



## As if dementia reviews weren't complex enough.....

Cochrane Dementia Group's adventures with NIHR Complex Reviews Support Unit (NIHR CRSU)





- Why add more complexity
- NMA
- DTA
- Overviews
- Prognosis
- The good, the bad and the complex

- Dementia is a public health priority
- Limited evidence based therapy
- Established Cochrane Group,
- Diverse portfolio,
- Program grants
- Social media profile
- etc
- etc





#### SUPPORTED BY



- "....group has a narrow focus....."
- "...simple reviews..."
- "....niche topics...."
- ".....need for prioritisation......"
- ".....limited evidence of impact....."





No conclusions can be made......

Further high quality trials are needed......

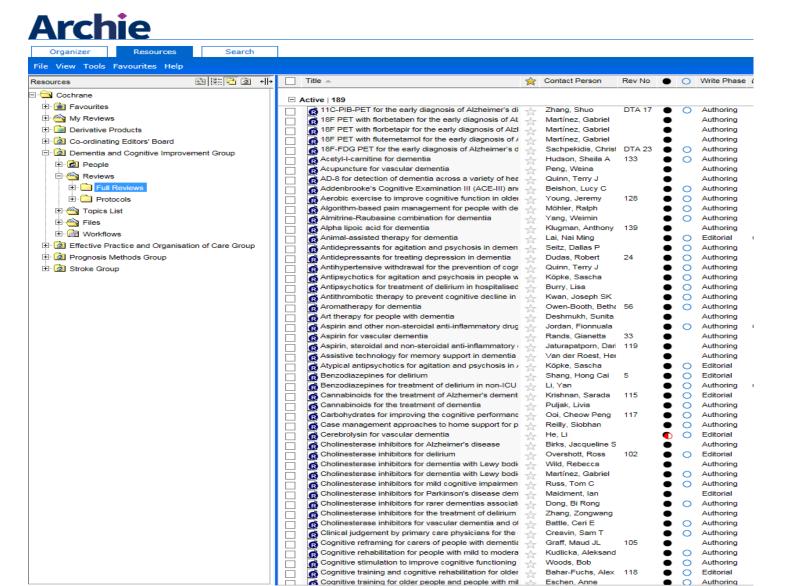


What are our most important reviews?

- What are the strengths of the group?
- What do stake holders want?

Which new areas can we start to develop?





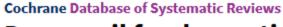


What are our most important reviews?

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#### Donepezil for dementia due to Alzheimer's disease

Cochrane Systematic Review - Intervention | Version published: 18 June 2018 | see what's new

https://doi.org/10.1002/14651858\_CD001190\_pub3 f2

New search Concl

Jacqueline S B View authors' decla

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#### Rivastigmine for Alzheimer's disease

Cochrane Systematic Review - Intervention | Version published: 22 September 2015 | see what's new

https://doi.org/1



#### Galantamine for Alzheimer's disease and mild cognitive impairment

Cochrane Systematic Review - Intervention | Version published: 25 January 2006 | see what's new

https://doi.org/10.1002/2 Jacqueline View authors' d



Clement Loy | Lon View authors' declaration

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#### Memantine for dementia

Cochrane Systematic Review - Intervention | Version published: 20 March 2019 | see what's new

https://doi.org/10.1002/14651858.CD003154.pub6 3

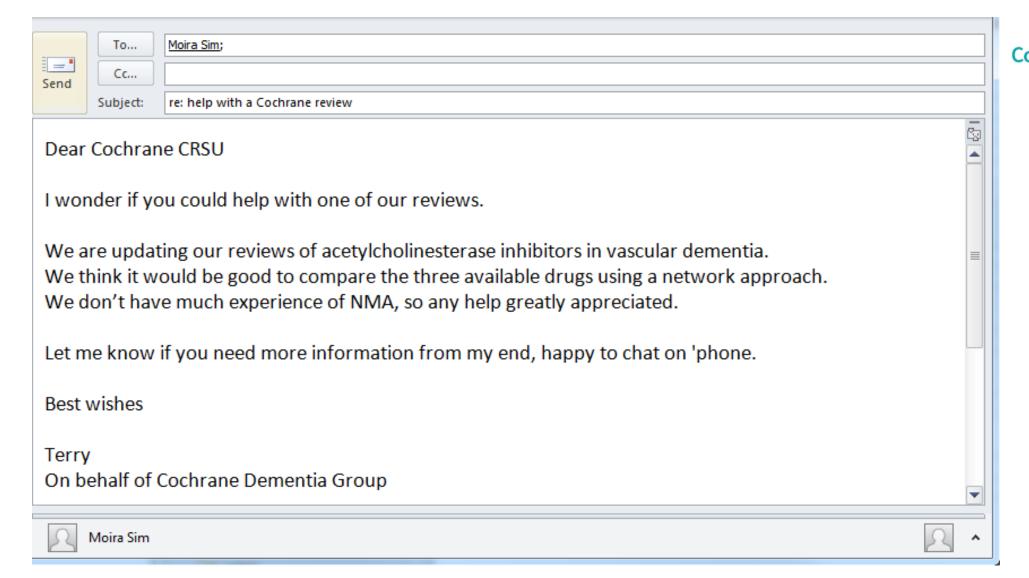
Conclusions changed New search



View article information

Rupert McShane | Maggie J Westby | Emmert Roberts | Neda Minakaran | Lon Schneider | Lucy E Farrimond Nicola Maayan | Jennifer Ware | Jean Debarros

View authors' declarations of interest







**Cochrane Database of Systematic Reviews** 

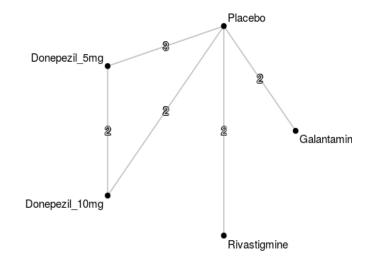
## Cholinesterase inhibitors for vascular dementia and other vascular cognitive impairments: a network meta-analysis

Cochrane Systematic Review - Intervention - Protocol | Version published: 10 April 2019 https://doi.org/10.1002/14651858.CD013306 3

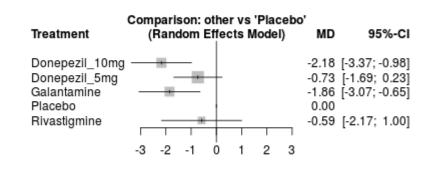
Am score 4

View article information

☑ Ceri E Battle | Azmil H Abdul-Rahim | Susan D Shenkin | Jonathan Hewitt View authors' declarations of interest



- More informative review
- Authors needed support with app
- Issues with incorporating NMA into review template





CD Number	Review Title	Full text downloads
CD005563	Interventions for preventing delirium in hospitalised non-ICU patients	7,741
CD001120	Reminiscence therapy for dementia	6,711
CD011145	Mini-Mental State Examination (MMSE) for the detection of dementia in clinically unevaluated people aged 65 and over in community and primary care populations	6,179

"There is STRONG evidence supporting multi-component interventions to prevent delirium in hospitalised patients"



- 1. Sleep protocol, avoid sedatives, reorientation, early mobilisation
- 2. Avoid sedatives, reorientation, avoid catheters
- 3. Sleep protocol, environmental factors, nurse training, screening
- 4. Screening, reorientation, early mobilisation
- 5. Avoid sedatives, nurse training, screening
- 6. Sleep protocol, nurse training, early mobilisation
- 7. Early mobilisation, nurse training, screening
- 8. Early mobilisation, avoid sedatives, avoid urinary catheters
- 9. Environmental factors, nurse raining, screening, avoid sedatives, avoid catheters
- 10. Nurse training, sleep protocol, early mobilisation



Any multicomponent intervention

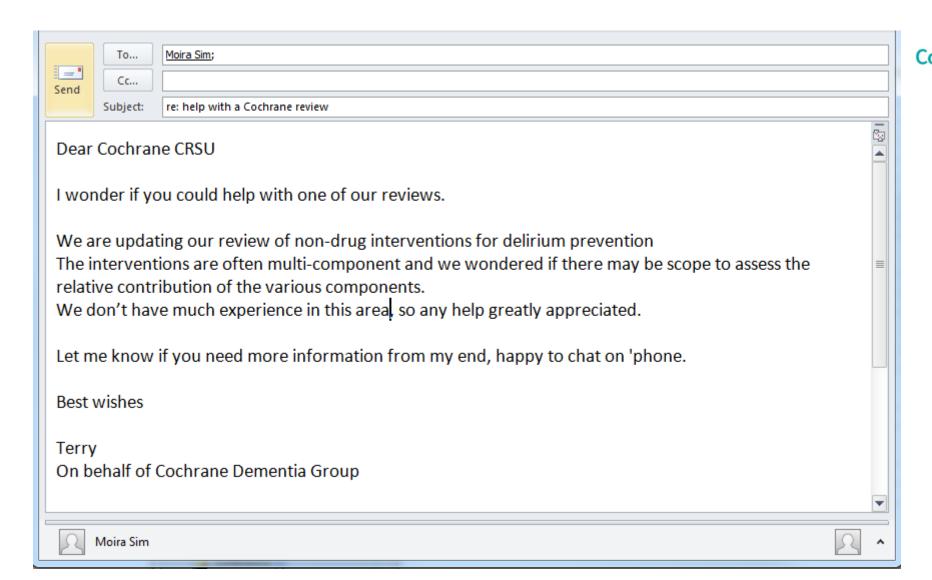
**Usual care** 



sleep protocol, avoid
sedatives, reorientation,
early mobilisation, avoid
catheters, environmental
factors, nurse training,
screening,

**Usual care** 







**Cochrane Database of Systematic Reviews** 

## Non-pharmacological interventions for preventing delirium in hospitalised non-ICU patients

Cochrane Systematic Review - Intervention - Protocol | Version published: 15 April 2019 https://doi.org/10.1002/14651858.CD013307 3



**■** Jennifer K Burton | Najma Siddiqi | Elizabeth A Teale | Amanda Barugh | Alex J Sutton View authors' declarations of interest

- More complex analysis offers a more useful result
- Good to liaise with NIHR CRSU early
- Approach to analysis needs to be flexible depending on the data



Cochrane Database of Systematic Reviews

## Blood pressure lowering in patients without prior cerebrovascular disease for prevention of cognitive impairment and dementia

Cochrane Systematic Review - Intervention | Version published: 07 October 2009 see what's new https://doi.org/10.1002/14651858.CD004034.pub3 3

New search Conclusions changed Am score 18 Used in 1 guideline View article information

■ Bernadette McGuinness | Stephen Todd | Peter Passmore | Roger Bullock

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Can we create a network to compare individual drug classes?

10.			



**Cochrane Database of Systematic Reviews** 

#### Blood pressure lowering in patients without prior cerebrovascular disease for prevention of cognitive impairment and dementia

Cochrane Systematic Review - Intervention | Version published: 07 October 2009 | see what's new https://doi.org/10.1002/14651858.CD004034.pub3 [3]

New search

Conclusions changed



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> Can we create a network to compare individual drug classes?

No.

But, here are some other things you could do.....



What are our most important reviews?

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Which new areas can we start to develop?



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CD005563	Interventions for preventing delirium in hospitalised non-ICU patients	7,741
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CD011145	Mini-Mental State Examination (MMSE) for the detection of dementia in clinically unevaluated people aged 65 and over in community and primary care populations	6,179



**Cochrane Database of Systematic Reviews** 

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 Systematic Review - Diagnostic | Version published: 13 January 2016 | see what's new

https://doi.org/10.1002/146

Am score 50 Used in

✓ Sam T Creavin | Susal | Victoria M Thom | Kirs | Emma Phillips | Sophi

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Sarah Cullum

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## Mini-Cog for the diagnosis of Alzheimer's disease dementia and other dementias within a community setting

Cochrane Systematic Review - Diagnostic | Version published: 03 February 2015

https://doi.org/10.1002/14651858.CD010860.pub2 @



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Bruce A Fage | Calvin CH Cha ■ Dallas P Seitz

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**Cochrane Database of Systematic Reviews** 

## Montreal Cognitive Assessment for the diagnosis of Alzheimer's disease and other dementias

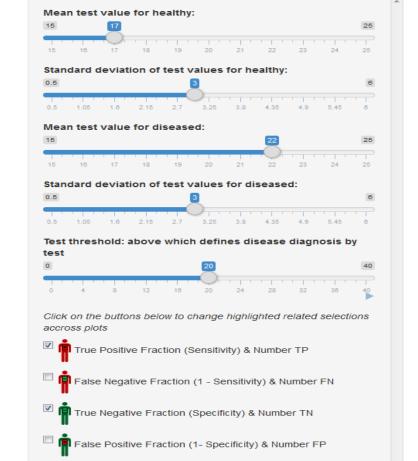
Cochrane Systematic Review - Diagnostic | Version published: 29 October 2015 https://doi.org/10.1002/14651858.CD010775.pub2 3



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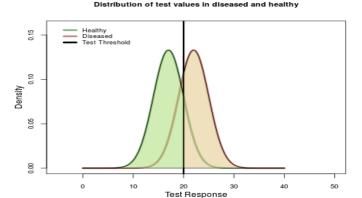
■ Daniel HJ Davis | Sam T Creavin | Jennifer LY Yip | Anna H Noel-Storr | Carol Brayne | Sarah Cullum View authors' declarations of interest

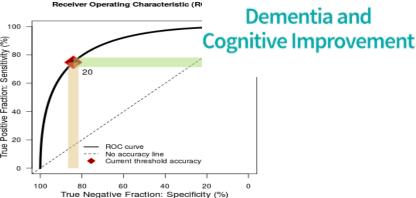




Prevalence: % of tested population with disease (does not

affect Test Accuracy tab)



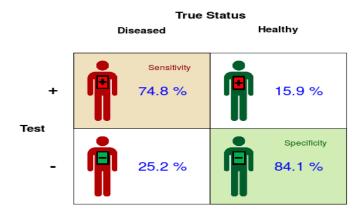


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The fraction of diseased patients correctly diagnosed by a test is often referred to as test sensitivity and the fraction of healthy patients correctly diagnosed by a test as specificity. These quantities are used to describe the performance of a diagnostic test, and both will vary with the test threshold used.

If 1 - specificity is plotted against sensitivity for all threshold values, a Receiver Operating Characteristic (ROC) plot is created (above right figure). This summarises test performance across all thresholds giving the possible trade-offs that can be achieved between False Negatives and False Positives (plotted above).

Explore how changing the means and variances of the test distributions in the diseased and healthy affect the ROC curve.



Performance of a test relating to **specified distribution** and **threshold values**:

**Selected threshold** above which test diagnoses patients as diseased is **20**.

At this test threshold **74.8**% of diseased patients are correctly diagnosed by the test (**sensitivity**), and **25.2**% are incorrectly diagnosed as healthy.

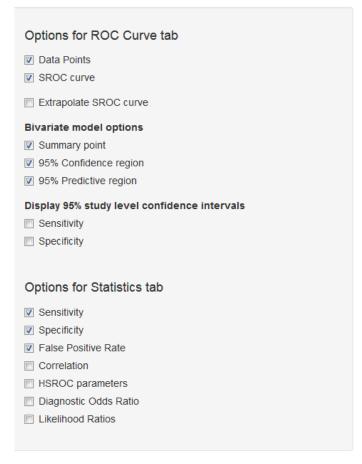
**84.1**% of healthy patients are correctly diagnosed by the test (**specificity**), and **15.9**% are incorrectly diagnosed as diseased.





# Cochrane Dementia and Cognitive Improvement

#### Meta-Analysis of Diagnostic Test Accuracy Studies



how	30 → entries								Search:	
	Author	♦ Year ♦	<b>TP</b>	FN ∜	FP <b></b>	<b>TN</b>	<b>N</b> ≑	Sensitivity	Specificity	<b>♦ FPR</b>
1	Aalto	2006	47	9	101	738	895	0.839	0.880	0.120
2	Aertgeerts01	2001	126	51	272	1543	1992	0.712	0.850	0.150
3	Aertgeerts02	2002	19	10	12	192	233	0.655	0.941	0.059
4	Bradley03	2003	36	3	78	276	393	0.923	0.780	0.220
5	Bradley07	2007	130	19	211	959	1319	0.872	0.820	0.180
6	Bush	1998	84	2	68	89	243	0.977	0.567	0.433
7	Gomez	2006	68	0	112	423	603	1.000	0.791	0.209
3	Gordon	2001	752	0	3226	2977	6955	1.000	0.480	0.520
9	Gual	2002	59	5	55	136	255	0.922	0.712	0.288
10	Rumpf	2002	142	50	571	2788	3551	0.740	0.830	0.170
11	Seale	2006	137	24	107	358	626	0.851	0.770	0.230
12	Selin	2006	57	3	103	437	600	0.950	0.809	0.191
13	Tsai	2005	34	1	21	56	112	0.971	0.727	0.273
14	Tuunanen	2007	152	51	88	254	545	0.749	0.743	0.257

Showing 1 to 14 of 14 entries Previous 1 N



- Q. What is the accuracy of MMSE for diagnosis of dementia?
- Q. Which test should I use to screen for dementia in my patients?



**Cochrane Database of Systematic Reviews** 

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 Systematic Review - Diagnostic | Version published: 13 January 2016 | see what's new

https://doi.org/10.1002/146

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## Mini-Cog for the diagnosis of Alzheimer's disease dementia and other dementias within a community setting

Cochrane Systematic Review - Diagnostic | Version published: 03 February 2015

https://doi.org/10.1002/14651858.CD010860.pub2 @



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## Montreal Cognitive Assessment for the diagnosis of Alzheimer's disease and other dementias

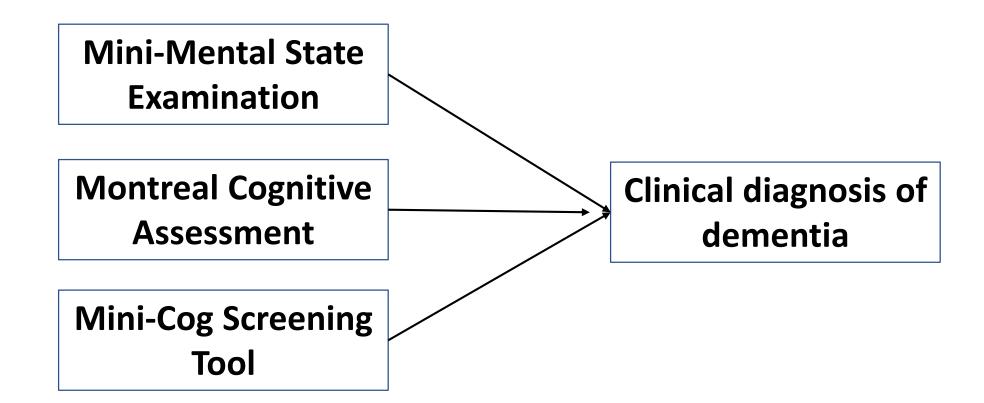
Cochrane Systematic Review - Diagnostic | Version published: 29 October 2015 https://doi.org/10.1002/14651858.CD010775.pub2 3



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Dementia and **Mini-Mental State Cognitive Improvement Examination** Clinical diagnosis of dementia **Mini-Cog Screening Montreal Cognitive Tool Assessment** 









Journal of Clinical Epidemiology

Journal of Clinical Epidemiology 99 (2018) 64-74

#### ORIGINAL ARTICLE

Network meta-analysis of diagnostic test accuracy studies identifies and ranks the optimal diagnostic tests and thresholds for health care policy and decision-making

Rhiannon K. Owen<sup>a,\*</sup>, Nicola J. Cooper<sup>a</sup>, Terence J. Quinn<sup>b</sup>, Rosalind Lees<sup>b</sup>, Alex J. Sutton<sup>a</sup>

<sup>a</sup>Department of Health Sciences, University of Leicester, Leicester, UK

<sup>b</sup>Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, UK

Accepted 7 March 2018; Published online 13 March 2018

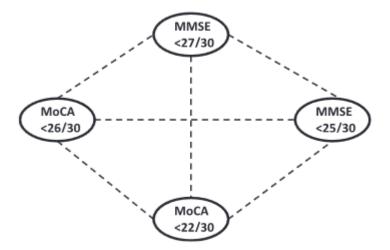


Fig. 1. Network of comparative studies. MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment.

**Table 4.** Estimated mean difference (95% CrI) in sensitivity (top right) and specificity (bottom left) between each test-threshold combination (row—column) obtained from a model incorporating threshold constraints and assuming a common heterogeneity and correlation parameter across tests

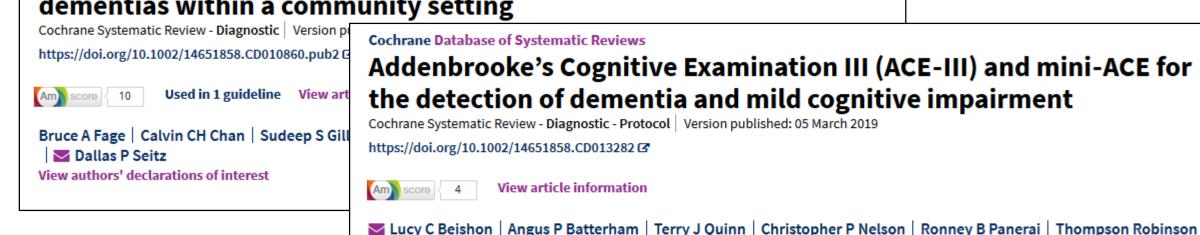
Test-threshold	MMSE <25	MMSE <27	MoCA <22	MoCA <26
MMSE <25	-	0.17 (0.08, 0.26)	0.10 (-0.01, 0.22)	0.25 (0.15, 0.35)
MMSE <27	0.26 (0.15, 0.39)	-	-0.07 (-0.18, 0.03)	0.08 (0.02, 0.16)
MoCA <22	0.07 (-0.01, 0.18)	-0.19 (-0.33, -0.06)	-	0.14 (0.07, 0.25)
MoCA <26	0.49 (0.38, 0.61)	0.23 (0.08, 0.37)	0.42 (0.31, 0.52)	-

Above the leading diagonal gives estimates of the mean difference (row—column) in sensitivity (95% CrI), and below the leading diagonal gives estimates of the mean difference in specificity (95% CrI).



**Cochrane Database of Systematic Reviews** 

## Mini-Cog for the diagnosis of Alzheimer's disease dementia and other dementias within a community setting



- 'User friendly interface very helpful for authors
- Still requires a knowledge of DTA theory to interpret the results

Victoria J Haunton

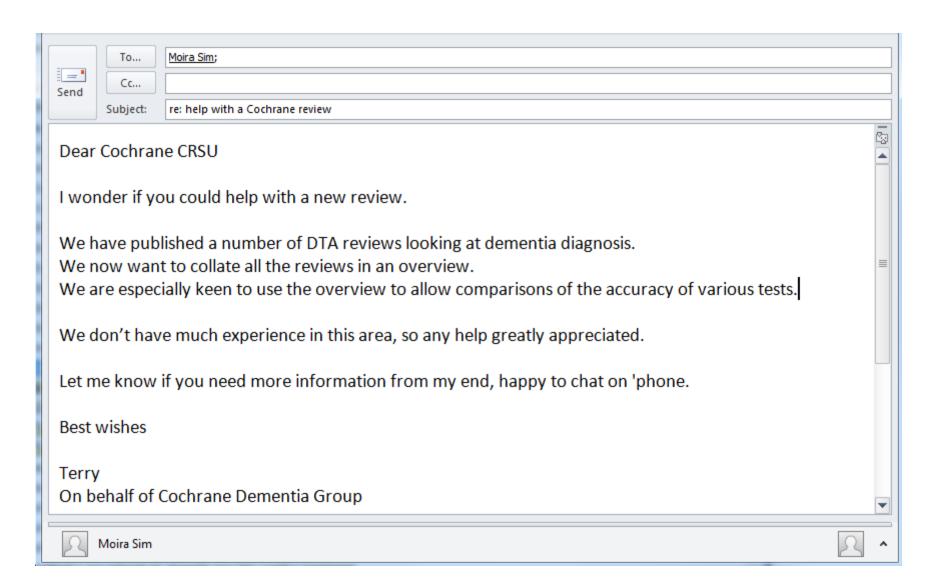
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Potential for even more complexity, but this is needed to give clinically useful results



- Increasing number of SRs looking at accuracy of single dementia tests
- Methodology for indirect comparisons of accuracy across reviews
- An overview of DTA could:
- Collate the available literature
- Assess the quality of evidence
- Compare accuracy of various tests
- Create an 'evidence map' highlighting where new reviews or new research studies are needed





Cochrane
Dementia and
Cognitive Improvement

Informant based screening tools for diagnosis of dementia, an overview of test accuracy studies

#### **Protocol information**

# Review type: Overview Authors Sara Nafisi<sup>1</sup>, Martin Taylor-Rowan<sup>2</sup>, Amit Patel<sup>3</sup>, Terry J Quinn<sup>4</sup> <sup>1</sup>Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, Glasgow, UK <sup>2</sup>Cardiovascular Science, University of Glasgow, Glasgow, UK <sup>3</sup>Other <sup>4</sup>Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, UK Citation example: Nafisi S, Taylor-Rowan M, Patel N, Stir To Informant based screening tools for diagnosis of dementia, an overview of test accuracy studies. Cochrane Database of System on Teviews , Issue . Art. No.: . DOI: . Contact person Terry J Quinn

- Useful peer review
- Learned a lot about overview strengths, limitations and methodological challenges
- Liaise with Cochrane before doing anything too novel



What are our most important reviews?

- What are the strengths of the group?
- What do stake holders want?

Which new areas can we start to develop?





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The Cochrane Dementia and Cognitive Improvement Group publish systematic reviews, metaanalyses and methodological guidance. Our remit extends beyond dementia and we are keen to develop our portfolio in the areas of vascular cognitive impairement and post stroke problems. We hope you can help us select review titles that tackle questions of greatest relevance to the stroke and VCI community.

To help us in our prioritisation work we would be grateful if you complete the three questions below and overleaf. Hopefully this should only take a few minutes and it will be incredibly helpful for our group.

If you have other ideas or thoughts that you want to share, please get in touch. There is space for free text comments and email contact details at the end of the questionnaire.





Organisation for Psychological Research into Stroke

Cochrane
Dementia and
Cognitive Improvement

2. Traditionally Cochrane has focussed on clinical trials, but we now have methods that allow us to collate evidence from other types of research. For the table below, please rank (1-5) order of importance (1=most; 5=least important) \*









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18F PET with florbetaben for the early diagnosis of Alzheimer's disease dementia and other dementias in people with mild cognitive impairment (MCI)

Cochrane Systematic Review - Diagnostic | Version published: 22 November 2017

https://doi.org/10.1002/14651858.CD012883 [3]



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**Cochrane Database of Systematic Reviews** 

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)

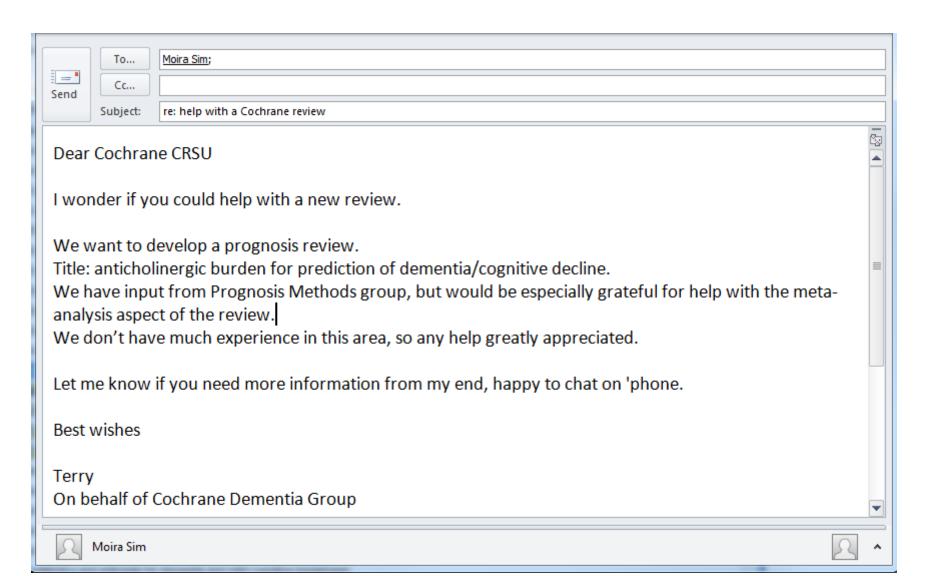
Cochrane Systematic Review - Diagnostic | Version published: 22 March 2017

https://doi.org/10.1002/14651858.CD010803.pub2 3



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Anticholinergic burden (prognostic factor) for prediction of dementia or cognitive decline in older adults with no known cognitive syndrome.

#### Protocol information

Review type: Flexible (Prognosis)

**Authors** 

Terry J Quinn<sup>1</sup>, Phyo Kyaw K Myint<sup>2</sup>, Jenny McCleery<sup>3</sup>, Martin Taylor-Rowan<sup>4</sup>

<sup>1</sup>Institute of Cardiovascular and Medical Sciences, University of Glasgow, Glasgow, UK

<sup>2</sup>Division of Applied Health Sciences, School of Medicine, Medical Sciences and Nutrition, University of Aberdeen, Aberdeen, UK

3Oxford Health NHS Foundation Trust, Banbury, UK

Cardiovascular Science, University of Glasgow, Glasgow, UK

Citation example: Quinn TJ, Myint PKK, McCleery J, Taylor-Rowan M. Anticholinergic burden (prognostic factor) for prediction of dementia or cognitive decline in older adults with no known cognitive syndrome.. Cochrane Database of Systematic Reviews , Issue . Art. No.: . DOI: .

- If you thought DTA was complex......
- New territory for NIHR CRSU
- Working in partnership with Prognosis Methods
- Watch this space



- Why add more complexity
- NMA
- DTA
- Overviews
- Prognosis
- The good, the bad and the complex