HEALTH TECHNOLOGY ASSESSMENT (WINCHESTER, ENGLAND)

Various

Health Technol Assess. 2017 May; 21(26): 1–192. PMCID: PMC5494514

doi: 10.3310/hta21260 PMID: 28625273

Development of a core outcome set for disease modification trials in mild to moderate dementia: a systematic review, patient and public consultation and consensus recommendations.

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Abstract

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BACKGROUND

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There is currently no disease-modifying treatment available to halt or delay the progression of the disease pathology in dementia. An agreed core set of the best-available and most appropriate outcomes for disease modification would facilitate the design of trials and ensure consistency across disease modification trials, as well as making results comparable and meta-analysable in future trials.

OBJECTIVES

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To agree a set of core outcomes for disease modification trials for mild to moderate dementia with the UK dementia research community and patient and public involvement (PPI).

DATA SOURCES

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We included disease modification trials with quantitative outcomes of efficacy from (1) references from related systematic reviews in workstream 1; (2) searches of the Cochrane Dementia and Cognitive Improvement Group study register, Cochrane Central Register of Controlled Trials, Cumulative Index to Nursing and Allied Health Literature, EMBASE, Latin American and Caribbean Health Sciences Literature and PsycINFO on 11 December 2015, and clinical trial registries [International Standard Randomised Controlled Trial Number (ISRCTN) and clinicaltrials.gov] on 22 and 29 January 2016; and (3) hand-searches of reference lists of relevant systematic reviews from database searches.

REVIEW METHODS

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The project consisted of four workstreams. (1) We obtained related core outcome sets and work from co-applicants. (2) We systematically reviewed published and ongoing disease modification trials to identify the outcomes used in different domains. We extracted outcomes used in each trial, recording how many used each outcome and with how many participants. We divided outcomes into the domains measured and searched for validation data. (3) We consulted with PPI participants about recommended outcomes. (4) We presented all the synthesised information at a conference attended by the wider body of National Institute for Health Research (NIHR) dementia researchers to reach consensus on a core set of outcomes.

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RESULTS

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We included 149 papers from the 22,918 papers screened, referring to 125 individual trials. Eighty-one outcomes were used across trials, including 72 scales [31 cognitive, 12 activities of daily living (ADLs), 10 global, 16 neuropsychiatric and three quality of life] and nine biological techniques. We consulted with 18 people for PPI. The conference decided that only cognition and biological markers are core measures of disease modification. Cognition should be measured by the Mini Mental State Examination (MMSE) or the Alzheimer's Disease Assessment Scale - Cognitive subscale (ADAS-Cog), and brain changes through structural magnetic resonance imaging (MRI) in a subset of participants. All other domains are important but not core. We recommend using the Neuropsychiatric Inventory for neuropsychiatric symptoms: the Disability Assessment for Dementia for ADLs, the Dementia Quality of Life Measure for quality of life and the Clinical Dementia Rating scale to measure dementia globally.

LIMITATIONS

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Most of the trials included participants with Alzheimer's disease, so recommendations may not apply to other types of dementia. We did not conduct economic analyses. The PPI consultation was limited to members of the Alzheimer's Society Research Network.

CONCLUSIONS

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Cognitive outcomes and biological markers form the core outcome set for future disease modification trials, measured by the MMSE or ADAS-Cog, and structural MRI in a subset of participants.

FUTURE WORK

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We envisage that the core set may be superseded in the future, particularly for other types of dementia. There is a need to develop an algorithm to compare scores on the MMSE and ADAS-Cog.

STUDY REGISTRATION

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The project was registered with Core Outcome Measures in Effectiveness Trials [www.comet-initiative.org/studies/details/819?

result=true (accessed 7 April 2016)]. The systematic review protocol is registered as PROSPERO CRD42015027346.

FUNDING

Go to:

The National Institute for Health Research Health Technology Assessment programme.

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