

Conceptualizing disease: building unifying models to support the development of PROs and cost-effectiveness analyses. A case study in Alzheimer's Disease (AD)

Wild D, Mealing S, Gallop K, Nixon A, Lloyd A, Briggs A, Sculpher M

Oxford Outcomes Ltd, Oxford, United Kingdom

INTRODUCTION

Conceptual models are used in Patient Reported Outcomes (PRO) research to explore a disease or treatment. They are developed for a number of reasons including the selection, adaptation or development of a PRO measure and the development of an endpoint model. They have long been used in psychology and health education to explore the relations between concepts.

Approaches similar to conceptual models are also used by decision analysts and health economists to understand the underlying mechanism and natural history of a particular disease. These models typically form the basis from which a cost-effectiveness model is constructed. However, in the models constructed by a health economist here is perhaps less emphasis on patient experience than those constructed by a PRO analyst where this is more of the focus.

However, there is we believe considerable potential for using a shared approach to developing models which will meet the aims of both groups. Such a unified approach we believe can only lead to greater validity and a convergence of the science.

METHODS

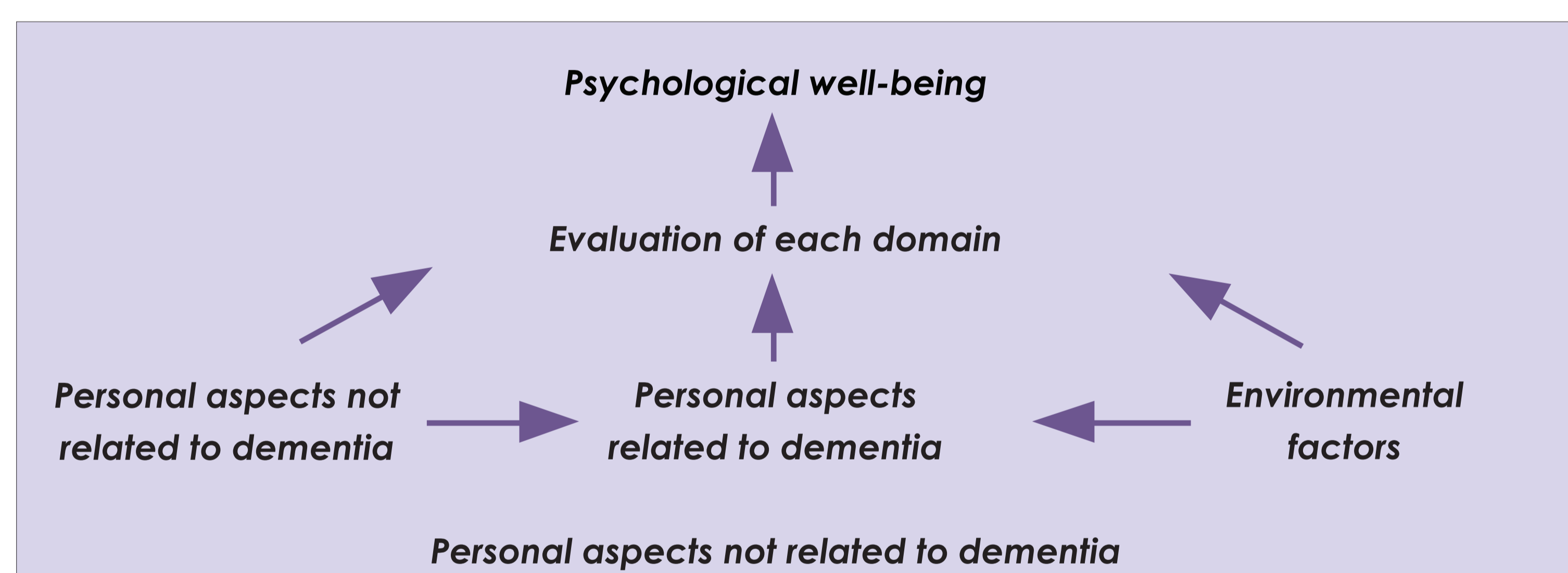
To explore the potential for a shared approach the authors reviewed two models of the same disease - Alzheimer's disease (AD). The authors reviewed the structure of a health economic model of the disease which described the progression from diagnosis to death. They also reviewed a published QoL model of AD from a patient perspective (Jonker et al, 2004). The patient oriented conceptual model and the economic model are presented below:

Conceptual Model

The introduction of drugs used to treat AD has increased levels of interest in measuring quality of life (QoL) in dementia patients (Brod et al, 1999). Jonker et al (2004) propose a model of QoL in dementia (see figure 2).

The conceptual model of AD developed by Jonker et al (2004) extends work by Lawton (1994). Lawton suggested a hierarchical view of QoL in dementia, with psychological well-being as the ultimate outcome. This model includes the interrelationships between dimensions. The model is disease specific, however, not all dimensions of the model are influenced by the disease. The model identifies the causal pathways that link different types of outcomes. According to this model, QoL can be measured at three levels. The relative importance of the domains may vary across patients, although it is assumed that for all patients with dementia, a number of these are important and contribute to psychological well-being, the central outcome measure. The model focuses on the dementia patient, and does not consider the subsequent impact on the caregiver's QoL, if the patient is being cared for at home. The model is more generic and less detailed than other conceptual models, which perhaps makes it less useful from a health economic perspective.

Figure 1 – Conceptual Model



Economic Model

AD is a common and incurable ailment of the elderly. It is degenerative and during the later stages of the illness individuals are unable to undertake everyday tasks and thus require large amounts of specialist care. AD thus constitutes a significant burden on the budget of any health care provider.

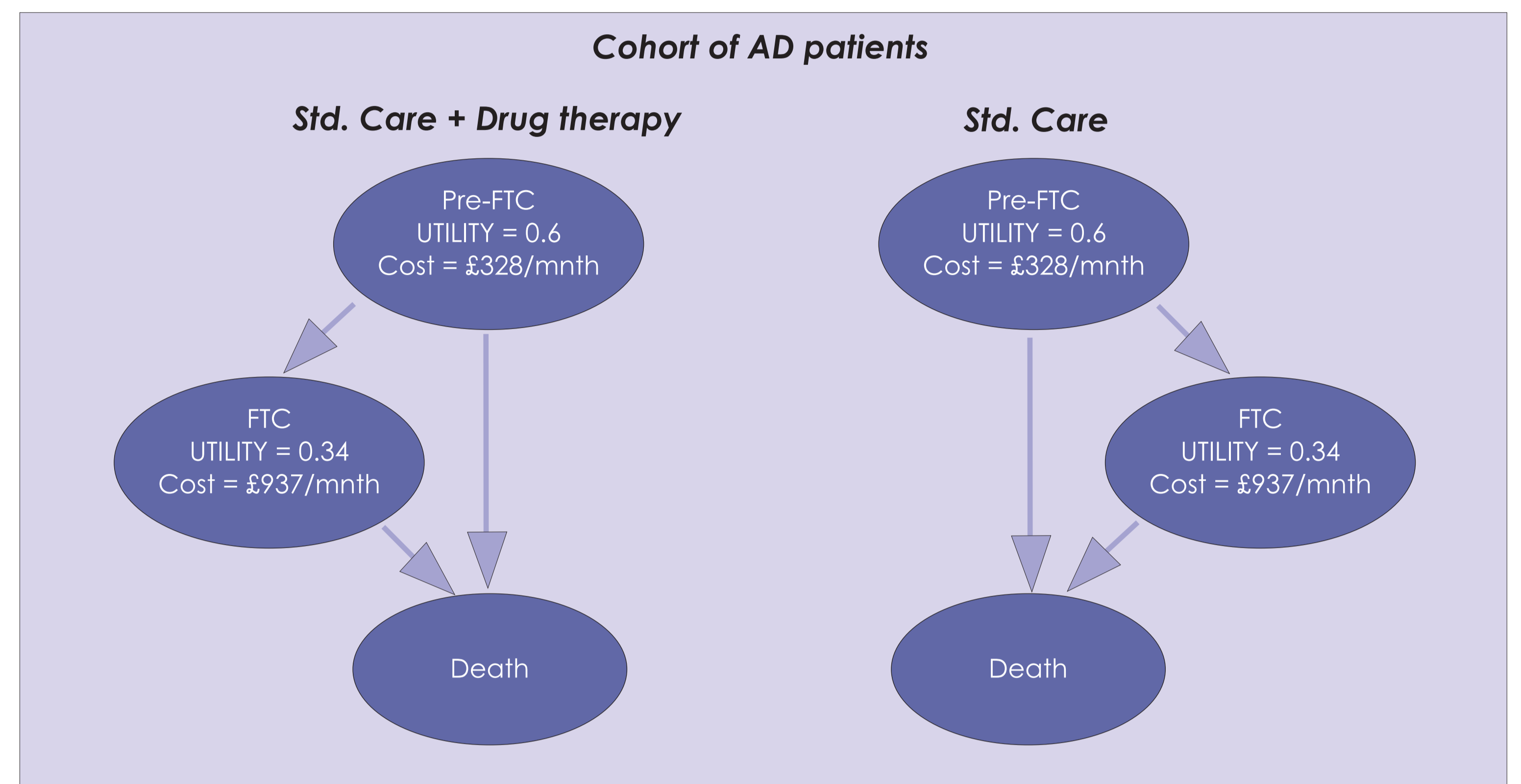
The economic model is based around the concept of the need for full time care (FTC - either in an institution or at home). The rationale behind this approach being that prior to this point, care tends to be less intensive and is usually provided by family and friends and thus the cost to health care providers is relatively minor. The need for full time care is also a proxy for severe disease and is associated with a reduction in an individuals' quality of life. Three licensed products exist (galantamine, rivastigmine and donepezil) that aim to extend the period of time a patient can live without the need to full time care. The schematic of the model is shown in figure 1.

Structurally, the model has two components. A short term module covering an initial six month period, and a long term module with a 10 year time horizon. At the start of the model, matched cohorts of patients were generated using the following patient characteristics: Age, age at onset of disease, duration of illness, gender, cognitive function

(as measured using the ADAD-COG instrument), the presence of extrapyramidal symptoms, and the presence of hallucinations or delusions.

In the long term module, mathematical functions were used to calculate the time dependant probabilities of moving from pre-FTC to FTC, and from either state to death. Baseline characteristics and change in ADAS-COG during the short term module were used as independent variables in all risk equations. The model has been implemented as a patient level simulation (Caro et al, 2001) and, after modification, a closed cohort Markov model (Loveman et al, 2006).

Figure 2 Economic Model



RESULTS

A large number of points of overlap were identified. These included the impacts of AD on day to day functioning of the patient which will have an impact on caregiver burden, and will influence the ability of the caregiver to work and impact on other resource utilisation. This may, in turn, have an impact on the time to institutionalisation which is where the major cost burden of AD is.

If the economic and conceptual modeling had been undertaken concurrently, however, the conceptual models insight into the multi-factorial influences on patients' health (in terms of psychological well-being) may have led to different approaches to the economic modeling. In particular, although a patient's entry into full time care may represent a step-change in the cost of caring for AD patients, it is not clear whether this is a major driver for patients' health status. Structuring the economic model around health states, defined in terms of the key determinants of psychological health on which medical interventions may impact, would be an alternative approach. These health states would effectively use patients' health (as reported by patients and their carers) to characterize the natural history of AD, including the likely increase in severity over time. The costs of care (including that related to institutionalization) would be quantified as a function of that severity.

CONCLUSIONS

The synergy found between PRO and health economic models lead us to suggest that there is merit in developing many models simultaneously and as early as possible in the drug development life cycle. This is likely to increase the validity of each of the models, as well as having a positive impact on related research, for example, the development of health states for utility elicitation.

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