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Diagnosing Alzheimer's disease: A systematic review of economic evaluations

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Abstract

Background: The objective of this study is to systematically review the literature on economic evaluations of interventions for the early diagnosis of Alzheimer's disease (AD) and related disorders and to describe their general and methodological characteristics. We focused on the diagnostic aspects of the decision models to assess the applicability of existing decision models for the evaluation of the recently revised diagnostic research criteria for AD.

Methods: PubMed and the National Institute for Health Research Economic Evaluation database were searched for English-language publications related to economic evaluations on diagnostic technologies. Trial-based economic evaluations were assessed using the Consensus on Health Economic Criteria list. Modeling studies were assessed using the framework for quality assessment of decision-analytic models.

Results: The search retrieved 2109 items, from which eight decision-analytic modeling studies and one trial-based economic evaluation met all eligibility criteria.

Conclusions: Diversity among the study objective and characteristics was considerable and, despite considerable methodological quality, several flaws were indicated. Recommendations were focused on diagnostic aspects and the applicability of existing models for the evaluation of recently revised diagnostic research criteria for AD.

Keywords: Alzheimer's disease; Neurodegenerative disorder; Dementia; Early diagnosis; Diagnostic intervention; Biomarker; Economic evaluation; Health technology assessment; Cost-effectiveness; Costs; Modeling; Decision-analytic model; Quality assessment; Review

1. Introduction

Alzheimer's disease (AD) and other dementing disorders are common in the elderly, with a worldwide prevalence estimated in 2010 at 35.6 million, which will increase to 115.4 million in 2050. AD has a substantial impact on the person who suffers from the disease, his or her family, and society [1,2]. The total worldwide cost of AD and other dementing disorders was estimated at $604 billion in 2010 [3].

Earlier diagnosis and early intervention are considered important mechanisms to manage the worldwide impact of the disease. Early diagnosis can be described as a "timely" recognition of mild dementia in response to a patient's complaints to ensure that disabled individuals receive the necessary support and care or as the "symptomatic predementia" diagnosis when cognition is impaired but functioning not yet affected (typically referred to as mild cognitive impairment) [4].

Until recently, the diagnosis of AD was largely based on clinical judgment using the NINCDS-ADRDA criteria [5]. These criteria were recently revised [6–8] to enhance diagnostic accuracy and enable an early diagnosis even when only very mild clinical symptoms are present. Biomarkers in cerebrospinal fluid (CSF), positron emission

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tomography (PET), magnetic resonance imaging (MRI), and photon emission tomography (SPECT) are attributed a more prominent role in the new diagnostic research criteria. However, validation of these research criteria is needed before the role of new biomarkers can be adopted in clinical practice [9].

The ultimate goal of diagnostic testing is to guide disease management to improve patient outcomes and patient well-being. Tests that lack this potential are considered obsolete [10,11]. Furthermore, because health-care resources are scarce and must be allocated efficiently, decision-makers require evidence of the cost-effectiveness of diagnostic tests before adoption in clinical practice. Such evidence can be generated by decision-analytic models which are defined as a set of mathematical relationships that form a structure reflecting the natural progression of a disease. By simulating patient cohorts, these models enable the estimation of the likelihood of each consequence and its corresponding costs and effects [12,13]. Trial-based economic evaluations, in which costs and health-care outcomes are measured during clinical trials, can also provide evidence of cost-effectiveness.

Decision-analytic models of AD have been reviewed extensively by Cohen et al [14]. However, this review only included models that project disease progression, excluding possible relevant evidence on the evaluation of diagnostic techniques. Furthermore, the applicability of existing decision models to evaluate the recently revised research criteria has not been elaborated. This raises the urgent need for a review of economic evaluations of diagnostic interventions for AD.

The objective of this study was to systematically review the literature on economic evaluations of interventions for the early diagnosis of AD and related disorders and to describe their general and methodological characteristics. Using these results, recommendations for future studies were focused on the diagnostic aspects of the decision models to assess the applicability of existing decision models for the evaluation of the recently revised diagnostic research criteria for AD.

2. Methods

2.1. Search strategy

A systematic literature review was performed to identify economic evaluations of diagnostic interventions for AD or related dementias. The following eligibility criteria were applied:

1. The study should focus on a population, either an empirical (primary data) or a theoretical (model), which is suffering from or suspected of suffering from AD or related disorders (vascular dementia, dementia with Lewy bodies, and frontotemporal dementia). The population should consist of previously undiagnosed individuals. Studies of neurodegenerative disorders were excluded (e.g., Parkinson's, Huntington's disease, or depression).
2. The population reflects humans, 55 years of age or older.
3. The intervention is a diagnostic technology, tool, questionnaire, process, procedure, or protocol used for a timely or symptomatic predementia diagnosis of AD or related dementias in a clinical setting. Screening tools and risk, severity, or progression analyses were excluded (screening tools such as the Mini-Mental State Examination [MMSE] or DNA risk assessment).
4. The study reports primary patient and/or cost data or uses a mathematical model that is based on such data. Reviews, case studies, and publications that merely describe methodological issues were excluded.
5. The study is an economic evaluation: either a cost-consequence [15] analysis or a full economic evaluation (cost-effectiveness, cost-utility, or cost-benefit analyses). Partial economic evaluations, which do not include a comparison between different strategies or do not analyze both costs and consequences [16], were excluded.

PubMed and the National Institute for Health Research Economic Evaluation Database databases [17,18] were searched through March 2011. Medical subject headings and free text words on dementia, diagnosis, and economic evaluation were used to identify relevant English-language articles with an available abstract (see Appendix 1 for the full search query).

Two reviewers (R.H. and C.W.) independently assessed titles. A title was excluded if both reviewers agreed that it explicitly met one of the exclusion criteria. The same reviewers independently assessed abstracts of the remaining titles. An abstract was excluded if either reviewer considered that it did not meet all five inclusion and exclusion criteria. Dissimilarities in the reviewers' assessments were resolved by discussion. The full article was assessed if the remaining abstracts had dissimilarities that could not be otherwise resolved. If an article was not accessible, the author was contacted to request a copy of the original publication. A third reviewer (J.S.) resolved the remaining differences in the reviewer's assessments; this third reviewer made the final decision as to whether the article would be included. See Appendix 2 for an overview of the study selection process.

2.2. Analyses

General study characteristics of all of the included articles are described in Table 1. For modeling studies, the model type was scored separately for the diagnostic and treatment part of the model. A Markov model is characterized by mutually exclusive disease states that represent the possible consequences of the options under evaluation. Disease progression is reflected by the transition of a patient's disease states over discrete time periods [12]. We used the