

## PROGRESS REPORT

<b>Report Type</b>	Submit Summary Progress Report
<b>Due Date</b>	16/09/2013
<b>Submitted Date</b>	

## PROJECT DETAILS

<b>Programme</b>	<b>Research Type</b>
Systematic Reviews Programme Grants	Secondary Research
<b>Project Reference Number</b>	<b>Chief Investigator</b>
10/4001/05	McShane, Rupert
<b>Project Title</b>	
A Programme of Diagnostic Test Accuracy Reviews and of Updates of Intervention Reviews in Dementia	
<b>Name and Address of Host Institution</b>	
University of Oxford	
<b>Start Date (Current)</b>	
01/09/2010	
<b>End Date (Original)</b>	<b>End Date (Current)</b>
31/08/2013	31/03/2014
<b>Draft Final Report Due Date</b>	
31/03/2014	
<b>R&amp;D Costs (Original)</b>	<b>R&amp;D Costs (Current)</b>
392,380.00	392,380.00

### Details of Contract Variations Awarded

Requested Date	Additional Time Granted (months)	Additional Funds Granted (£)
10/09/2013	7	
<b>Extension Totals</b>	7	

**PROJECT PROGRESS**

Question	Response
<p><b>Progress Summary</b> Please Provide a summary of progress since your last report</p>	<p>Our programme consists of 12 Diagnostic Test Accuracy (DTA) reviews of imaging, laboratory biomarkers and simple clinical tests, and 15 updates of systematic reviews of interventions currently in use in the NHS. In addition, 11 DTA reviews directly associated with this programme are on going.</p> <p>DTA reviews – Since the last progress report, six DTA protocols have been published (11 published total, including a generic protocol), two are ready to publish, one has been re-submitted for editorial review and four will be resubmitted within the next month. The protocols for the five remaining reviews are in preparation. In addition, two DTA reviews have been submitted for DTA Editorial team approval, 11 reviews are being drafted with the goal of submitting for in-house editorial approval by the end of the year, and six more by the end of the programme grant (March 2014).</p> <p>Intervention updates – Two updates have been published since the last report (five published total) and one is almost ready for publication. Four more have been submitted, three are in the final stages of preparation and two are progressing well. We are expecting all updates to be published by the end of this project grant (March 2014).</p> <p>We have used our funds strategically to help authors progress their reviews by outsourcing three review updates and part of the quality assessment task for four DTA reviews. In addition, we have identified new authors to help with particularly challenging analytical issues and recruited medical students to help scan the thousands of titles generated by the searches.</p>
<p><b>Milestone Update</b> With reference to the milestones you outlined in your latest approved full proposal or protocol, please list the milestones that have been completed.</p>	<p>Key millstones with regard to progress and publication of DTA reviews and review updates are presented in the attached tables:</p> <ul style="list-style-type: none"> <li>• Table 1. DTA reviews progress</li> <li>• Table 2. Review updates progress</li> <li>• Table 3. Dissemination activities</li> </ul>

Question	Response
<p><b>Ongoing Problems</b> Please outline any ongoing problems</p>	<p>The main challenge we have faced in progressing our reviews to completion within the original timeframe has been that, because DTA reviews are a new venture, fewer people have the ability and capacity to provide high quality editorial review than for intervention reviews – which have been going for 20 years. This results in delay in editorial process. This applies to both halves of the twin track editorial process for DTA reviews: the CRG and the DTA Editorial Unit. Indeed, our programme is a major and welcome part of the drive to increase exactly this capacity.</p> <p>Other problems we have faced include difficulty in recruiting authors (who also lack experience in this area), variable quality and poor reporting of DTA studies, and poor indexing of citation databases for this type of work with the result that typically searches yield over 10,000 studies which need screening. ALOIS (A register of DTA studies in dementia) and STARDdem (Standards for the Reporting of Diagnostic accuracy studies in dementia) will help mitigate some of these issues.</p> <p>In addition, we have felt that we have had to encourage authors to start work on ‘review stage’ processes, such as identification of likely included studies and data extraction BEFORE sign off of protocols. This is not entirely satisfactory because it increases the risk that some processes may need to be repeated. However, it is an important way to try to maintain momentum. This is always challenging in Cochrane reviews, but is doubly so when faced with the (entirely understandable) twin track editorial process.</p> <p>The result has been that our programme of work has progressed reasonably well, as described above.</p>
<p><b>Staff Changes</b> Please list any changes to project staff since your last report</p>	<p>There has been no change in staff since the last progress report.</p>
<p><b>Additional Comments</b> Please note any additional comments relating to this progress report</p>	



**PPI UPDATE**

The ways in which patients and the public have been actively involved in the proposed research during the last reporting period (if applicable).

Summary account of public involvement over the last reporting period with reference to the intentions stated in the application form.

**FEEDBACK**

We regularly review our processes and your comments are highly valued – please use this space to make any observations you may have regarding your experience

**UPLOADS**

The following pages contain the following uploads:

Upload Name
Additional Documentation

**Table 1. Progress of DTA reviews (10<sup>th</sup> October 2013)**

Title	Stage
1. IQCODE for the diagnosis of Alzheimer's disease dementia and other dementias within a community setting	Protocol published. New search performed. Included studies identified. Data extracted and entered into RevMan5. Included & Excluded studies tables and quality assessment completed. Analyses completed. Comments from in-house ET addressed. Review updated and submitted for DTA approval.
2. Plasma and CSF Aβ for the longitudinal prediction of Alzheimer's disease dementia and other dementias in people with cognitive decline but no dementia	Protocol published. New search performed. Included studies identified. Data extracted and entered into RevMan5. Included & Excluded studies tables/quality assessment and analyses completed. Address the comments from in-house ET. Review updated and submitted for DTA approval.
3. <sup>11</sup> C-PIB PET for the early diagnosis of Alzheimer's disease dementia in people with Mild Cognitive Impairment (MCI)	Protocol published. New search performed. Included studies identified. Data extracted and entered into RevMan5. Included & Excluded studies tables and quality assessment completed. Analyses completed. Writing review with the goal of submitting for in-house editorial approval by 15 <sup>th</sup> November 13.
4. The role of 18F-FDG-PET in the early diagnosis of Alzheimer's disease dementia and other dementias in people with mild cognitive impairment (MCI)	Protocol published. Included studies identified from the first search, data extracted and quality assessment completed. New search performed. New included studies identified. Data extraction almost completed (waiting for responses from a few authors who were contacted for some additional information). Included & Excluded studies tables almost completed. QUADAS 2 assessment and analyses to be performed. Writing review with the goal of submitting for in-house editorial approval by 30 <sup>th</sup> November 13.
5. Dopamine transporter imaging for the diagnosis of dementia with Lewy bodies	Protocol published. Search performed. Identifying included studies and data extraction in progress. Writing review with the goal of submitting for in-house editorial approval by 31 <sup>st</sup> December 13.
6. The role of MRI in the early diagnosis of Alzheimer's disease or other dementias in persons with Mild Cognitive Impairment (MCI)	Protocol published. Included studies identified. Data extracted and entered into RevMan5. Included & Excluded studies tables/quality assessment and analyses completed. New search performed. Identifying new included studies and data extraction in progress. Writing review with the goal of submitting for in-house editorial approval by 31 <sup>st</sup> December 13.
7. Mini-Cog for the cross-sectional diagnosis of Alzheimer's disease dementia and other dementias within a community setting	Protocol approved for publication. Included studies identified and data extracted. Analyses completed. Writing review with the goal of submitting for in-house editorial approval by 15 <sup>th</sup> November 13.
8. The Montreal Cognitive Assessment for the	Protocol published. Included studies identified and data extracted. Included & Excluded studies tables



diagnosis of Alzheimer's disease and other dementia disorders	and QUADAS 2 assessment to be completed. Analyses to be performed. Writing review with the goal of submitting for in-house editorial approval by 30 <sup>th</sup> November 13.
9. IQCODE for the cross-sectional diagnosis of Alzheimer's disease dementia and other dementias within a general practice (primary care) setting	Protocol published. New search performed. Included studies identified and data extracted. Quality assessment and analyses completed. Writing review with the goal of submitting for in-house editorial approval by 30 <sup>th</sup> November 13.
10. IQCODE for the cross-sectional diagnosis of Alzheimer's disease dementia and other dementias within a secondary care setting	Protocol published. New search performed. Included studies identified and data extracted. Quality assessment and analyses completed. Writing review with the goal of submitting for in-house editorial approval by 31 <sup>th</sup> January 14.
11. CSF Tau and the CSF Aβeta/Tau Ratio for the diagnosis of Alzheimer's disease dementia and other dementias in people with cognitive decline but no dementia	Protocol approved for publication. Data extraction, Included & Excluded studies tables and QUADAS 2 assessment to be completed. Analyses to be performed. Writing review with the goal of submitting for in-house editorial approval by 31 <sup>st</sup> December 13.
12. Mini-Mental State Examination (MMSE) for the detection of Alzheimer's dementia and other dementias in people with Mild Cognitive Impairment (MCI)	Protocol published. Search performed. Identifying included studies in progress. Data extraction, Included & Excluded studies tables and QUADAS 2 assessment to be completed. Analyses to be performed. Writing review with the goal of submitting for in-house editorial approval by 31 <sup>st</sup> January 14.
13. Plasma and CSF Aβeta42 for the differential diagnosis of Alzheimer's disease dementia in participants diagnosed with any dementia subtypes in specialist care setting	Protocol re-submitted for DTA approval. Included studies identified from the first search and data extracted. Quality assessment completed. New search performed. Identifying new included studies and data extraction in progress. Included & Excluded studies tables to be completed. Analyses to be performed. Writing review with the goal of submitting for in-house editorial approval by 31 <sup>st</sup> December 13.
14. APOE ε4 allele for the diagnosis of Alzheimer's and other dementia disorders in people with MCI in a community setting	Protocol to be re-submitted for DTA editorial approval by 15 <sup>th</sup> November. New search performed. Included studies identified and data extracted. Quality assessment and analyses completed. Writing review with the goal of submitting for in-house editorial approval by 31 <sup>th</sup> January 14.
15. APOE ε4 allele for the diagnosis of Alzheimer's and other dementia disorders in people with MCI in a primary care setting	Protocol to be re-submitted for DTA editorial approval by 15 <sup>th</sup> November. New search performed. Included studies identified and data extracted. Quality assessment and analyses completed. Writing review with the goal of submitting for in-house editorial approval by 31 <sup>th</sup> January 14.
16. APOE ε4 allele for the diagnosis of Alzheimer's and other dementia disorders in	Protocol to be re-submitted for DTA editorial approval by 15 <sup>th</sup> November. New search performed. Included studies identified and data extracted. Quality assessment and analyses completed. Writing

people with MCI in a secondary care setting	review with the goal of submitting for in-house editorial approval by 31 <sup>th</sup> January 14.
17. rCBF SPECT for the detection of frontotemporal dementia in people with suspected dementia	Protocol to be re-submitted for DTA editorial approval by 30 <sup>th</sup> October. Search performed. Identifying new included studies in progress. Data extraction and Included & Excluded studies tables to be completed. Analyses to be performed. Writing review with the goal of submitting for in-house editorial approval by 31 <sup>st</sup> January 14.
<b>Contingency plan: 5 ongoing DTA reviews</b>	
18. Neuropsychological tests for the diagnosis of Alzheimer's disease dementia and other dementias: a generic protocol for cross-sectional and delayed-verification studies	Generic Protocol published. This generic protocol is providing valuable information for those preparing a diagnostic accuracy review in dementia.
19. Mini-Cog for the cross-sectional diagnosis of Alzheimer's disease dementia and other dementias within a primary care setting	Protocol drafted. Submit the protocol for DTA editorial approval by 30 <sup>th</sup> October. Included studies identified and data extracted. Analyses completed. Writing review with the goal of submitting for in-house editorial approval by 31 <sup>st</sup> December 13.
20. Mini-Cog for the cross-sectional diagnosis of Alzheimer's disease dementia and other dementias within a secondary care setting	Protocol drafted. Submit the protocol for DTA editorial approval by 30 <sup>th</sup> October. Included studies identified and data extracted. Analyses completed. Writing review with the goal of submitting for in-house editorial approval by 31 <sup>st</sup> December 13.
21. Mini-Mental State Examination (MMSE) for the detection of Alzheimer's dementia and other dementias in people over 65 within a community setting	Protocol to be drafted. Search performed. Identifying included studies in progress.
22. Mini-Mental State Examination (MMSE) for the detection of Alzheimer's dementia and other dementias in people over 65 within a primary healthcare setting	Protocol to be drafted. Search performed. Identifying included studies in progress.
23. Mini-Mental State Examination (MMSE) for the detection of Alzheimer's dementia and other dementias in people over 65 within a secondary healthcare setting	Protocol to be drafted. Search performed. Identifying included studies in progress.



**Table 2. Progress of Intervention reviews (update up to 10<sup>th</sup> October '13)**

<b>Published</b>	
1. Huperzine A for vascular dementia – Z Hao	Published Issue 8 August 2011
2. Metal attenuating compounds for the treatment of AD – Liz Sampson	Published Issue 2 February 2012
3. Aspirin for vascular dementia – Gianetta Rands	Published Issue 11 November 2012
4. Driving assessment for maintaining mobility and safety in drivers with dementia – Alan Martin	Published Issue 5 May 2013
5. Thiamine for Wernicke-Korsakoff syndrome in people at risk from alcohol abuse – Ed Day	Published Issue 7 July 2013
<b>Ongoing</b>	
6. Aromatherapy for dementia – Lene Thorgrimsen Forrester	Submitted – Awaiting approval
7. Light therapy for managing cognitive, sleep, functional, behavioural, or psychiatric disturbances in dementia – Catherine Blake	Submitted – Awaiting approval
8. Respite care for people with dementia and their carers – Karla Soares-Weiser	Submitted – Awaiting approval
9. Physical activity programs for persons with dementia – Catherine Blake	Almost ready to publish
10. Propentofylline for dementia – Andrew Ntanda	With authors – Addressing comments
11. Validation therapy for dementia – Martin Neal	With authors – Addressing comments
12. Memantine for dementia – Rupert McShane	With author – Update ongoing
13. Statins for treatment of dementia – Bernadette McGuinness	With authors – Update ongoing
14. Ginkgo for cognitive impairment in dementia – Jacqueline Birks	With authors – Update ongoing
15. Rivastigmine for AD – Jacqueline Birks	With authors – Update ongoing

**Table 3 – Project dissemination activities**

Papers
<p>1. Noel-Storr A, Flicker L, Ritchie CW et al. Systematic review of the body of evidence for the use of biomarkers in the diagnosis of dementia. <i>Alzheimer &amp; Dementia</i> 2012. <i>Alzheimer &amp; Dementia</i> 2013; 9(3): e96-e105.</p>
Conferences
<p><u>Oral presentations &amp; symposium talks</u></p> <p>2. Oral presentation: Ritchie CW, Flicker L, Noel-Storr A, McShane R. A systematic review of the quality and reporting standards of longitudinal biomarker studies in dementia and recommendations. <i>Alzheimer's Association International Conference (AAIC)</i>, 16-21 July 2011, Paris, France.</p> <p>3. Oral presentation: McShane R, Quinn T, Noel-Storr A. Reporting and quality of longitudinal studies of diagnostic accuracy in MCI: A systematic literature review. <i>Alzheimer's Association International Conference (AAIC)</i>, 16-21 July 2011, Paris, France.</p> <p>4. Symposium talk: Noel-Storr A, Flicker L, Ritchie CW, McShane R. Reporting standards in diagnostic test accuracy studies in dementia: a review and recommendations. <i>4<sup>th</sup> Clinical Trials Conference on Alzheimer's Disease (CTAD)</i>, 3-5 November 2011, San Diego, CA, US.</p> <p>5. Symposium talk: Smailagic N, Noel-Storr, McShane R. PET-PiB biomarker for longitudinal diagnosis of Alzheimer's dementia and other dementias. <i>4<sup>th</sup> Clinical Trials Conference on Alzheimer's Disease (CTAD)</i>, 3-5 November 2011, San Diego, CA, US.</p> <p>6. Oral presentation: Ritchie CW, Flicker L, Noel-Storr A, McShane. A systematic review of the quality and reporting standards of longitudinal biomarker studies in dementia and recommendations. <i>27<sup>th</sup> International Conference of Alzheimer's Disease International</i>, 7-10 March 2012, London, UK.</p> <p>7. Oral presentation: Flicker L, Noel-Storr A, Ritchie CW, McShane R. Review of standards for the reporting of diagnostic accuracy studies. <i>Research and Standardization in Alzheimer's Disease (RASAD) International Conference</i>, 26-29 March 2012, Melbourne, Australia.</p> <p>8. Oral presentation: Flicker L, Ritchie CW, Noel-Storr A, McShane R, STARDdem Working Group. <b>Harmonisation of reporting standards for studies of diagnostic test accuracy in dementia and related conditions: the STARDdem (STAndards for the Reporting of Diagnostic accuracy studies-Dementia) criteria.</b> <i>Alzheimer's Association International Conference (AAIC)</i>, 14-19 July 2012, Vancouver, Canada.</p> <p>9. Oral presentation: Flicker L, Ritchie C, Noel-Storr A, McShane R. Harmonisation of Reporting Standards for Studies of Diagnostic Test Accuracy in Dementia and Related Conditions: the STARDdem (STAndards for the Reporting of Diagnostic accuracy studies-Dementia) Criteria. <i>International Psychogeriatric Association (IPA) International Meeting</i>, 7-11 September 2012, Cairns, Australia.</p> <p>10. Oral presentation: McShane R, Noel-Storr A, Flicker L, Ritchie CW, Wilcock G. Harmonisation of reporting standards for studies of diagnostic test accuracy in dementia: the STARDdem (STAndards for the Reporting of Diagnostic accuracy studies-Dementia) criteria. 5th Clinical Trials Conference in Alzheimer's Disease 29 Oct-3 November 2012, Monte Carlo, Monaco.</p> <p>11. Symposium talk: Wilcock G. et al. Harmonisation of reporting standards for studies of diagnostic test accuracy in dementia: the STARDdem (STAndards for the Reporting of Diagnostic accuracy studies-Dementia) criteria consensus meeting. Satellite symposium 5th Clinical Trials Conference in Alzheimer's Disease 28 October 2012, Monte Carlo, Monaco.</p> <p>12. Symposium talk: Noel-Storr A, et al. Scoping the evidence base - risk of overdiagnosis in dementia. 20th Cochrane Colloquium 30-3 October 2012, Auckland, New Zealand.</p>

13. Noel-Storr AH, Struthers C, McShane R et al. Many hands make light work – or do they? Results of two pilot studies looking at the effects of crowdsourcing. Oral presentation for the Cochrane Colloquium, Quebec 19-23 September 2013. [winner of Thomas Chalmers Award 2013]

Poster presentations

14. Noel-Storr A, McShane R. ALOIS: the next phase: a register of diagnostic studies. *Alzheimer's Association International Conference (AAIC)*, 16-21 July 2011, Paris, France.
15. McShane R, Ritchie CW, Quinn T, Noel-Storr A. Quality and reporting of studies of diagnostic tests in dementia. *Alzheimer's Association International Conference (AAIC)*, 16-21 July 2011, Paris, France.
16. Noel-Storr A, McShane R. ALOIS: the next phase: a register of diagnostic studies. *International Psychogeriatric Association (IPA)*, 6-9 September 2011, Hague, The Netherlands.
17. Noel-Storr A, Beecher D. The development of a methodological filter for studies of diagnostic accuracy in dementia. *19<sup>th</sup> Cochrane Colloquium*, 19-22 October 2011, Madrid, Spain.
18. McShane R, Flicker L, Ritchie CW, Noel-Storr A. The quality and reporting of longitudinal studies of diagnostic tests: a systematic review. *19<sup>th</sup> Cochrane Colloquium*, 19-22 October 2011, Madrid, Spain.
19. Quinn T, McShane R, Fearon P, Noel-Storr A, Stott DJ. IQCODE for diagnosis of dementia – systematic review and meta-analysis. *27<sup>th</sup> International Conference of Alzheimer's Disease International*, 7-10 March 2012, London, UK.
20. McShane R, Flicker L, Ritchie CW, Noel-Storr A. The quality and reporting of longitudinal studies of diagnostic tests: a systematic review. *17<sup>th</sup> Annual Cochrane Contributors Meeting*, 20-22 March, 2012, Loughborough, UK.
21. Noel-Storr A, Beecher D. The development of a methodological filter for studies of diagnostic accuracy in dementia. *17<sup>th</sup> Annual Cochrane Contributors Meeting*, 20-22 March, 2012, Loughborough, UK.
22. Ritchie CW, Flicker L, Smailagic N, Noel-Storr A, McShane R. Plasma and CSF Abeta for the diagnosis of Alzheimer's disease dementia and other dementias in mild cognitive impairment: a Cochrane systematic review. *Alzheimer's Association International Conference (AAIC)*, 14-19 July 2012, Vancouver, Canada.
23. Creavin S, Ewins E, Rayment D, Noel-Storr A, Cullum S. Crowdsourcing citation screening for a Cochrane diagnostic test accuracy review on the mini-mental state examination. Poster presentation for International Congress 2-5 July 2013 [YouTube link: <http://www.youtube.com/watch?v=ufwQZKuYkuE> ]
24. Noel-Storr AH. Search methods for diagnostic test accuracy reviews in dementia: an overview of a programme grant. Poster presentation for the Cochrane Colloquium, Quebec 19-23 September 2013.