinesterase inhibitors on the Executive interview, and Trail Making Test parts A and B. The impact of cholinesterase inhibitors on the Vascular

ADAS-Cog score (1 study, WMD 0.04, 95% CI -1.57 to 1.65, P = 0.96; high quality evidence), the Clinical Dementia Rating Scale Sum of Boxes (1 study, WMD -0.09, 95% CI -0.48 to 0.03, P = 0.65; high quality evidence) Disability Assessment for Dementia scale (1 study, WMD 0.58, 95% CI -2.72 to 3.88, P = 0.73; moderate quality evidence), and other measures was unclear. One study included patients with FTD. This trial consisted of an open-label treatment period followed by a randomised, double-blind, placebo-controlled phase. No data of primary outcomes were reported in this study. In the included studies, the most common side effect was gastrointestinal symptoms. For all conditions, compared to the treatment group, the placebo group experienced significantly less nausea (6 studies, 44/257 vs. 22/246, OR 2.10, 95% CI 1.22 to 3.62, P = 0.007; high quality evidence), diarrhoea (6 studies, 40/257 vs. 13/246, OR 3.26, 95% CI 1.72 to 6.19, P = 0.0003; moderate quality evidence) and vomiting (3 studies, 17/192 vs. 3/182, OR 5.76, 95% CI 1.67 to 19.87, P = 0.006; moderate quality evidence). Authors' conclusions: The sample sizes of most included trials were small, and some of the results were extracted from only one study. There were no poolable data for HD, CADASIL and FTD patients and there were no results for patients with PSP. Current evidence shows that the efficacy on cognitive function and activities of daily living of cholinesterase inhibitors in people with HD, CADASIL, MS, PSP or FTD is unclear, although cholinesterase inhibitors are associated with more gastrointestinal side effects compared with placebo.

Lins S, Hayder-Beichel D, Rücker G, Motschall E, Antes G, Meyer G, et al. Efficacy and experiences of telephone counselling for informal carers of people with dementia. *Cochrane Database of Systematic Reviews*. 2014; 9. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009126.pub2/abstract>

**Background:** Informal carers of people with dementia can suffer from depressive symptoms, emotional distress and other physiological, social and financial consequences. **Objectives:** This review focuses on three main objectives: To: 1) produce a quantitative review of the efficacy of telephone counselling for informal carers of people with dementia; 2) synthesize qualitative studies to explore carers' experiences of receiving telephone counselling and counsellors' experiences of conducting telephone counselling; and 3) integrate 1) and 2) to identify aspects of the intervention that are valued and work well, and those interventional components that should be improved or redesigned. **Search methods:** The Cochrane Dementia and Cognitive Improvement Group's Specialized Register, The Cochrane Library, MEDLINE, MEDLINE in Process, EMBASE, CINAHL, PSYINDEX, PsycINFO, Web of Science, DIMDI databases, Springer database, Science direct and trial registers were searched on 3 May 2011 and updated on 25 February 2013. A Forward Citation search was conducted for included studies in Web of Science and Google Scholar. We used the Related Articles service of PubMed for included studies, contacted experts and hand-searched abstracts of five congresses. **Selection criteria:** Randomised controlled trials (RCTs) or cross-over trials that compared telephone counselling for informal carers of people with dementia against no treatment, usual care or friendly calls for chatting were included. Evaluation of efficacy. Qualitative studies with qualitative methods of data collection and analysis were also included to address experiences with telephone counselling. **Data collection and analysis:** Two authors independently screened articles for inclusion criteria, extracted data and assessed the quantitative trials with the Cochrane 'Risk of bias' tool and the qualitative studies with the Critical Appraisal Skills Program (CASP) tool. The authors conducted meta-analyses, but reported some results in narrative form due to clinical heterogeneity. The authors synthesised the qualitative data and integrated quantitative RCT data with the qualitative data. **Main results:** Nine RCTs and two qualitative studies were included. Six studies investigated telephone counselling without additional intervention, one study combined telephone counselling with video sessions, and two studies combined it with video sessions and a workbook. All quantitative studies had a high risk of bias in terms of blinding of participants and outcome assessment. Most studies provided no information about random sequence generation and allocation concealment. The quality of the qualitative studies ('thin descriptions') was assessed as moderate. Meta-analyses indicated a reduction of depressive symptoms for telephone counselling without additional intervention (three trials, 163 participants: standardised mean difference (SMD) 0.32, 95% confidence interval (CI) 0.01 to 0.63, P value 0.04; moderate quality evidence). The estimated effects on other outcomes (burden, distress, anxiety, quality of life, self-efficacy, satisfaction and social support) were uncertain and differences could not be excluded (burden: four trials, 165 participants: SMD 0.45, 95% CI -0.01 to 0.90, P value 0.05; moderate quality evidence; support: two trials, 67 participants: SMD 0.25, 95% CI -0.24 to 0.73, P value 0.32; low quality evidence). None of the quantitative studies included reported adverse effects or harm due to telephone counselling. Three analytical themes (barriers and facilitators for successful implementation of telephone counselling, counsellor's emotional attitude and content of telephone counselling) and 16 descriptive themes that present the carers' needs for telephone counselling were identified in the thematic synthesis. Integration of quantitative and qualitative data shows potential for improvement. For example, no RCT reported that the counsellor provided 24-hour availability or that there was debriefing of the counsellor. Also, the qualitative studies covered a limited range of ways of performing telephone counselling. **Authors' conclusions:** There is evidence that telephone counselling can reduce depressive symptoms for carers of people with dementia and that telephone counselling meets important needs of the carer. This result needs to be confirmed in future studies that evaluate efficacy through robust RCTs and the experience aspect through qualitative studies with rich data.

Liu J, Wang L-N, Wu L-Y, Wang Y-P. Treatment of epilepsy for people with Alzheimer's disease. *Cochrane Database of Systematic Reviews*. 2016; 11. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011922.pub2/abstract>

Background: Any type of seizure can be observed in Alzheimer's disease (AD). Antiepileptic drugs seem to prevent the recurrence of epileptic seizures in most people with AD. There are pharmacological and non-pharmacological treatments for epilepsy in people with AD. There are no current systematic reviews to evaluate the efficacy and tolerability of the treatment. This review aims to review those different modalities. Objectives: To assess the efficacy and tolerability of the treatment of epilepsy for people with Alzheimer's disease (AD) (including sporadic AD and dominantly inherited AD). Search methods: We searched the Cochrane Epilepsy Group Specialized Register (1 February 2016), the Cochrane Central Register of Controlled Trials (1 February 2016), MEDLINE (Ovid, 1 February 2016) and ClinicalTrials.gov (1 February 2016). In an effort to identify further published, unpublished and ongoing trials, we searched ongoing trials' registers, reference lists and relevant conference proceedings, and contacted authors and pharmaceutical companies. Selection criteria: We included randomised and quasi-randomised controlled trials investigating treatment for epilepsy in people with AD, with the outcomes of proportion of seizure freedom or experiencing adverse events. Data collection and analysis: Two review authors independently screened the titles and abstracts of identified records, selected studies for inclusion, extracted data, cross-checked the data for accuracy and assessed the methodological quality. We performed no meta-analyses due to the limited available data. Main results: We included one randomised controlled trial with 95 participants. Concerning the proportion of participants with seizure freedom, no significant differences were found in levetiracetam (LEV) versus lamotrigine (LTG) (risk ratio (RR) 1.20, 95% confidence interval (CI) 0.53 to 2.71), in levetiracetam versus phenobarbital (PB) (RR 1.01, 95% CI 0.47 to 2.19), or in LTG versus PB (RR 0.84, 95% CI 0.35 to 2.02). It seemed that LEV could improve cognition and LTG could relieve depression; while PB and LTG could worsen cognition, and LEV and PB could worsen mood. We judged the quality of the evidence to be very low. Authors' conclusions: This review does not provide sufficient evidence to support LEV, PB and LTG for the treatment of epilepsy in people with AD. Regarding the efficacy and tolerability, no significant differences were found between LEV, PB and LTG. In the future, large randomised, double-blind, controlled, parallel-group clinical trials are required to determine the efficacy and tolerability of treatment for epilepsy in people with AD.

Maayan N, Soares-Weiser K, Lee H. Respite care for people with dementia and their carers. Cochrane Database of Systematic Reviews. 2014; 1. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004396.pub3/abstract>

Background: Caring for someone with dementia can be emotionally and physically demanding. Respite care is any intervention designed to give rest or relief to caregivers. It is not clear what positive and negative effects such care may have on them, or on people with dementia. Objectives: To assess the benefits and harms of respite care for people with dementia and their caregivers, in particular the effect of respite care on rates of institutionalisation. Search methods: The trials were identified from a search of ALOIS, the Specialized Register of the Cochrane Dementia and Cognitive Improvement Group, using the terms respite\* OR daycare OR caregiver\* relief. ALOIS contains up-to-date records from all major healthcare databases and many ongoing trial databases. Selection criteria: Randomised controlled trials comparing respite care with a control intervention for people with dementia. Data collection and analysis: Two review authors carried out study selection independently and reached a consensus through discussion. Data were extracted by a single review author. The review authors contacted all investigators for methodological details not reported in the text and for additional data for three studies included in the previous version of the review. Main results: Four trials are now included in the review, with 753 participants. They were different in many ways including the intervention, duration, outcomes and control group so pooling of data was not possible. Overall, the quality of the evidence was rated as very low. Re-analysis of outcomes using data from the published studies found no significant effects of respite care compared to no respite care on any caregiver variable. When respite care was compared to polarity therapy a significant effect was found in favour of polarity therapy for caregiver perceived stress (n = 38, MD 5.80, 95% CI 1.43 to 10.17), but not for other measures of psychological health and other caregiver outcomes. No studies reported evaluable data on outcomes related to the people with dementia. Authors' conclusions: Current evidence does not demonstrate any benefits or adverse effects from the use of respite care for people with dementia or their caregivers. These results should be treated with caution, however, as they may reflect the lack of high quality research in this area rather than an actual lack of benefit. Given the frequency with which respite care is advocated and provided, well-designed trials are needed in this area.

Martin Alan J, Marottoli R, O'Neill D. Driving assessment for maintaining mobility and safety in drivers with dementia. Cochrane Database of Systematic Reviews. 2013; 8. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006222.pub4/abstract>

Background: Demographic changes are leading to an increase in the number of older drivers: as dementia is an age-related disease, there is also an increase in the numbers of drivers with dementia. Dementia can impact on both the mobility and safety of drivers, and the impact of formal assessment of driving is unknown in terms of either mobility or safety. Those involved in assessment of older drivers need to be aware of the evidence of positive and negative effects of driving assessment. Cognitive tests are felt by some authors to have poor face and construct validity for assessing driving performance; extrapolating from values in one large-scale prospective cohort study, the cognitive test that most strongly predicted future crashes would, if used as a screening tool, potentially prevent six crashes per 1000 people over 65 years of age screened, but at the price of stopping the driving of 121 people who would not have had a crash. Objectives: Primary objectives: 1. to assess whether driving

assessment facilitates continued driving in people with dementia; 2. to assess whether driving assessment reduces accidents in people with dementia. Secondary objective: 1. to assess the quality of research on assessment of drivers with dementia. Search methods: ALOIS, the Cochrane Dementia Group's Specialized Register was searched on 13 September 2012 using the terms: driving or driver\* or "motor vehicle\*" or "car accident\*" or "traffic accident\*" or automobile\* or traffic. This register contains records from major healthcare databases, ongoing trial databases and grey literature sources and is updated regularly. Selection criteria: We sought randomised controlled trials prospectively evaluating drivers with dementia for outcomes such as transport mobility, driving cessation or motor vehicle accidents following driving assessment. Data collection and analysis: Each review author retrieved studies and assessed for primary and secondary outcomes, study design and study quality. Main results: No studies were found that met the inclusion criteria. A description and discussion of the driving literature relating to assessment of drivers with dementia relating to the primary objectives is presented. Authors' conclusions: In an area with considerable public health impact for drivers with dementia and other road users, the available literature fails to demonstrate the benefit of driver assessment for either preserving transport mobility or reducing motor vehicle accidents. Driving legislation and recommendations from medical practitioners requires further research that addresses these outcomes in order to provide the best outcomes for both drivers with dementia and the general public.

McCleery J, Cohen Daniel A, Sharpley Ann L. Pharmacotherapies for sleep disturbances in dementia. Cochrane Database of Systematic Reviews. 2016; 11. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009178.pub3/abstract>

Background: Sleep disturbances, including reduced nocturnal sleep time, sleep fragmentation, nocturnal wandering, and daytime sleepiness are common clinical problems in dementia, and are associated with significant caregiver distress, increased healthcare costs, and institutionalisation. Drug treatment is often sought to alleviate these problems, but there is significant uncertainty about the efficacy and adverse effects of the various hypnotic drugs in this vulnerable population. Objectives: To assess the effects, including common adverse effects, of any drug treatment versus placebo for sleep disorders in people with dementia, through identification and analysis of all relevant randomised controlled trials (RCTs). Search methods: We searched ALOIS ([www.medicine.ox.ac.uk/alois](http://www.medicine.ox.ac.uk/alois)), the Cochrane Dementia and Cognitive Improvement Group's Specialized Register, in March 2013 and again in March 2016, using the terms: sleep, insomnia, circadian, hypersomnia, parasomnia, somnolence, rest-activity, sundowning. Selection criteria: We included RCTs that compared a drug with placebo, and that had the primary aim of improving sleep in people with dementia who had an identified sleep disturbance at baseline. Trials could also include non-pharmacological interventions, as long as both drug and placebo groups had the same exposure to them. Data collection and analysis: Two review authors independently extracted data on study design, risk of bias, and results from the included study reports. We obtained additional information from study authors where necessary. We used the mean difference as the measure of treatment effect, and where possible, synthesized results using a fixed-effect model. Main results: We found six RCTs eligible for inclusion for three drugs: melatonin (222 participants, four studies, but only two yielded data on our primary sleep outcomes suitable for meta-analysis), trazodone (30 participants, one study), and ramelteon (74 participants, one study, no peer-reviewed publication, limited information available). The participants in the trazodone study and almost all participants in the melatonin studies had moderate-to-severe dementia due to Alzheimer's disease (AD); those in the ramelteon study had mild-to-moderate AD. Participants had a variety of common sleep problems at baseline. All primary sleep outcomes were measured using actigraphy. In one study of melatonin, drug treatment was combined with morning bright light therapy. Only two studies made a systematic assessment of adverse effects. Overall, the evidence was at low risk of bias, although there were areas of incomplete reporting, some problems with participant attrition, related largely to poor tolerance of actigraphy and technical difficulties, and a high risk of selective reporting in one trial that contributed very few participants. The risk of bias in the ramelteon study was unclear due to incomplete reporting. We found no evidence that melatonin, at doses up to 10 mg, improved any major sleep outcome over 8 to 10 weeks in patients with AD who were identified as having a sleep disturbance. We were able to synthesize data for two of our primary sleep outcomes: total nocturnal sleep time (mean difference (MD) 10.68 minutes, 95% CI -16.22 to 37.59; N = 184; two studies), and the ratio of daytime sleep to night-time sleep (MD -0.13, 95% CI -0.29 to 0.03; N = 184; two studies). From single studies, we found no difference between melatonin and placebo groups for sleep efficiency, time awake after sleep onset, or number of night-time awakenings. From two studies, we found no effect of melatonin on cognition or performance of activities of daily living (ADL). No serious adverse effects of melatonin were reported in the included studies. We considered this evidence to be of low quality. There was low-quality evidence that trazodone 50 mg given at night for two weeks improved total nocturnal sleep time (MD 42.46 minutes, 95% CI 0.9 to 84.0; N = 30; one study), and sleep efficiency (MD 8.53%, 95% CI 1.9 to 15.1; N = 30; one study) in patients with moderate-to-severe AD, but it did not affect the amount of time spent awake after sleep onset (MD -20.41, 95% CI -60.4 to 19.6; N = 30; one study), or the number of nocturnal awakenings (MD -3.71, 95% CI -8.2 to 0.8; N = 30; one study). No effect was seen on daytime sleep, cognition, or ADL. No serious adverse effects of trazodone were reported. Results from a phase 2 trial investigating ramelteon 8 mg administered at night were available in summary form in a sponsor's synopsis. Because the data were from a single, small study and reporting was incomplete, we considered this evidence to be of low quality in general terms. Ramelteon had no effect on total nocturnal sleep time at one week (primary outcome) or eight weeks (end of treatment) in patients with mild-to-moderate AD. The synopsis reported few significant differences from placebo for any sleep, behavioural, or

cognitive outcomes; none were likely to be of clinical significance. There were no serious adverse effects from ramelteon. Authors' conclusions: We discovered a distinct lack of evidence to help guide drug treatment of sleep problems in dementia. In particular, we found no RCTs of many drugs that are widely prescribed for sleep problems in dementia, including the benzodiazepine and non-benzodiazepine hypnotics, although there is considerable uncertainty about the balance of benefits and risks associated with these common treatments. From the studies we identified for this review, we found no evidence that melatonin (up to 10mg) helped sleep problems in patients with moderate to severe dementia due to AD. There was some evidence to support the use of a low dose (50 mg) of trazodone, although a larger trial is needed to allow a more definitive conclusion to be reached on the balance of risks and benefits. There was no evidence of any effect of ramelteon on sleep in patients with mild to moderate dementia due to AD. This is an area with a high need for pragmatic trials, particularly of those drugs that are in common clinical use for sleep problems in dementia. Systematic assessment of adverse effects is essential.

McCleery J, Morgan S, Bradley Kevin M, Noel-Storr Anna H, Ansorge O, Hyde C. Dopamine transporter imaging for the diagnosis of dementia with Lewy bodies. *Cochrane Database of Systematic Reviews*. 2015; 1. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010633.pub2/abstract>

**Background:** Dementia with Lewy bodies (DLB) is a common cause of neurodegenerative dementia of old age. Its accurate recognition can be important in clinical management and is essential for the development of disease-modifying treatments. The current clinical diagnostic criteria are limited particularly by relatively poor sensitivity. Dopamine transporter (DAT) imaging using single-photon emission computed tomography (SPECT) is the most highly developed supplementary test for DLB, and is now incorporated as a suggestive feature in the consensus diagnostic criteria. However, there is uncertainty about its accuracy and its place in clinical practice. It is most commonly used in people who are already suspected of having DLB. **Objectives:** We had two objectives in this review: (A) to estimate the accuracy of DAT imaging for the diagnosis of DLB in people with dementia in secondary care (specialist dementia services), and (B) to estimate the accuracy of DAT imaging for the diagnosis of DLB in people with dementia in secondary care who are already suspected of having DLB on the basis of a prior clinical work-up. **Search methods:** We searched MEDLINE (1946 to February 2013), Embase (1980 to February 2013), BIOSIS Previews (1926 to February 2013), PsycINFO (1806 to February 2013), CINAHL (1982 to February 2013), LILACS (February 2013) and Web of Science and Conference Proceedings (ISI Web of Science) (1945 to February 2013). Several of these sources contain conference abstracts. We also searched four specialised databases containing diagnostic reviews: Meta-analyses van Diagnostisch Onderzoek (MEDION; February 2013), Database of Abstracts of Reviews of Effects (DARE; February 2013), Health Technology Assessment Database (HTA; February 2013), and Aggressive Research Intelligence Facility (ARIF; February 2013). We checked reference lists of relevant studies and reviews for potential additional studies. Terms for electronic database searching were devised in conjunction with the team at the Cochrane Dementia and Cognitive Improvement Group. **Selection criteria:** Study design: We included test accuracy studies with delayed verification, diagnostic case-control studies, and two-gate studies with alternative diagnosis controls. Participants: (A) participants with dementia in secondary care, (B) participants in secondary care meeting consensus clinical criteria (other than the DAT imaging criterion) for possible or probable DLB, or both. Index test: SPECT or positron emission tomography (PET) imaging of brain dopamine transporters. Reference standard: Neuropathological diagnosis at autopsy. **Data collection and analysis:** Two review authors independently selected studies for inclusion and extracted data. We extracted results into a 2x2 table, showing the binary test results cross-classified with the binary reference standard. We used this data to calculate sensitivities, specificities, and their 95% confidence intervals. We used the QUADAS-2 tool plus some additional items to assess methodological quality. **Main results:** We included one study that was applicable to our first objective (A). It reported data on 22 participants who met consensus clinical criteria for DLB or National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria for Alzheimer's disease, or both (a two-gate design with alternative diagnosis controls). The index test was SPECT scanning using the ligand 123I-FP-CIT. We considered the study to be at high risk of bias in the participant selection and index test domains (QUADAS-2). 123I-FP-CIT SPECT analysed semiquantitatively had a sensitivity of 1.00 (95% confidence interval (CI) 0.66 to 1.00) and a specificity of 0.92 (95% CI 0.64 to 1.00) for the diagnosis of DLB (n = 22, 1 study). Analysed visually, the sensitivity was 0.86 (95% CI 0.42 to 1.00) and the specificity was 0.83 (95% CI 0.52 to 0.98) (n = 19, 1 study). We considered that the study also provided the best available data to address our second objective (B). At baseline, 1 participants were clinically suspected of having DLB. In this group, 123I-FP-CIT SPECT scanning analysed semiquantitatively had a sensitivity of 1.00 (95% CI 0.63 to 1.00) and a specificity of 1.00 (95% CI 0.59 to 1.00) for the diagnosis of DLB (n = 15, 1 study). Analysed visually, accuracy in this group was lower with a sensitivity of 0.83 (95% CI 0.36 to 1.00) and a specificity of 0.71 (95% CI 0.29 to 0.96) (n = 13, 1 study). **Authors' conclusions:** Only one study has used a neuropathological reference standard to assess the accuracy of DAT imaging for the diagnosis of DLB. The small size of the included study means that sensitivity and specificity estimates are imprecise. However, data from this study suggest that DAT imaging is more accurate than clinical diagnosis. Clinical diagnosis is therefore unsuitable to use as a reference standard for assessing the accuracy of DAT imaging. No studies using a neuropathological reference standard have directly addressed the common clinical scenario where the use of DAT imaging is considered as a diagnostic test in a person with possible DLB, or assessed the accuracy of DAT imaging in people with mild dementia. However, the data from the included study suggest that, where there is moderately severe dementia and a strong pre-existing suspicion of DLB (probable

DLB), then a normal (123I)-FP-CIT SPECT scan may be an accurate means of excluding the diagnosis. Semiquantitative ratings of 123I-FP-CIT SPECT scans appeared to be more accurate than visual ratings in all analyses.

McGuinness B, Cardwell Chris R, Passmore P. Statin withdrawal in people with dementia. *Cochrane Database of Systematic Reviews*. 2016; 9. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD012050.pub2/abstract>

**Background:** There are approximately 24 million people worldwide with dementia; this is likely to increase to 81 million by 2040. Dementia is a progressive condition, and usually leads to death eight to ten years after first symptoms. End-of-life care should emphasise treatments that optimise quality of life and physicians should minimise unnecessary or non-beneficial interventions. Statins are 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors; they have become the cornerstone of pharmacotherapy for the management of hypercholesterolaemia but their ability to provide benefit is unclear in the last weeks or months of life. Withdrawal of statins may improve quality of life in people with advanced dementia, as they will not be subjected to unnecessary polypharmacy or side effects. However, they may help to prevent further vascular events in people of advanced age who are at high risk of such events. **Objectives:** To evaluate the effects of withdrawal or continuation of statins in people with dementia on: cognitive outcomes, adverse events, behavioural and functional outcomes, mortality, quality of life, vascular morbidity, and healthcare costs. **Search methods:** We searched ALOIS ([medicine.ox.ac.uk/alois/](http://medicine.ox.ac.uk/alois/)), the Cochrane Dementia and Cognitive Improvement Group Specialised Register on 11 February 2016. We also ran additional searches in MEDLINE, EMBASE, PsycINFO, CINAHL, Clinical.Trials.gov and the WHO Portal/ICTRP on 11 February 2016, to ensure that the searches were as comprehensive and as up-to-date as possible. **Selection criteria:** We included all randomised, controlled clinical trials with either a placebo or 'no treatment' control group. We applied no language restrictions. **Data collection and analysis:** Two review authors independently assessed whether potentially relevant studies met the inclusion criteria, using standard methodological procedures expected by Cochrane. We found no studies suitable for inclusion therefore analysed no data. **Main results:** The search strategy identified 28 unique references, all of which were excluded. **Authors' conclusions:** We found no evidence to enable us to make an informed decision about statin withdrawal in dementia. Randomised controlled studies need to be conducted to assess cognitive and other effects of statins in participants with dementia, especially when the disease is advanced.

McGuinness B, Craig D, Bullock R, Malouf R, Passmore P. Statins for the treatment of dementia. *Cochrane Database of Systematic Reviews*. 2014; 7. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD007514.pub3/abstract>

**Background:** The use of statin therapy in established Alzheimer's disease (AD) or vascular dementia (VaD) is a relatively unexplored area. In AD,  $\beta$ -amyloid protein (A $\beta$ ) is deposited in the form of extracellular plaques and previous studies have determined A $\beta$  generation is cholesterol dependent. Hypercholesterolaemia has also been implicated in the pathogenesis of VaD. Due to the role of statins in cholesterol reduction, it is biologically plausible they may be efficacious in the treatment of AD and VaD. **Objectives:** To assess the clinical efficacy and safety of statins in the treatment of AD and VaD. To evaluate if the efficacy of statins in the treatment of AD and VaD depends on cholesterol level, ApoE genotype or cognitive level. **Search methods:** We searched ALOIS, the Specialized Register of the Cochrane Dementia and Cognitive Improvement Group, The Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL and LILACS, as well as many trials registries and grey literature sources (20 January 2014). **Selection criteria:** Double-blind, randomised controlled trials of statins given for at least six months in people with a diagnosis of dementia. **Data collection and analysis:** Two independent authors extracted and assessed data against the inclusion criteria. We pooled data where appropriate and entered them into a meta-analysis. We used standard methodological procedures expected by The Cochrane Collaboration. **Main results:** We identified four studies (1154 participants, age range 50 to 90 years). All participants had a diagnosis of probable or possible AD according to standard criteria and most participants were established on a cholinesterase inhibitor. The primary outcome in all studies was change in Alzheimer's Disease Assessment Scale - cognitive subscale (ADAS-Cog) from baseline. When we pooled data, there was no significant benefit from statin (mean difference -0.26, 95% confidence interval (CI) -1.05 to 0.52, P value = 0.51). All studies provided change in Mini Mental State Examination (MMSE) from baseline. There was no significant benefit from statins in MMSE when we pooled the data (mean difference -0.32, 95% CI -0.71 to 0.06, P value = 0.10). Three studies reported treatment-related adverse effects. When we pooled data, there was no significant difference between statins and placebo (odds ratio 1.09, 95% CI 0.58 to 2.06, P value = 0.78). There was no significant difference in behaviour, global function or activities of daily living in the statin and placebo groups. We assessed risk of bias as low for all studies. We found no studies assessing role of statins in treatment of VaD. **Authors' conclusions:** Analyses from the studies available, including two large randomised controlled trials, indicate that statins have no benefit on the primary outcome measures of ADAS-Cog or MMSE.

McGuinness B, Craig D, Bullock R, Passmore P. Statins for the prevention of dementia. *Cochrane Database of Systematic Reviews*. 2016; 1. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003160.pub3/abstract>

**Background:** This is an update of a Cochrane review first published in 2001 and then updated in 2009.



Vascular risk factors including high cholesterol levels increase the risk of dementia due to Alzheimer's disease and of vascular dementia. Some observational studies have suggested an association between statin use and lowered incidence of dementia. Objectives: To evaluate the efficacy and safety of statins for the prevention of dementia in people at risk of dementia due to their age and to determine whether the efficacy and safety of statins for this purpose depends on cholesterol level, apolipoprotein E (ApoE) genotype or cognitive level. Search methods: We searched ALOIS (the Specialized Register of the Cochrane Dementia and Cognitive Improvement Group), The Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL, LILACS, ClinicalTrials.gov and the World Health Organization (WHO) Portal on 11 November 2015. Selection criteria: We included double-blind, randomised, placebo-controlled trials in which statins were administered for at least 12 months to people at risk of dementia. Data collection and analysis: We used standard methodological procedures expected by Cochrane. Main results: We included two trials with 26,340 participants aged 40 to 82 years of whom 11,610 were aged 70 or older. All participants had a history of, or risk factors for, vascular disease. The studies used different statins (simvastatin and pravastatin). Mean follow-up was 3.2 years in one study and five years in one study. The risk of bias was low. Only one study reported on the incidence of dementia (20,536 participants, 31 cases in each group; odds ratio (OR) 1.00, 95% confidence interval (CI) 0.61 to 1.65, moderate quality evidence, downgraded due to imprecision). Both studies assessed cognitive function, but at different times using different scales, so we judged the results unsuitable for a meta-analysis. There were no differences between statin and placebo groups on five different cognitive tests (high quality evidence). Rates of treatment discontinuation due to non-fatal adverse events were less than 5% in both studies and there was no difference between statin and placebo groups in the risk of withdrawal due to adverse events (26,340 participants, 2 studies, OR 0.94, 95% CI 0.83 to 1.05). Authors' conclusions: There is good evidence that statins given in late life to people at risk of vascular disease do not prevent cognitive decline or dementia. Biologically, it seems feasible that statins could prevent dementia due to their role in cholesterol reduction and initial evidence from observational studies was very promising. However, indication bias may have been a factor in these studies and the evidence from subsequent RCTs has been negative. There were limitations in the included studies involving the cognitive assessments used and the inclusion of participants at moderate to high vascular risk only.

Moniz Cook Esme D, Swift K, James I, Malouf R, De Vugt M, Verhey F. Functional analysis-based interventions for challenging behaviour in dementia. *Cochrane Database of Systematic Reviews*. 2012; 2. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006929.pub2/abstract>

Background: Functional analysis (FA) for the management of challenging behaviour is a promising behavioural intervention that involves exploring the meaning or purpose of an individual's behaviour. It extends the ABC approach of behavioural analysis, to overcome the restriction of having to derive a single explanatory hypothesis for the person's behaviour. It is seen as a first line alternative to traditional pharmacological management for agitation and aggression. FA typically requires the therapist to develop and evaluate hypotheses-driven strategies that aid family and staff caregivers to reduce or resolve a person's distress and its associated behavioural manifestations. Objectives: To assess the effects of functional analysis-based interventions for people with dementia (and their caregivers) living in their own home or in other settings. Search methods: We searched ALOIS: the Cochrane Dementia and Cognitive Improvement Group's Specialized Register on 3 March 2011 using the terms: FA, behaviour (intervention, management, modification), BPSD, psychosocial and Dementia. Selection criteria: Randomised controlled trials (RCTs) with reported behavioural outcomes that could be associated with functional analysis for the management of challenging behaviour in dementia. Data collection and analysis: Four reviewers selected trials for inclusion. Two reviewers worked independently to extract data and assess trial quality, including bias. Meta-analyses for reported incidence, frequency, severity of care recipient challenging behaviour and mood (primary outcomes) and caregiver reaction, burden and mood were performed. Details of adverse effects were noted. Main results: Eighteen trials are included in the review. The majority were in family care settings. For fourteen studies, FA was just one aspect of a broad multi-component programme of care. Assessing the effect of FA was compromised by ill-defined protocols for the duration of component parts of these programmes (i.e. frequency of the intervention or actual time spent). Therefore, establishing the real effect of the FA component was not possible. Overall, positive effects were noted at post-intervention for the frequency of reported challenging behaviour (but not for incidence or severity) and for caregiver reaction (but not burden or depression). These effects were not seen at follow-up. Authors' conclusions: The delivery of FA has been incorporated within wide ranging multi-component programmes and study designs have varied according to setting - i.e. family care, care homes and hospital, with surprisingly few studies located in care homes. Our findings suggest potential beneficial effects of multi-component interventions, which utilise FA. Whilst functional analysis for challenging behaviour in dementia care shows promise, it is too early to draw conclusions about its efficacy.

Murphy E, Froggatt K, Connolly S, O'Shea E, Sampson Elizabeth L, Casey D, et al. Palliative care interventions in advanced dementia. *Cochrane Database of Systematic Reviews*. 2016; 12. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011513.pub2/abstract>

Background: Dementia is a chronic, progressive and ultimately fatal neurodegenerative disease. Advanced dementia is characterised by profound cognitive impairment, inability to communicate verbally and complete functional dependence. Usual care of people with advanced dementia is not underpinned universally by a palliative approach. Palliative care has focused traditionally on care of people with cancer but for more than a decade, there

have been increased calls worldwide to extend palliative care services to include all people with life-limiting illnesses in need of specialist care, including people with dementia. Objectives: To assess the effect of palliative care interventions in advanced dementia and to report on the range of outcome measures used. Search methods: We searched ALOIS, the Cochrane Dementia and Cognitive Improvement Group's Specialized Register on 4 February 2016. ALOIS contains records of clinical trials identified from monthly searches of several major healthcare databases, trial registries and grey literature sources. We ran additional searches across MEDLINE (OvidSP), Embase (OvidSP), PsycINFO (OvidSP), CINAHL (EBSCOhost), LILACS (BIREME), Web of Science Core Collection (ISI Web of Science), ClinicalTrials.gov and the World Health Organization ICTRP trial portal to ensure that the searches were as comprehensive and as up-to-date as possible. Selection criteria: We searched for randomised (RCT) and non-randomised controlled trials (nRCT), controlled before-and-after studies (CBA) and interrupted time series studies evaluating the impact of palliative care interventions for adults with dementia of any type, staged as advanced dementia by a recognised and validated tool. Participants could be people with advanced dementia, their family members, clinicians or paid care staff. We included clinical interventions and non-clinical interventions. Comparators were usual care or another palliative care intervention. We did not exclude studies on the basis of outcomes measured and recorded all outcomes measured in included studies. Data collection and analysis: Two review authors independently assessed for inclusion all the potential studies we identified as a result of the search strategy. We resolved any disagreement through discussion or, when required, consulted with the rest of the review team. We independently extracted data and conducted assessment of methodological quality, using standard Cochrane methods. Main results: We identified two studies of palliative care interventions for people with advanced dementia. We did not pool data due to the heterogeneity between the two trials in terms of the interventions and the settings. The two studies measured 31 different outcomes, yet they did not measure the same outcome. There are six ongoing studies that we expect to include in future versions of this review. Both studies were at high risk of bias, in part because blinding was not possible. This and small sample sizes meant that the overall certainty of all the evidence was very low. One individually randomised RCT (99 participants) evaluated the effect of a palliative care team for people with advanced dementia hospitalised for an acute illness. While this trial reported that a palliative care plan was more likely to be developed for participants in the intervention group (risk ratio (RR) 5.84, 95% confidence interval (CI) 1.37 to 25.02), the plan was only adopted for two participants, both in the intervention group, while in hospital. The palliative care plan was more likely to be available on discharge in the intervention group (RR 4.50, 95% CI 1.03 to 19.75). We found no evidence that the intervention affected mortality in hospital (RR 1.06, 95% CI 0.53 to 2.13), decisions to forgo cardiopulmonary resuscitation in hospital or the clinical care provided during hospital admission, but for the latter, event rates were low and the results were associated with a lot of uncertainty. One cluster RCT (256 participants, each enrolled with a family carer) evaluated the effect of a decision aid on end-of-life feeding options on surrogate decision-makers of nursing home residents with advanced dementia. Data for 90 participants (35% of the original study) met the definition of advanced dementia for this review and were re-analysed for the purposes of the review. In this subset, intervention surrogates had lower scores for decisional conflict measured on the Decisional Conflict Scale (mean difference -0.30, 95% CI -0.61 to 0.01, reduction of 0.3 to 0.4 units considered meaningful) and were more likely than participants in the control group to discuss feeding options with a clinician (RR 1.57, 95% CI 0.93 to 2.64), but imprecision meant that there was significant uncertainty about both results. Authors' conclusions: Very little high quality work has been completed exploring palliative care interventions in advanced dementia. There were only two included studies in this review, with variation in the interventions and in the settings that made it impossible to conduct a meta-analysis of data for any outcome. Thus, we conclude that there is insufficient evidence to assess the effect of palliative care interventions in advanced dementia. The fact that there are six ongoing studies at the time of this review indicates an increased interest in this area by researchers, which is welcome and needed.

Orgeta V, Qazi A, Spector Aimee E, Orrell M. Psychological treatments for depression and anxiety in dementia and mild cognitive impairment. *Cochrane Database of Systematic Reviews*. 2014; 1. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009125.pub2/abstract>

Background: Experiencing anxiety and depression is very common in people with dementia and mild cognitive impairment (MCI). Psychological interventions have been suggested as a potential treatment for these populations. Current research suggests that people with dementia and MCI have limited opportunities for psychological treatments aimed at improving their well-being. A systematic review of the evidence on their effectiveness is likely to be useful in terms of improving outcomes for patients and for future recommendations for practice. Objectives: The main objective of this review was to assess the effectiveness of psychological interventions in reducing anxiety and depression in people with dementia or mild cognitive impairment (MCI). Search methods: We searched the Cochrane Dementia and Cognitive Improvement Group Specialized Register and additional sources for both published and unpublished data. Selection criteria: We included randomised controlled trials (RCTs) comparing a psychological intervention with usual care or a placebo intervention (social contact control) in people with dementia or MCI. Data collection and analysis: Two review authors worked independently to select trials, extract data and assess studies for risk of bias, using a data extraction form. We contacted authors when further information was not available from the published articles. Main results: Six RCTs involving 439 participants with dementia were included in the review, but no studies of participants with MCI were identified. The studies included people with dementia living in the community or in nursing home care and were carried out in several countries. Only one of the studies was classified as low risk of

bias. Five studies were at unclear or high risk of bias due to uncertainties around randomisation, blinding and selective reporting of results. The studies used the different psychological approaches of cognitive behavioural therapy (CBT), interpersonal therapy and counselling. Two studies were of multimodal interventions including a specific psychological therapy. The comparison groups received either usual care, attention-control educational programs, diagnostic feedback or services slightly above usual care. Meta-analysis showed a positive effect of psychological treatments on depression (6 trials, 439 participants, standardised mean difference (SMD) -0.22; 95% confidence interval (CI) -0.41 to -0.03, moderate quality evidence) and on clinician-rated anxiety (2 trials, 65 participants, mean difference (MD) -4.57; 95% CI -7.81 to -1.32, low quality evidence), but not on self-rated anxiety (2 trials, SMD 0.05; 95% CI -0.44 to 0.54) or carer-rated anxiety (1 trial, MD -2.40; 95% CI -4.96 to 0.16). Results were compatible with both benefit and harm on the secondary outcomes of patient quality of life, activities of daily living (ADLs), neuropsychiatric symptoms and cognition, or on carers' self-rated depressive symptoms, but most of the studies did not measure these outcomes. There were no reports of adverse events. Authors' conclusions: We found evidence that psychological interventions added to usual care can reduce symptoms of depression and clinician-rated anxiety for people with dementia. We conclude that psychological interventions have the potential to improve patient well-being. Further high quality studies are needed to investigate which treatments are most effective and to evaluate the effect of psychological interventions in people with MCI.

Quinn Terry J, Fearon P, Noel-Storr Anna H, Young C, McShane R, Stott David J. Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) for the diagnosis of dementia within community dwelling populations. *Cochrane Database of Systematic Reviews*. 2014; 4. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010079.pub2/abstract>

**Background:** Various tools exist for initial assessment of possible dementia with no consensus on the optimal assessment method. Instruments that use collateral sources to assess change in cognitive function over time may have particular utility. The most commonly used informant dementia assessment is the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE). A synthesis of the available data regarding IQCODE accuracy will help inform cognitive assessment strategies for clinical practice, research and policy. **Objectives:** Our primary objective was to determine the diagnostic accuracy of the informant based questionnaire IQCODE, for detection of all cause (undifferentiated) dementia in community-dwelling adults with no previous cognitive assessment. We sought to describe the accuracy of IQCODE (the index test) against a clinical diagnosis of dementia (the reference standard). Our secondary objective was to describe the effect of heterogeneity on the summary estimates. We were particularly interested in the traditional 26-item scale versus the 16-item short form; and language of administration. We explored the effect of varying the threshold IQCODE score used to define 'test positivity'. **Search methods:** We searched the following sources on 28 January 2013: ALOIS (Cochrane Dementia and Cognitive Improvement Group), MEDLINE (OvidSP), EMBASE (OvidSP), PsycINFO (OvidSP), BIOSIS Previews (ISI Web of Knowledge), Web of Science with Conference Proceedings (ISI Web of Knowledge), LILACS (BIREME). We also searched sources relevant or specific to diagnostic test accuracy: MEDION (Universities of Maastricht and Leuven); DARE (York University); ARIF (Birmingham University). We used sensitive search terms based on MeSH terms and other controlled vocabulary. **Selection criteria:** We selected those studies performed in community settings that used (not necessarily exclusively) the IQCODE to assess for presence of dementia and, where dementia diagnosis was confirmed, with clinical assessment. Our intention with limiting the search to a 'community' setting was to include those studies closest to population level assessment. Within our predefined community inclusion criteria, there were relevant papers that fulfilled our definition of community dwelling but represented a selected population, for example stroke survivors. We included these studies but performed sensitivity analyses to assess the effects of these less representative populations on the summary results. **Data collection and analysis:** We screened all titles generated by the electronic database searches and abstracts of all potentially relevant studies were reviewed. Full papers were assessed for eligibility and data extracted by two independent assessors. For quality assessment (risk of bias and applicability) we used the QUADAS 2 tool. We included test accuracy data on the IQCODE used at predefined diagnostic thresholds. Where data allowed, we performed meta-analyses to calculate summary values of sensitivity and specificity with corresponding 95% confidence intervals (CIs). We pre-specified analyses to describe the effect of IQCODE format (traditional or short form) and language of administration for the IQCODE. **Main results:** From 16,144 citations, 71 papers described IQCODE test accuracy. We included 10 papers (11 independent datasets) representing data from 2644 individuals ( $n = 379$  (14%) with dementia). Using IQCODE cut-offs commonly employed in clinical practice (3.3, 3.4, 3.5, 3.6) the sensitivity and specificity of IQCODE for diagnosis of dementia across the studies were generally above 75%. Taking an IQCODE threshold of 3.3 (or closest available) the sensitivity was 0.80 (95% CI 0.75 to 0.85); specificity was 0.84 (95% CI 0.78 to 0.90); positive likelihood ratio was 5.2 (95% CI 3.7 to 7.5) and the negative likelihood ratio was 0.23 (95% CI 0.19 to 0.29). Comparative analysis suggested no significant difference in the test accuracy of the 16 and 26-item IQCODE tests and no significant difference in test accuracy by language of administration. There was little difference in sensitivity across our predefined diagnostic cut-points. There was substantial heterogeneity in the included studies. Sensitivity analyses removing potentially unrepresentative populations in these studies made little difference to the pooled data estimates. The majority of included papers had potential for bias, particularly around participant selection and sampling. The quality of reporting was suboptimal particularly regarding timing of assessments and descriptors of reproducibility and inter-observer variability. **Authors' conclusions:** Published data suggest that if using the IQCODE for community dwelling older adults, the 16 item

IQCODE may be preferable to the traditional scale due to lesser test burden and no obvious difference in accuracy. Although IQCODE test accuracy is in a range that many would consider 'reasonable', in the context of community or population settings the use of the IQCODE alone would result in substantial misdiagnosis and false reassurance. Across the included studies there were issues with heterogeneity, several potential biases and suboptimal reporting quality.

Reilly S, Miranda-Castillo C, Malouf R, Hoe J, Toot S, Challis D, et al. Case management approaches to home support for people with dementia. *Cochrane Database of Systematic Reviews*. 2015; 1. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008345.pub2/abstract>

**Background:** Over 35 million people are estimated to be living with dementia in the world and the societal costs are very high. Case management is a widely used and strongly promoted complex intervention for organising and co-ordinating care at the level of the individual, with the aim of providing long-term care for people with dementia in the community as an alternative to early admission to a care home or hospital. **Objectives:** To evaluate the effectiveness of case management approaches to home support for people with dementia, from the perspective of the different people involved (patients, carers, and staff) compared with other forms of treatment, including ?treatment as usual?, standard community treatment and other non-case management interventions. **Search methods:** We searched the following databases up to 31 December 2013: ALOIS, the Specialised Register of the Cochrane Dementia and Cognitive Improvement Group, The Cochrane Library, MEDLINE, EMBASE, PsycINFO, CINAHL, LILACS, Web of Science (including Science Citation Index Expanded (SCI-EXPANDED) and Social Science Citation Index), Campbell Collaboration/SORO database and the Specialised Register of the Cochrane Effective Practice and Organisation of Care Group. We updated this search in March 2014 but results have not yet been incorporated. **Selection criteria:** We include randomised controlled trials (RCTs) of case management interventions for people with dementia living in the community and their carers. We screened interventions to ensure that they focused on planning and co-ordination of care. **Data collection and analysis:** We used standard methodological procedures as required by The Cochrane Collaboration. Two review authors independently extracted data and made 'Risk of bias' assessments using Cochrane criteria. For continuous outcomes, we used the mean difference (MD) or standardised mean difference (SMD) between groups along with its confidence interval (95% CI). We applied a fixed- or random-effects model as appropriate. For binary or dichotomous data, we generated the corresponding odds ratio (OR) with 95% CI. We assessed heterogeneity by the  $I^2$  statistic. **Main results:** We include 13 RCTs involving 9615 participants with dementia in the review. Case management interventions in studies varied. We found low to moderate overall risk of bias; 69% of studies were at high risk for performance bias. The case management group were significantly less likely to be institutionalised (admissions to residential or nursing homes) at six months (OR 0.82, 95% CI 0.69 to 0.98,  $n = 5741$ , 6 RCTs,  $I^2 = 0\%$ ,  $P = 0.02$ ) and at 18 months (OR 0.25, 95% CI 0.10 to 0.61,  $n = 363$ , 4 RCTs,  $I^2 = 0\%$ ,  $P = 0.003$ ). However, the effects at 10 - 12 months (OR 0.95, 95% CI 0.83 to 1.08,  $n = 5990$ , 9 RCTs,  $I^2 = 48\%$ ,  $P = 0.39$ ) and 24 months (OR 1.03, 95% CI 0.52 to 2.03,  $n = 201$ , 2 RCTs,  $I^2 = 0\%$ ,  $P = 0.94$ ) were uncertain. There was evidence from one trial of a reduction in the number of days per month in a residential home or hospital unit in the case management group at six months (MD -5.80, 95% CI -7.93 to -3.67,  $n = 88$ , 1 RCT,  $P < 0.0001$ ) and at 12 months (MD -7.70, 95% CI -9.38 to -6.02,  $n = 88$ , 1 RCT,  $P < 0.0001$ ). One trial reported the length of time until participants were institutionalised at 12 months and the effects were uncertain (hazard ratio (HR): 0.66, 95% CI 0.38 to 1.14,  $P = 0.14$ ). There was no difference in the number of people admitted to hospital at six (4 RCTs, 439 participants), 12 (5 RCTs, 585 participants) and 18 months (5 RCTs, 613 participants). For mortality at 4 - 6, 12, 18 - 24 and 36 months, and for participants' or carers' quality of life at 4, 6, 12 and 18 months, there were no significant effects. There was some evidence of benefits in carer burden at six months (SMD -0.07, 95% CI -0.12 to -0.01,  $n = 4601$ , 4 RCTs,  $I^2 = 26\%$ ,  $P = 0.03$ ) but the effects at 12 or 18 months were uncertain. Additionally, some evidence indicated case management was more effective at reducing behaviour disturbance at 18 months (SMD -0.35, 95% CI -0.63 to -0.07,  $n = 206$ , 2 RCTs,  $I^2 = 0\%$ ,  $P = 0.01$ ) but effects were uncertain at four (2 RCTs), six (4 RCTs) or 12 months (5 RCTs). The case management group showed a small significant improvement in carer depression at 18 months (SMD -0.08, 95% CI -0.16 to -0.01,  $n = 2888$ , 3 RCTs,  $I^2 = 0\%$ ,  $P = 0.03$ ). Conversely, the case management group showed greater improvement in carer well-being in a single study at six months (MD -2.20, 95% CI -4.14 to -0.26,  $n = 65$ , 1 RCT,  $P = 0.03$ ) but the effects were uncertain at 12 or 18 months. There was some evidence that case management reduced the total cost of services at 12 months (SMD -0.07, 95% CI -0.12 to -0.02,  $n = 5276$ , 2 RCTs,  $P = 0.01$ ) and incurred lower dollar expenditure for the total three years (MD -705.00, 95% CI -1170.31 to -239.69,  $n = 5170$ , 1 RCT,  $P = 0.003$ ). Data on a number of outcomes consistently indicated that the intervention group received significantly more community services. **Authors' conclusions:** There is some evidence that case management is beneficial at improving some outcomes at certain time points, both in the person with dementia and in their carer. However, there was considerable heterogeneity between the interventions, outcomes measured and time points across the 13 included RCTs. There was some evidence from good-quality studies to suggest that admissions to care homes and overall healthcare costs are reduced in the medium term; however, the results at longer points of follow-up were uncertain. There was not enough evidence to clearly assess whether case management could delay institutionalisation in care homes. There were uncertain results in patient depression, functional abilities and cognition. Further work should be undertaken to investigate what components of case management are associated with improvement in outcomes. Increased consistency in measures of outcome would support future meta-analysis.

Richter T, Meyer G, Möhler R, Köpke S. Psychosocial interventions for reducing antipsychotic medication in care home residents. *Cochrane Database of Systematic Reviews*. 2012; 12. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008634.pub2/abstract>

**Background:** Antipsychotic medication is regularly prescribed in care homes to control 'behavioural and psychological symptoms of dementia' despite moderate efficacy, significant adverse effects, and available non-pharmacological alternatives. **Objectives:** To evaluate the effectiveness of psychosocial interventions to reduce antipsychotic medication in care home residents. **Search methods:** The Cochrane Dementia and Cognitive Improvement Group's Specialized Register, MEDLINE, EMBASE, CINAHL, PsycINFO, LILACS, a number of trial registers and grey literature sources were searched on 19th December 2011. **Selection criteria:** Individual or cluster-randomised controlled trials comparing a psychosocial intervention aimed at reducing antipsychotic medication with usual care in care home residents or comparing two different approaches. **Data collection and analysis:** Two review authors independently assessed the retrieved articles for relevance and methodological quality and extracted data. **Critical appraisal of studies** addressed risk of bias through selection bias, performance bias, attrition bias, and detection bias, as well as criteria related to cluster design. **Authors of relevant studies** were contacted for additional information. **Owing to clinical heterogeneity of interventions, statistical heterogeneity was not assessed and no meta-analysis performed.** **Study results** are presented in a narrative form. **Main results:** Four cluster-randomised controlled studies met the inclusion criteria. All of them investigated complex interventions comprising educational approaches. Three studies offered education and training for nursing staff, one study offered multidisciplinary team meetings as main component of the intervention. There was one high-quality study, but overall the methodological quality of studies was moderate. The studies revealed consistent results for the primary end point. All studies documented a decrease of the proportion of residents with antipsychotic drug use or a reduction in days with antipsychotic use per 100 days per resident, respectively. **In summary, the reviewed evidence on psychosocial interventions targeting professionals is consistent with a reduction of antipsychotic medication prescription in care home residents. However, owing to heterogeneous approaches, summary effect sizes cannot be determined.** **Authors' conclusions:** There is evidence to support the effectiveness of psychosocial interventions for reducing antipsychotic medication in care home residents. However, the review was based on a small number of heterogeneous studies with important methodological shortcomings. The most recent and methodologically most rigorous study showed the most pronounced effect.

Ritchie C, Smailagic N, Noel-Storr Anna H, Takwoingi Y, Flicker L, Mason Sam E, et al. Plasma and cerebrospinal fluid amyloid beta for the diagnosis of Alzheimer's disease dementia and other dementias in people with mild cognitive impairment (MCI). *Cochrane Database of Systematic Reviews*. 2014; 6. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008782.pub4/abstract>

**Background:** According to the latest revised National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (now known as the Alzheimer's Association) (NINCDS-ADRDA) diagnostic criteria for Alzheimer's disease dementia of the National Institute on Aging and Alzheimer Association, the confidence in diagnosing mild cognitive impairment (MCI) due to Alzheimer's disease dementia is raised with the application of biomarkers based on measures in the cerebrospinal fluid (CSF) or imaging. These tests, added to core clinical criteria, might increase the sensitivity or specificity of a testing strategy. However, the accuracy of biomarkers in the diagnosis of Alzheimer's disease dementia and other dementias has not yet been systematically evaluated. A formal systematic evaluation of sensitivity, specificity, and other properties of plasma and CSF amyloid beta (A $\beta$ ) biomarkers was performed. **Objectives:** To determine the accuracy of plasma and CSF A $\beta$  levels for detecting those patients with MCI who would convert to Alzheimer's disease dementia or other forms of dementia over time. **Search methods:** The most recent search for this review was performed on 3 December 2012. We searched MEDLINE (OvidSP), EMBASE (OvidSP), BIOSIS Previews (ISI Web of Knowledge), Web of Science and Conference Proceedings (ISI Web of Knowledge), PsycINFO (OvidSP), and LILACS (BIREME). We also requested a search of the Cochrane Register of Diagnostic Test Accuracy Studies (managed by the Cochrane Renal Group). No language or date restrictions were applied to the electronic searches and methodological filters were not used so as to maximise sensitivity. **Selection criteria:** We selected those studies that had prospectively well defined cohorts with any accepted definition of cognitive decline, but no dementia, with baseline CSF or plasma A $\beta$  levels, or both, documented at or around the time the above diagnoses were made. We also included studies which looked at data from those cohorts retrospectively, and which contained sufficient data to construct two by two tables expressing plasma and CSF A $\beta$  biomarker results by disease status. Moreover, studies were only selected if they applied a reference standard for Alzheimer's dementia diagnosis, for example the NINCDS-ADRDA or Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria. **Data collection and analysis:** We screened all titles generated by the electronic database searches. Two review authors independently assessed the abstracts of all potentially relevant studies. We assessed the identified full papers for eligibility and extracted data to create standard two by two tables. Two independent assessors performed quality assessment using the QUADAS-2 tool. Where data allowed, we derived estimates of sensitivity at fixed values of specificity from the model we fitted to produce the summary receiver operating characteristic (ROC) curve. **Main results:** Alzheimer's disease dementia was evaluated in 14 studies using CSF A $\beta$ 42. Of the 1349 participants included in the meta-analysis, 436 developed Alzheimer's dementia. Individual study estimates of sensitivity were between 36% and 100% while the specificities were between 29% and 91%. Because of the variation in assay

thresholds, we did not estimate summary sensitivity and specificity. However, we derived estimates of sensitivity at fixed values of specificity from the model we fitted to produce the summary ROC curve. At the median specificity of 64%, the sensitivity was 81% (95% CI 72 to 87). This equated to a positive likelihood ratio (LR+) of 2.22 (95% CI 2.00 to 2.47) and a negative likelihood ratio (LR?) of 0.31 (95% CI 0.21 to 0.48). The accuracy of CSF A $\beta$ 42 for all forms of dementia was evaluated in four studies. Of the 464 participants examined, 188 developed a form of dementia (Alzheimer's disease and other forms of dementia). The thresholds used were between 209 mg/ml and 512 ng/ml. The sensitivities were between 56% and 75% while the specificities were between 47 and 76%. At the median specificity of 75%, the sensitivity was estimated to be 63% (95% CI 22 to 91) from the meta-analytic model. This equated to a LR+ of 2.51 (95% CI 1.30 to 4.86) and a LR? of 0.50 (95% CI 0.16 to 1.51). The accuracy of CSF A $\beta$ 42 for non-Alzheimer's disease dementia was evaluated in three studies. Of the 385 participants examined, 61 developed non-Alzheimer's disease dementia. Since there were very few studies and considerable variation between studies, the results were not meta-analysed. The sensitivities were between 8% and 63% while the specificities were between 35% and 67%. Only one study examined the accuracy of plasma A $\beta$ 42 and the plasma A $\beta$ 42/A $\beta$ 40 ratio for Alzheimer's disease dementia. The sensitivity of 86% (95% CI 81 to 90) was the same for both tests while the specificities were 50% (95% CI 44 to 55) and 70% (95% CI 64 to 75) for plasma A $\beta$ 42 and the plasma A $\beta$ 42/A $\beta$ 40 ratio respectively. Of the 565 participants examined, 245 developed Alzheimer's dementia and 87 non-Alzheimer's disease dementia. There was substantial heterogeneity between studies. The accuracy of A $\beta$ 42 for the diagnosis of Alzheimer's disease dementia did not differ significantly ( $P = 0.8$ ) between studies that pre-specified the threshold for determining test positivity ( $n = 6$ ) and those that only determined the threshold at follow-up ( $n = 8$ ). One study excluded a sample of MCI non-Alzheimer's disease dementia converters from their analysis. In sensitivity analyses, the exclusion of this study had no impact on our findings. The exclusion of eight studies (950 patients) that were considered at high ( $n = 3$ ) or unclear ( $n = 5$ ) risk of bias for the patient selection domain also made no difference to our findings. Authors' conclusions: The proposed diagnostic criteria for prodromal dementia and MCI due to Alzheimer's disease, although still being debated, would be fulfilled where there is both core clinical and cognitive criteria and a single biomarker abnormality. From our review, the measure of abnormally low CSF A $\beta$  levels has very little diagnostic benefit with likelihood ratios suggesting only marginal clinical utility. The quality of reports was also poor, and thresholds and length of follow-up were inconsistent. We conclude that when applied to a population of patients with MCI, CSF A $\beta$  levels cannot be recommended as an accurate test for Alzheimer's disease.

Ritchie C, Smailagic N, Noel-Storr Anna H, Ukoumunne O, Ladds Emma C, Martin S. CSF tau and the CSF tau/ABeta ratio for the diagnosis of Alzheimer's disease dementia and other dementias in people with mild cognitive impairment (MCI). *Cochrane Database of Systematic Reviews*. 2017; 3. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010803.pub2/abstract>

**Background:** Research suggests that measurable change in cerebrospinal fluid (CSF) biomarkers occurs years in advance of the onset of clinical symptoms (Beckett 2010). In this review, we aimed to assess the ability of CSF tau biomarkers (t-tau and p-tau) and the CSF tau (t-tau or p-tau)/ABeta ratio to enable the detection of Alzheimer's disease pathology in patients with mild cognitive impairment (MCI). These biomarkers have been proposed as important in new criteria for Alzheimer's disease dementia that incorporate biomarker abnormalities. **Objectives:** To determine the diagnostic accuracy of 1) CSF t-tau, 2) CSF p-tau, 3) the CSF t-tau/ABeta ratio and 4) the CSF p-tau/ABeta ratio index tests for detecting people with MCI at baseline who would clinically convert to Alzheimer's disease dementia or other forms of dementia at follow-up. **Search methods:** The most recent search for this review was performed in January 2013. We searched MEDLINE (OvidSP), Embase (OvidSP), BIOSIS Previews (Thomson Reuters Web of Science), Web of Science Core Collection, including Conference Proceedings Citation Index (Thomson Reuters Web of Science), PsycINFO (OvidSP), and LILACS (BIREME). We searched specialized sources of diagnostic test accuracy studies and reviews. We checked reference lists of relevant studies and reviews for additional studies. We contacted researchers for possible relevant but unpublished data. We did not apply any language or data restriction to the electronic searches. We did not use any methodological filters as a method to restrict the search overall. **Selection criteria:** We selected those studies that had prospectively well-defined cohorts with any accepted definition of MCI and with CSF t-tau or p-tau and CSF tau (t-tau or p-tau)/ABeta ratio values, documented at or around the time the MCI diagnosis was made. We also included studies which looked at data from those cohorts retrospectively, and which contained sufficient data to construct two by two tables expressing those biomarker results by disease status. Moreover, studies were only selected if they applied a reference standard for Alzheimer's disease dementia diagnosis, for example, the NINCDS-ADRDA or Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria. **Data collection and analysis:** We screened all titles generated by the electronic database searches. Two review authors independently assessed the abstracts of all potentially relevant studies, and the full papers for eligibility. Two independent assessors performed data extraction and quality assessment. Where data allowed, we derived estimates of sensitivity at fixed values of specificity from the model we fitted to produce the summary receiver operating characteristic (ROC) curve. **Main results:** In total, 1282 participants with MCI at baseline were identified in the 15 included studies of which 1172 had analysable data; 430 participants converted to Alzheimer's disease dementia and 130 participants to other forms of dementia. Follow-up ranged from less than one year to over four years for some participants, but in the majority of studies was in the range one to three years. Conversion to Alzheimer's disease dementia The accuracy of the CSF t-tau was evaluated in seven studies (291 cases and 418

non-cases). The sensitivity values ranged from 51% to 90% while the specificity values ranged from 48% to 88%. At the median specificity of 72%, the estimated sensitivity was 75% (95% CI 67 to 85), the positive likelihood ratio was 2.72 (95% CI 2.43 to 3.04), and the negative likelihood ratio was 0.32 (95% CI 0.22 to 0.47). Six studies (164 cases and 328 non-cases) evaluated the accuracy of the CSF p-tau. The sensitivities were between 40% and 100% while the specificities were between 22% and 86%. At the median specificity of 47.5%, the estimated sensitivity was 81% (95% CI: 64 to 91), the positive likelihood ratio was 1.55 (CI 1.31 to 1.84), and the negative likelihood ratio was 0.39 (CI: 0.19 to 0.82). Five studies (140 cases and 293 non-cases) evaluated the accuracy of the CSF p-tau/ABeta ratio. The sensitivities were between 80% and 96% while the specificities were between 33% and 95%. We did not conduct a meta-analysis because the studies were few and small. Only one study reported the accuracy of CSF t-tau/ABeta ratio. Our findings are based on studies with poor reporting. A significant number of studies had unclear risk of bias for the reference standard, participant selection and flow and timing domains. According to the assessment of index test domain, eight of 15 studies were of poor methodological quality. The accuracy of these CSF biomarkers for other dementias had not been investigated in the included primary studies. Investigation of heterogeneity The main sources of heterogeneity were thought likely to be reference standards used for the target disorders, sources of recruitment, participant sampling, index test methodology and aspects of study quality (particularly, inadequate blinding). We were not able to formally assess the effect of each potential source of heterogeneity as planned, due to the small number of studies available to be included. Authors' conclusions: The insufficiency and heterogeneity of research to date primarily leads to a state of uncertainty regarding the value of CSF testing of t-tau, p-tau or p-tau/ABeta ratio for the diagnosis of Alzheimer's disease in current clinical practice. Particular attention should be paid to the risk of misdiagnosis and overdiagnosis of dementia (and therefore over-treatment) in clinical practice. These tests, like other biomarker tests which have been subject to Cochrane DTA reviews, appear to have better sensitivity than specificity and therefore might have greater utility in ruling out Alzheimer's disease as the aetiology to the individual's evident cognitive impairment, as opposed to ruling it in. The heterogeneity observed in the few studies awaiting classification suggests our initial summary will remain valid. However, these tests may have limited clinical value until uncertainties have been addressed. Future studies with more uniformed approaches to thresholds, analysis and study conduct may provide a more homogenous estimate than the one that has been available from the included studies we have identified.

Rolinski M, Fox C, Maidment I, McShane R. Cholinesterase inhibitors for dementia with Lewy bodies, Parkinson's disease dementia and cognitive impairment in Parkinson's disease. *Cochrane Database of Systematic Reviews*. 2012; 3. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006504.pub2/abstract>

Background: Previous Cochrane reviews have considered the use of cholinesterase inhibitors in both Parkinson's disease with dementia (PDD) and dementia with Lewy bodies (DLB). The clinical features of DLB and PDD have much in common and are distinguished primarily on the basis of whether or not parkinsonism precedes dementia by more than a year. Patients with both conditions have particularly severe deficits in cortical levels of the neurotransmitter acetylcholine. Therefore, blocking its breakdown using cholinesterase inhibitors may lead to clinical improvement. Objectives: To assess the efficacy, safety and tolerability of cholinesterase inhibitors in patients with dementia with Lewy bodies (DLB), Parkinson's disease with dementia (PDD), and cognitive impairment in Parkinson's disease falling short of dementia (CIND-PD) (considered as separate phenomena and also grouped together as Lewy body disease). Search methods: The trials were identified from a search of ALOIS, the Specialised Register of the Cochrane Dementia and Cognitive Improvement Group (on 30 August 2011) using the search terms Lewy, Parkinson, PDD, DLB, LBD. This register consists of records from major healthcare databases (MEDLINE, EMBASE, PsycINFO, CINAHL) and many ongoing trial databases and is updated regularly. Reference lists of relevant studies were searched for additional trials. Selection criteria: Randomised, double-blind, placebo-controlled trials assessing the efficacy of treatment with cholinesterase inhibitors in DLB, PDD and CIND-PD. Data collection and analysis: Data were extracted from published reports by one review author (MR). The data for each 'condition' (that is DLB, PDD or CIND-PD) were considered separately and, where possible, also pooled. Statistical analysis was conducted using Review Manager 5.0. Main results: Six trials met the inclusion criteria for this review, in which a total of 1236 participants were randomised. Four of the trials were of a parallel group design and two cross-over trials were included. Four of the trials included participants with a diagnosis of PDD (Aarsland 2002a; Dubois 2007; Emre 2004; Ravina 2005), of which Dubois 2007 remains unpublished (n = 550). Leroi 2004 included patients with cognitive impairment and Parkinson's disease (both with and without dementia). Patients with DLB were included in only one of the trials (McKeith 2000). For global assessment, three trials comparing cholinesterase inhibitor treatment to placebo in PDD (Aarsland 2002a; Emre 2004; Ravina 2005) reported a difference in the Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change (ADCS-CGIC) score of -0.38, favouring the cholinesterase inhibitors (95% confidence interval (CI) -0.56 to -0.24, P < 0.0001). A clinically meaningful improvement was observed in 19.8% of patients receiving cholinesterase inhibitors, compared to 14.5% of those in the placebo group. For cognitive function, a pooled estimate of the effect of cholinesterase inhibitors on cognitive function measures was consistent with the presence of a therapeutic benefit (standardised mean difference (SMD) -0.34, 95% CI -0.46 to -0.23, P < 0.00001). There was evidence of a positive effect of cholinesterase inhibitors on the Mini-Mental State Examination (MMSE) in patients with PDD (weighted mean difference (WMD) 1.09, 95% CI 0.45 to 1.73, P = 0.0008) and in the single PDD and CIND-PD trial (WMD 1.05, 95% CI 0.42 to 1.68, P = 0.01) but not in the single DLB trial. For behavioural disturbance, analysis of the pooled continuous data relating to behavioural disturbance rating scales favoured



treatment with cholinesterase inhibitors (SMD -0.20, 95% CI -0.36 to -0.04, P = 0.01). For activities of daily living, combined data for the ADCS and the Unified Parkinson's Disease Rating Scale (UPDRS) activities of daily living rating scales favoured treatment with cholinesterase inhibitors (SMD -0.20, 95% CI -0.38 to -0.02, P = 0.03). For safety and tolerability, those taking a cholinesterase inhibitor were more likely to experience an adverse event (318/452 versus 668/84; odds ratio (OR) 1.64, 95% CI 1.26 to 2.15, P = 0.0003) and to drop out (128/465 versus 45/279; OR 1.94, 95% CI 1.33 to 2.84, P = 0.0006). Adverse events were more common amongst those taking rivastigmine (357/421 versus 173/240; OR 2.28, 95% CI 1.53 to 3.38, P < 0.0001) but not those taking donepezil (311/421 versus 145/212; OR 1.24, 95% CI 0.86 to 1.80, P = 0.25). Parkinsonian symptoms in particular tremor (64/739 versus 12/352; OR 2.71, 95% CI 1.44 to 5.09, P = 0.002), but not falls (P = 0.39), were reported more commonly in the treatment group but this did not have a significant impact on the UPDRS (total and motor) scores (P = 0.71). Fewer deaths occurred in the treatment group than in the placebo group (4/465 versus 9/279; OR 0.28, 95% CI 0.09 to 0.84, P = 0.03). Authors' conclusions: The currently available evidence supports the use of cholinesterase inhibitors in patients with PDD, with a positive impact on global assessment, cognitive function, behavioural disturbance and activities of daily living rating scales. However, almost half of the trial data, which could potentially change this conclusion, have not been made public. The effect in DLB remains unclear. There is no current disaggregated evidence to support their use in CIND-PD.

Russ Tom C, Morling Joanne R. Cholinesterase inhibitors for mild cognitive impairment. Cochrane Database of Systematic Reviews. 2012; 9. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009132.pub2/abstract>

Background: Mild cognitive impairment is hypothesised to represent a pre-clinical stage of dementia but forms a heterogeneous group with variable prognosis. Objectives: To assess the safety and efficacy of cholinesterase inhibitors in people with mild cognitive impairment. Search methods: Trials were identified from the Cochrane Dementia and Cognitive Improvement Group's Specialised Register, which is frequently updated from the major healthcare databases (MEDLINE, EMBASE, CINAHL, PsycINFO and Lilacs) as well as trial registers and grey literature. Selection criteria: Double-blind, placebo-controlled randomised trials of any cholinesterase inhibitor in people with mild cognitive impairment. Data collection and analysis: Data were extracted from the published reports of the included studies, combined by meta-analysis where appropriate, and treatment efficacy and risk of adverse events were estimated. Main results: Nine studies (from eight published reports) of 5149 individuals with mild cognitive impairment (however defined) were included in the review. Limited pooling of results was possible owing to different lengths of trials. Meta-analysis of the three studies reporting conversion to dementia gives no strong evidence of a beneficial effect of cholinesterase inhibitors on the progression to dementia at one, two or three years. The risk ratio (RR) for conversion at two years was significantly different from unity (0.67; 95% confidence interval (CI) 0.55 to 0.83), but this is based on only two studies reported in the same article. There was essentially no effect of cholinesterase inhibitors on cognitive test scores. Based on the results from 4207 individuals, there were significantly more adverse events in the cholinesterase inhibitor groups (RR 1.09; 95% CI 1.02 to 1.16), but no more serious adverse events or deaths. Gastrointestinal side effects were much more common (diarrhoea: RR 2.10; 95% CI 1.30 to 3.39; nausea: RR 2.97; 95% CI 2.57 to 3.42; vomiting: RR 4.42; 95% CI 3.23 to 6.05). Cardiac problems were no more likely in either group (RR 0.71; 95% CI 0.25 to 2.02). Other side effects reported significantly more often in the cholinesterase inhibitor group were muscle spasms/leg cramps (RR 7.52; 95% CI 4.34 to 13.02), headache (RR 1.34; 95% CI 1.05 to 1.71), syncope or dizziness (RR 1.62; 95% CI 1.36 to 1.93), insomnia (RR 1.66; 95% CI 1.36 to 2.02) and abnormal dreams (RR 4.25; 95% CI 2.57 to 7.04). Authors' conclusions: There is very little evidence that cholinesterase inhibitors affect progression to dementia or cognitive test scores in mild cognitive impairment. This weak evidence is overwhelmed by the increased risk of adverse events, particularly gastrointestinal. Cholinesterase inhibitors should not be recommended for mild cognitive impairment.

Sampson Elizabeth L, Jenagaratnam L, McShane R. Metal protein attenuating compounds for the treatment of Alzheimer's dementia. Cochrane Database of Systematic Reviews. 2014; 2. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005380.pub5/abstract>

Background: Alzheimer's dementia (AD) may be caused by the formation of extracellular senile plaques comprised of beta-amyloid (A $\beta$ ). In vitro and mouse model studies have demonstrated that metal protein attenuating compounds (MPACs) promote the solubilisation and clearance of A $\beta$ . Objectives: To evaluate the efficacy of metal protein attenuating compounds (MPACs) for the treatment of cognitive impairment due to Alzheimer's dementia. Search methods: We searched ALOIS, the Cochrane Dementia and Cognitive Improvement Group Specialized Register, on 29 July 2010 using the terms: Clioquinol OR PBT1 OR PBT2 OR "metal protein" OR MPACS OR MPAC. Selection criteria: Randomised double-blind trials in which treatment with an MPAC was administered to participants with Alzheimer's dementia in a parallel group comparison with placebo were included. Data collection and analysis: Three review authors (RM, LJ, ELS) independently assessed the quality of trials according to the Cochrane Handbook for Systematic Reviews of Interventions. The primary outcome measure of interest was cognitive function (as measured by psychometric tests). The secondary outcome measures of interest were in the following areas: quality of life, functional performance, effect on carer, biomarkers, safety and adverse effects, and death. Main results: Two MPAC trials were identified. One trial compared clioquinol (PBT1) with placebo in 36 patients and 32 had sufficient data for per protocol analysis. There was no statistically significant

difference in cognition (as measured on the Alzheimer's Disease Assessment Scale - Cognition (ADAS-Cog)) between the active treatment and placebo groups at 36 weeks. The difference in mean change from baseline ADAS-Cog score in the clioquinol arm compared with the placebo arm at weeks 24 and 36 was a difference of 7.37 (95% confidence interval (CI) 1.51 to 13.24) and 6.36 (95% CI -0.50 to 13.23), respectively. There was no significant impact on non-cognitive symptoms or clinical global impression. One participant in the active treatment group developed neurological symptoms (impaired visual acuity and colour vision) which resolved on cessation of treatment and were possibly attributable to the drug. In the second trial a successor compound, PBT2, was compared with placebo in 78 participants with mild Alzheimer's dementia; all were included in the intention-to-treat analysis. There was no significant difference in the Neuropsychological Test Battery (NTB) composite or memory between placebo and PBT2 in the least squares mean change from baseline at week 12. However, two executive function component tests of the NTB showed significant improvement over placebo in the PBT2 250 mg group from baseline to week 12: category fluency test (2.8 words, 95% CI 0.1 to 5.4; P = 0.041) and trail making part B (-48.0 s, 95% CI -83.0 to -13.0; P = 0.009). In the executive factor Z score, the difference in least squares mean change from baseline at week 12 for PBT2 250 mg compared with placebo was 0.27 (0.01 to 0.53; p=0.042). There was no significant effect on cognition on Mini-Mental State Examination (MMSE) or ADAS-Cog scales. PBT2 had a favourable safety profile. Authors' conclusions: There is an absence of evidence as to whether clioquinol (PBT1) has any positive clinical benefit for patients with AD, or whether the drug is safe. We have some concerns about the quality of the study methodology; there was an imbalance in treatment and control groups after randomisation (participants in the active treatment group had a higher mean pre-morbid IQ) and the secondary analyses of results stratified by baseline dementia severity. The planned phase III trial of PBT1 has been abandoned and this compound has been withdrawn from development. The second trial of PBT2 was more rigorously conducted and showed that after 12 weeks this compound appeared to be safe and well tolerated in people with mild Alzheimer's dementia. Larger trials are now required to demonstrate cognitive efficacy.

Smailagic N, Vacante M, Hyde C, Martin S, Ukoumunne O, Sachpekidis C. 18F-FDG PET for the early diagnosis of Alzheimer's disease dementia and other dementias in people with mild cognitive impairment (MCI). *Cochrane Database of Systematic Reviews*. 2015; 1. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010632.pub2/abstract>

Background:  $^{18}\text{F}$ -FDG uptake by brain tissue as measured by positron emission tomography (PET) is a well-established method for assessment of brain function in people with dementia. Certain findings on brain PET scans can potentially predict the decline of mild cognitive impairment (MCI) to Alzheimer's disease dementia or other dementias. Objectives: To determine the diagnostic accuracy of the  $^{18}\text{F}$ -FDG PET index test for detecting people with MCI at baseline who would clinically convert to Alzheimer's disease dementia or other forms of dementia at follow-up. Search methods: We searched the Cochrane Register of Diagnostic Test Accuracy Studies, MEDLINE, EMBASE, Science Citation Index, PsycINFO, BIOSIS previews, LILACS, MEDION, (Meta-analyses van Diagnostisch Onderzoek), DARE (Database of Abstracts of Reviews of Effects), HTA (Health Technology Assessment Database), ARIF (Aggressive Research Intelligence Facility) and C-EBLM (International Federation of Clinical Chemistry and Laboratory Medicine Committee for Evidence-based Laboratory Medicine) databases to January 2013. We checked the reference lists of any relevant studies and systematic reviews for additional studies. Selection criteria: We included studies that evaluated the diagnostic accuracy of  $^{18}\text{F}$ -FDG PET to determine the conversion from MCI to Alzheimer's disease dementia or to other forms of dementia, i.e. any or all of vascular dementia, dementia with Lewy bodies, and fronto-temporal dementia. These studies necessarily employ delayed verification of conversion to dementia and are sometimes labelled as 'delayed verification cross-sectional studies'. Data collection and analysis: Two blinded review authors independently extracted data, resolving disagreement by discussion, with the option to involve a third review author as arbiter if necessary. We extracted and summarised graphically the data for two-by-two tables. We conducted exploratory analyses by plotting estimates of sensitivity and specificity from each study on forest plots and in receiver operating characteristic (ROC) space. When studies had mixed thresholds, we derived estimates of sensitivity and likelihood ratios at fixed values (lower quartile, median and upper quartile) of specificity from the hierarchical summary ROC (HSROC) models. Main results: We included 14 studies (421 participants) in the analysis. The sensitivities for conversion from MCI to Alzheimer's disease dementia were between 25% and 100% while the specificities were between 15% and 100%. From the summary ROC curve we fitted we estimated that the sensitivity was 76% (95% confidence interval (CI): 53.8 to 89.7) at the included study median specificity of 82%. This equates to a positive likelihood ratio of 4.03 (95% CI: 2.97 to 5.47), and a negative likelihood ratio of 0.34 (95% CI: 0.15 to 0.75). Three studies recruited participants from the same Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort but only the largest ADNI study (Herholz 2011) is included in the meta-analysis. In order to demonstrate whether the choice of ADNI study or discriminating brain region (Chételat 2003) or reader assessment (Pardo 2010) make a difference to the pooled estimate, we performed five additional analyses. At the median specificity of 82%, the estimated sensitivity was between 74% and 76%. There was no impact on our findings. In addition to evaluating Alzheimer's disease dementia, five studies evaluated the accuracy of  $^{18}\text{F}$ -FDG PET for all types of dementia. The sensitivities were between 46% and 95% while the specificities were between 29% and 100%; however, we did not conduct a meta-analysis because of too few studies, and those studies which we had found recruited small numbers of participants. Our findings are based on studies with poor reporting, and the majority of included studies had an unclear risk of bias, mainly for the reference standard and participant selection domains. According to the

assessment of Index test domain, more than 50% of studies were of poor methodological quality. Authors' conclusions: It is difficult to determine to what extent the findings from the meta-analysis can be applied to clinical practice. Given the considerable variability of specificity values and lack of defined thresholds for determination of test positivity in the included studies, the current evidence does not support the routine use of  $^{18}\text{F}$ -FDG PET scans in clinical practice in people with MCI. The  $^{18}\text{F}$ -FDG PET scan is a high-cost investigation, and it is therefore important to clearly demonstrate its accuracy and to standardise the process of  $^{18}\text{F}$ -FDG PET diagnostic modality prior to its being widely used. Future studies with more uniform approaches to thresholds, analysis and study conduct may provide a more homogeneous estimate than the one available from the included studies we have identified.

Sydenham E, Dangour Alan D, Lim W-S. Omega 3 fatty acid for the prevention of cognitive decline and dementia. Cochrane Database of Systematic Reviews. 2012; 6. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005379.pub3/abstract>

Background: Evidence from observational studies suggests that diets high in omega-3 long-chain polyunsaturated fatty acids (PUFA) may protect people from cognitive decline and dementia. The strength of this potential protective effect has recently been tested in randomised controlled trials. Objectives: To assess the effects of omega-3 PUFA supplementation for the prevention of dementia and cognitive decline in cognitively healthy older people. Search methods: We searched ALOIS - the Cochrane Dementia and Cognitive Improvement Group's Specialized Register on 6 April 2012 using the terms: "omega 3", PUFA, "fatty acids", "fatty acid", fish, linseed, eicosapentaenoic, docosahexaenoic. Selection criteria: Randomised controlled trials of an omega-3 PUFA intervention which was provided for a minimum of six months to participants aged 60 years and over who were free from dementia or cognitive impairment at the beginning of the study. Two review authors independently assessed all trials. Data collection and analysis: The review authors sought and extracted data on incident dementia, cognitive function, safety and adherence, either from published reports or by contacting the investigators for original data. Data were extracted by two review authors. We calculated mean difference (MD) or standardised mean differences (SMD) and 95% confidence intervals (CI) on an intention-to-treat basis, and summarised narratively information on safety and adherence. Main results: Information on cognitive function at the start of a study was available on 4080 participants randomised in three trials. Cognitive function data were available on 3536 participants at final follow-up. In two studies participants received gel capsules containing either omega-3 PUFA (the intervention) or olive or sunflower oil (placebo) for six or 24 months. In one study, participants received margarine spread for 40 months; the margarine for the intervention group contained omega-3 PUFA. Two studies had cognitive health as their primary outcome; one study of cardiovascular disease included cognitive health as an additional outcome. None of the studies examined the effect of omega-3 PUFA on incident dementia. In two studies involving 3221 participants there was no difference between the omega-3 and placebo group in mini-mental state examination score at final follow-up (following 24 or 40 months of intervention); MD -0.07 (95% CI -0.25 to 0.10). In two studies involving 1043 participants, other tests of cognitive function such as word learning, digit span and verbal fluency showed no beneficial effect of omega-3 PUFA supplementation. Participants in both the intervention and control groups experienced either small or no cognitive declines during the studies. The main reported side-effect of omega-3 PUFA supplementation was mild gastrointestinal problems. Overall, minor adverse events were reported by fewer than 15% of participants, and reports were balanced between intervention groups. Adherence to the intervention was on average over 90% among people who completed the trials. All three studies included in this review are of high methodological quality. Authors' conclusions: Direct evidence on the effect of omega-3 PUFA on incident dementia is lacking. The available trials showed no benefit of omega-3 PUFA supplementation on cognitive function in cognitively healthy older people. Omega-3 PUFA supplementation is generally well tolerated with the most commonly reported side-effect being mild gastrointestinal problems. Further studies of longer duration are required. Longer-term studies may identify greater change in cognitive function in study participants which may enhance the ability to detect the possible effects of omega-3 PUFA supplementation in preventing cognitive decline in older people.

Van der Roest Henriëtte G, Wenborn J, Pastink C, Dröes R-M, Orrell M. Assistive technology for memory support in dementia. Cochrane Database of Systematic Reviews. 2017; 6. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009627.pub2/abstract>

Background: The sustained interest in electronic assistive technology in dementia care has been fuelled by the urgent need to develop useful approaches to help support people with dementia at home. Also the low costs and wide availability of electronic devices make it more feasible to use electronic devices for the benefit of disabled persons. Information Communication Technology (ICT) devices designed to support people with dementia are usually referred to as Assistive Technology (AT) or Electronic Assistive Technology (EAT). By using AT in this review we refer to electronic assistive devices. A range of AT devices has been developed to support people with dementia and their carers to manage their daily activities and to enhance safety, for example electronic pill boxes, picture phones, or mobile tracking devices. Many are commercially available. However, the usefulness and user-friendliness of these devices are often poorly evaluated. Although reviews of (electronic) memory aids do exist, a systematic review of studies focusing on the efficacy of AT for memory support in people with dementia is lacking. Such a review would guide people with dementia and their informal and professional carers in selecting appropriate AT devices. Objectives: Primary objective To assess the efficacy of AT for memory support in people with dementia

in terms of daily performance of personal and instrumental activities of daily living (ADL), level of dependency, and admission to long-term care. Secondary objective To assess the impact of AT on: users (autonomy, usefulness and user-friendliness, adoption of AT); cognitive function and neuropsychiatric symptoms; need for informal and formal care; perceived quality of life; informal carer burden, self-esteem and feelings of competence; formal carer work satisfaction, workload and feelings of competence; and adverse events. Search methods: We searched ALOIS, the Specialised Register of the Cochrane Dementia and Cognitive Improvement Group (CDCIG), on 10 November 2016. ALOIS is maintained by the Information Specialists of the CDCIG and contains studies in the areas of dementia prevention, dementia treatment and cognitive enhancement in healthy people. We also searched the following list of databases, adapting the search strategy as necessary: Centre for Reviews and Dissemination (CRD) Databases, up to May 2016; The Collection of Computer Science Bibliographies; DBLP Computer Science Bibliography; HCI Bibliography: Human-Computer Interaction Resources; and AgeInfo, all to June 2016; PiCarta; Inspec; Springer Link Lecture Notes; Social Care Online; and IEEE Computer Society Digital Library, all to October 2016; J-STAGE: Japan Science and Technology Information Aggregator, Electronic; and Networked Computer Science Technical Reference Library (NCSTRL), both to November 2016; Computing Research Repository (CoRR) up to December 2016; and OT seeker; and ADEAR, both to February 2017. In addition, we searched Google Scholar and OpenSIGLE for grey literature. Selection criteria: We intended to review randomised controlled trials (RCTs) and clustered randomised trials with blinded assessment of outcomes that evaluated an electronic assistive device used with the single aim of supporting memory function in people diagnosed with dementia. The control interventions could either be 'care (or treatment) as usual' or non-technological psychosocial interventions (including interventions that use non-electronic assistive devices) also specifically aimed at supporting memory. Outcome measures included activities of daily living, level of dependency, clinical and care-related outcomes (for example admission to long-term care), perceived quality of life and well-being, and adverse events resulting from the use of AT; as well as the effects of AT on carers. Data collection and analysis: Two review authors independently screened all titles and abstracts identified by the search. Main results: We identified no studies which met the inclusion criteria. Authors' conclusions: This review highlights the current lack of high-quality evidence to determine whether AT is effective in supporting people with dementia to manage their memory problems.

van der Steen Jenny T, van Soest-Poortvliet Mirjam C, van der Wouden Johannes C, Bruinsma Manon S, Scholten Rob JPM, Vink Annemiek C. Music-based therapeutic interventions for people with dementia. *Cochrane Database of Systematic Reviews*. 2017; 5. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003477.pub3/abstract>]

Background: Dementia is a clinical syndrome with a number of different causes which is characterised by deterioration in cognitive, behavioural, social and emotional functions. Pharmacological interventions are available but have limited effect to treat many of the syndrome's features. Less research has been directed towards non-pharmacological treatments. In this review, we examined the evidence for effects of music-based interventions as a treatment. Objectives: To assess the effects of music-based therapeutic interventions for people with dementia on emotional well-being including quality of life, mood disturbance or negative affect, behavioural problems, social behaviour, and cognition at the end of therapy and four or more weeks after the end of treatment. Search methods: We searched ALOIS, the Specialized Register of the Cochrane Dementia and Cognitive Improvement Group (CDCIG) on 14 April 2010 using the terms: music therapy, music, singing, sing, auditory stimulation. Additional searches were also carried out on 3 July 2015 in the major healthcare databases MEDLINE, Embase, psycINFO, CINAHL and LILACS; and in trial registers and grey literature sources. On 12 April 2016, we searched the major databases for new studies for future evaluation. Selection criteria: We included randomized controlled trials of music-based therapeutic interventions (at least five sessions) for people with dementia that measured any of our outcomes of interest. Control groups either received usual care or other activities. Data collection and analysis: Two reviewers worked independently to screen the retrieved studies against the inclusion criteria and then to extract data and assess methodological quality of the included studies. If necessary, we contacted trial authors to ask for additional data, including relevant subscales, or for other missing information. We pooled data using random-effects models. Main results: We included 17 studies. Sixteen studies with a total of 620 participants contributed data to meta-analyses. Participants in the studies had dementia of varying degrees of severity, but all were resident in institutions. Five studies delivered an individual music intervention; in the others, the intervention was delivered to groups of participants. Most interventions involved both active and receptive musical elements. The methodological quality of the studies varied. All were at high risk of performance bias and some were at high risk of detection or other bias. At the end of treatment, we found low-quality evidence that music-based therapeutic interventions may have little or no effect on emotional well-being and quality of life (standardized mean difference, SMD 0.32, 95% CI -0.08 to 0.71; 6 studies, 181 participants), overall behaviour problems (SMD -0.20, 95% CI -0.56 to 0.17; 6 studies, 209 participants) and cognition (SMD 0.21, 95% CI -0.04 to 0.45; 6 studies, 257 participants). We found moderate-quality evidence that they reduce depressive symptoms (SMD -0.28, 95% CI -0.48 to -0.07; 9 studies, 376 participants), but do not decrease agitation or aggression (SMD -0.08, 95% CI -0.29 to 0.14; 12 studies, 515 participants). The quality of the evidence on anxiety and social behaviour was very low, so effects were very uncertain. The evidence for all long-term outcomes was also of very low quality. Authors' conclusions: Providing people with dementia with at least five sessions of a music-based therapeutic intervention probably reduces depressive symptoms but has little or no effect on agitation or aggression. There may also be little or no effect on emotional well-being or quality of life, overall behavioural problems and cognition. We are

uncertain about effects on anxiety or social behaviour, and about any long-term effects. Future studies should employ larger sample sizes, and include all important outcomes, in particular 'positive' outcomes such as emotional well-being and social outcomes. Future studies should also examine the duration of effects in relation to the overall duration of treatment and the number of sessions.

van Ginneken N, Tharyan P, Lewin S, Rao Girish N, Meera SM, Pian J, et al. Non-specialist health worker interventions for the care of mental, neurological and substance-abuse disorders in low- and middle-income countries. *Cochrane Database of Systematic Reviews*. 2013; 11. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009149.pub2/abstract>]

**Background:** Many people with mental, neurological and substance-use disorders (MNS) do not receive health care. Non-specialist health workers (NSHWs) and other professionals with health roles (OPHRs) are a key strategy for closing the treatment gap. **Objectives:** To assess the effect of NSHWs and OPHRs delivering MNS interventions in primary and community health care in low- and middle-income countries. **Search methods:** We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (including the Cochrane Effective Practice and Organisation of Care (EPOC) Group Specialised Register) (searched 21 June 2012); MEDLINE, OvidSP; MEDLINE In Process & Other Non-Indexed Citations, OvidSP; EMBASE, OvidSP (searched 15 June 2012); CINAHL, EBSCOhost; PsycINFO, OvidSP (searched 18 and 19 June 2012); World Health Organization (WHO) Global Health Library (searched 29 June 2012); LILACS; the International Clinical Trials Registry Platform (WHO); OpenGrey; the metaRegister of Controlled Trials (searched 8 and 9 August 2012); Science Citation Index and Social Sciences Citation Index (ISI Web of Knowledge) (searched 2 October 2012) and reference lists, without language or date restrictions. We contacted authors for additional studies. **Selection criteria:** Randomised and non-randomised controlled trials, controlled before-and-after studies and interrupted-time-series studies of NSHWs/OPHR-delivered interventions in primary/community health care in low- and middle-income countries, and intended to improve outcomes in people with MNS disorders and in their carers. We defined an NSHW as any professional health worker (e.g. doctors, nurses and social workers) or lay health worker without specialised training in MNS disorders. OPHRs included people outside the health sector (only teachers in this review). **Data collection and analysis:** Review authors double screened, double data-extracted and assessed risk of bias using standard formats. We grouped studies with similar interventions together. Where feasible, we combined data to obtain an overall estimate of effect. **Main results:** The 38 included studies were from seven low- and 15 middle-income countries. Twenty-two studies used lay health workers, and most addressed depression or post-traumatic stress disorder (PTSD). The review shows that the use of NSHWs, compared with usual healthcare services: 1. may increase the number of adults who recover from depression or anxiety, or both, two to six months after treatment (prevalence of depression: risk ratio (RR) 0.30, 95% confidence interval (CI) 0.14 to 0.64; low-quality evidence); 2. may slightly reduce symptoms for mothers with perinatal depression (severity of depressive symptoms: standardised mean difference (SMD) -0.42, 95% CI -0.58 to -0.26; low-quality evidence); 3. may slightly reduce the symptoms of adults with PTSD (severity of PTSD symptoms: SMD -0.36, 95% CI -0.67 to -0.05; low-quality evidence); 4. probably slightly improves the symptoms of people with dementia (severity of behavioural symptoms: SMD -0.26, 95% CI -0.60 to 0.08; moderate-quality evidence); 5. probably improves/slightly improves the mental well-being, burden and distress of carers of people with dementia (carer burden: SMD -0.50, 95% CI -0.84 to -0.15; moderate-quality evidence); 6. may decrease the amount of alcohol consumed by people with alcohol-use disorders (drinks/drinking day in last 7 to 30 days: mean difference -1.68, 95% CI -2.79 to -0.57); low-quality evidence). It is uncertain whether lay health workers or teachers reduce PTSD symptoms among children. There were insufficient data to draw conclusions about the cost-effectiveness of using NSHWs or teachers, or about their impact on people with other MNS conditions. In addition, very few studies measured adverse effects of NSHW-led care - such effects could impact on the appropriateness and quality of care. **Authors' conclusions:** Overall, NSHWs and teachers have some promising benefits in improving people's outcomes for general and perinatal depression, PTSD and alcohol-use disorders, and patient- and carer-outcomes for dementia. However, this evidence is mostly low or very low quality, and for some issues no evidence is available. Therefore, we cannot make conclusions about which specific NSHW-led interventions are more effective.

Woods B, Aguirre E, Spector Aimee E, Orrell M. Cognitive stimulation to improve cognitive functioning in people with dementia. *Cochrane Database of Systematic Reviews*. 2012; 2. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005562.pub2/abstract>]

**Background:** Cognitive stimulation is an intervention for people with dementia which offers a range of enjoyable activities providing general stimulation for thinking, concentration and memory usually in a social setting, such as a small group. Its roots can be traced back to Reality Orientation (RO), which was developed in the late 1950s as a response to confusion and disorientation in older patients in hospital units in the USA. RO emphasised the engagement of nursing assistants in a hopeful, therapeutic process but became associated with a rigid, confrontational approach to people with dementia, leading to its use becoming less and less common. Cognitive stimulation is often discussed in normal ageing as well as in dementia. This reflects a general view that lack of cognitive activity hastens cognitive decline. With people with dementia, cognitive stimulation attempts to make use of the positive aspects of RO whilst ensuring that the stimulation is implemented in a sensitive, respectful and person-centred manner. There is often little consistency in the application and availability of psychological therapies in dementia services, so a systematic review of the available evidence regarding cognitive stimulation is important

in order to identify its effectiveness and to place practice recommendations on a sound evidence base. Objectives: To evaluate the effectiveness and impact of cognitive stimulation interventions aimed at improving cognition for people with dementia, including any negative effects. Search methods: The trials were identified from a search of the Cochrane Dementia and Cognitive Improvement Group Specialized Register, called ALOIS (updated 6 December 2011). The search terms used were: cognitive stimulation, reality orientation, memory therapy, memory groups, memory support, memory stimulation, global stimulation, cognitive psychostimulation. Supplementary searches were performed in a number of major healthcare databases and trial registers to ensure that the search was up to date and comprehensive. Selection criteria: All randomised controlled trials (RCTs) of cognitive stimulation for dementia which incorporated a measure of cognitive change were included. Data collection and analysis: Data were extracted independently by two review authors using a previously tested data extraction form. Study authors were contacted for data not provided in the papers. Two review authors conducted independent assessments of the risk of bias in included studies. Main results: Fifteen RCTs were included in the review. Six of these had been included in the previous review of RO. The studies included participants from a variety of settings, interventions that were of varying duration and intensity, and were from several different countries. The quality of the studies was generally low by current standards but most had taken steps to ensure assessors were blind to treatment allocation. Data were entered in the meta-analyses for 718 participants (407 receiving cognitive stimulation, 311 in control groups). The primary analysis was on changes that were evident immediately at the end of the treatment period. A few studies provided data allowing evaluation of whether any effects were subsequently maintained. A clear, consistent benefit on cognitive function was associated with cognitive stimulation (standardised mean difference (SMD) 0.41, 95% CI 0.25 to 0.57). This remained evident at follow-up one to three months after the end of treatment. In secondary analyses with smaller total sample sizes, benefits were also noted on self-reported quality of life and well-being (standardised mean difference: 0.38 [95% CI: 0.11, 0.65]); and on staff ratings of communication and social interaction (SMD 0.44, 95% CI 0.17 to 0.71). No differences in relation to mood (self-report or staff-rated), activities of daily living, general behavioural function or problem behaviour were noted. In the few studies reporting family caregiver outcomes, no differences were noted. Importantly, there was no indication of increased strain on family caregivers in the one study where they were trained to deliver the intervention. Authors' conclusions: There was consistent evidence from multiple trials that cognitive stimulation programmes benefit cognition in people with mild to moderate dementia over and above any medication effects. However, the trials were of variable quality with small sample sizes and only limited details of the randomisation method were apparent in a number of the trials. Other outcomes need more exploration but improvements in self-reported quality of life and well-being were promising. Further research should look into the potential benefits of longer term cognitive stimulation programmes and their clinical significance.

Xiao Y, Wang J, Jiang S, Luo H. Hyperbaric oxygen therapy for vascular dementia. Cochrane Database of Systematic Reviews. 2012; 7. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009425.pub2/abstract>

Background: Hyperbaric oxygen therapy (HBOT) has been used to treat a variety of conditions and has shown possible efficacy for treating vascular dementia (VaD) in experimental and preliminary clinical studies. Objectives: To assess the efficacy and safety of HBOT for VaD, used alone or as an adjuvant treatment. Search methods: We searched ALOIS: the Cochrane Dementia and Cognitive Improvement Group Specialised Register on 20 December 2011 using the terms: hyperbaric OR oxygen OR HBO OR HBOT. ALOIS contains records of clinical trials identified from monthly searches of a number of major healthcare databases, numerous trial registries and grey literature sources. We also searched the Chinese Biomedical Database (CBM), the Chinese National Knowledge Infrastructure (CNKI) and the VIP Chinese Science and Technique Journals Database on 10 November 2011 using the terms 'gaoyayang', 'xueguanxingchidai' and 'chidai'. In addition, we contacted authors of included studies for additional information. Selection criteria: Trials were eligible for inclusion if they were randomised controlled trials comparing HBOT to no intervention or to sham HBOT, or comparing HBOT plus another treatment to the same other treatment in patients with VaD. Data collection and analysis: Two review authors independently assessed trial quality and extracted data. Main results: One study involving 64 patients was included. It compared HBOT as an adjuvant to donepezil with donepezil alone. This one included study was judged to be of poor methodological quality. Patients receiving HBOT plus donepezil had significantly better cognitive function than the donepezil only group after 12 weeks of treatment, measured by the Mini-Mental State Examination (MMSE) (WMD 3.50; 95% CI 0.91 to 6.09) or by Hasegawa's Dementia Rating Scale (HDS) (WMD 3.10; 95% CI 1.16 to 5.04). There were no deaths or withdrawals, and the study did not mention safety assessment at all. Global function, behavioral disturbance and activities of daily living were not investigated in the study. Authors' conclusions: There is insufficient evidence to support HBOT as an effective treatment for patients with VaD. Future trials should be randomised, double-blind comparisons of HBOT to sham HBOT.

Zhang S, Smailagic N, Hyde C, Noel-Storr Anna H, Takwoingi Y, McShane R, et al. 11C-PIB-PET for the early diagnosis of Alzheimer's disease dementia and other dementias in people with mild cognitive impairment (MCI). Cochrane Database of Systematic Reviews. 2014; 7. [cited: url: <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010386.pub2/abstract>

Background: According to the latest revised National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (now known as the

Alzheimer's Association) (NINCDS-ADRDA) diagnostic criteria for Alzheimer's disease dementia, the confidence in diagnosing mild cognitive impairment (MCI) due to Alzheimer's disease dementia is raised with the application of imaging biomarkers. These tests, added to core clinical criteria, might increase the sensitivity or specificity of a testing strategy. However, the accuracy of biomarkers in the diagnosis of Alzheimer's disease dementia and other dementias has not yet been systematically evaluated. A formal systematic evaluation of the sensitivity, specificity, and other properties of positron emission tomography (PET) imaging with the 11C-labelled Pittsburgh Compound-B (11C-PIB) ligand was performed. Objectives: To determine the diagnostic accuracy of the 11C-PIB-PET scan for detecting participants with MCI at baseline who will clinically convert to Alzheimer's disease dementia or other forms of dementia over a period of time. Search methods: The most recent search for this review was performed on 12 January 2013. We searched MEDLINE (OvidSP), EMBASE (OvidSP), BIOSIS Previews (ISI Web of Knowledge), Web of Science and Conference Proceedings (ISI Web of Knowledge), PsycINFO (OvidSP), and LILACS (BIREME). We also requested a search of the Cochrane Register of Diagnostic Test Accuracy Studies (managed by the Cochrane Renal Group). No language or date restrictions were applied to the electronic searches and methodological filters were not used so as to maximise sensitivity. Selection criteria: We selected studies that had prospectively defined cohorts with any accepted definition of MCI with baseline 11C-PIB-PET scan. In addition, we only selected studies that applied a reference standard for Alzheimer's dementia diagnosis for example NINCDS-ADRDA or Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) criteria. Data collection and analysis: We screened all titles generated by electronic database searches. Two review authors independently assessed the abstracts of all potentially relevant studies. The identified full papers were assessed for eligibility and data were extracted to create two by two tables. Two independent assessors performed quality assessment using the QUADAS 2 tool. We used the hierarchical summary receiver operating characteristic (ROC) model to produce a summary ROC curve. Main results: Conversion from MCI to Alzheimer's disease dementia was evaluated in nine studies. The quality of the evidence was limited. Of the 274 participants included in the meta-analysis, 112 developed Alzheimer's dementia. Based on the nine included studies, the median proportion converting was 34%. The studies varied markedly in how the PIB scans were done and interpreted. The sensitivities were between 83% and 100% while the specificities were between 46% and 88%. Because of the variation in thresholds and measures of 11C-PIB amyloid retention, we did not calculate summary sensitivity and specificity. Although subject to considerable uncertainty, to illustrate the potential strengths and weaknesses of 11C-PIB-PET scans we estimated from the fitted summary ROC curve that the sensitivity was 96% (95% confidence interval (CI) 87 to 99) at the included study median specificity of 58%. This equated to a positive likelihood ratio of 2.3 and a negative likelihood ratio of 0.07. Assuming a typical conversion rate of MCI to Alzheimer's dementia of 34%, for every 100 PIB scans one person with a negative scan would progress and 28 with a positive scan would not actually progress to Alzheimer's dementia. There were limited data for formal investigation of heterogeneity. We performed two sensitivity analyses to assess the influence of type of reference standard and the use of a pre-specified threshold. There was no effect on our findings. Authors' conclusions: Although the good sensitivity achieved in some included studies is promising for the value of 11C-PIB-PET, given the heterogeneity in the conduct and interpretation of the test and the lack of defined thresholds for determination of test positivity, we cannot recommend its routine use in clinical practice. 11C-PIB-PET biomarker is a high cost investigation, therefore it is important to clearly demonstrate its accuracy and standardise the process of the 11C-PIB diagnostic modality prior to it being widely used.

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### **CENTRAL search for RCTs**

1998 results – number only