The course of mild cognitive impairment and the role of comorbidity

KNOWLEDGE VALORISATION

The goal of this valorisation paragraph is to describe how the knowledge resulting from the research in this dissertation can be made valuable for clinical and social use. This dissertation focuses on the natural course of cognitive decline in people with Mild Cognitive Impairment (MCI) and the influence of comorbidity on outcomes in this population.

Societal relevance

Dementia is a growing health problem, since the number of people with dementia is thought to dramatically rise due to the ageing population. This development poses a major challenge for society, health care systems and also has great economical impact. Already in 2011, dementia was the second most expensive medical disease in the Netherlands, with disease-associated costs of almost 5 billion euros. Furthermore, dementia is thought to have the highest disease burden of all medical illnesses for the patient, but has also a tremendous impact on the caregiver.

Currently, the transitional state between normal cognitive functioning and dementia is usually referred to as Mild Cognitive Impairment (MCI). MCI denominates a heterogeneous group of people with large individual variation in the level and pattern of cognitive impairment, course of decline over time and thus prognosis. Therefore, the uncertain MCI label often leads to negative reactions from patients and caregivers and may evoke anxiety, loss of self-confidence, feelings of depression etcetera.

Thus, there are multiple reasons for investigating the course of cognitive decline in MCI as has been done in this thesis. First, for patients and caregivers, a more accurate prognosis on the risk of developing dementia is important to end the uncertainty currently associated with the MCI label and it allows patients and caregivers to make arrangements for the future. In addition, when it is possible to differentiate between individuals who are likely to develop dementia and those who are not, clinicians will be able to initiate timely care, (psychological) treatment and support, which will likely reduce health care costs. Further, if pharmacological treatment becomes available in the future, these drugs are likely to be most effective in the early stages of the disease, which ultimately reduces the total disease burden for society and health care and also diminishes costs.

Target audience

The results described in this dissertation are relevant to various stakeholders who are involved in dealing with dementia and it's consequences.

First, the results are especially relevant for people with cognitive complaints and their families, since they often want to know the course of their cognitive

complaints, and whether patients are at increased risk of developing dementia and/or becoming care dependent in the near future.
Clinicians working in memory clinics are also important stakeholders, since they are the ones who have to inform patients with cognitive complaints about their risk of developing dementia in the future. The results of this thesis will aid them improving the accuracy of prognosis by increasing knowledge about which neuropsychological tests are important and early indicators of developing dementia pathology. As a result, they can better inform patients and their families about risks and what specific actions need to be taken. Further, support and education can be given at an early stage and when in the future disease-modifying treatment is available these patients will be an important target group.
Commercial organization concerned with neuropsychological test development could use the results to improve their products and create more dementia-sensitive test batteries. As it appears that especially cognitive decline in episodic memory, executive functioning and global cognitive functioning are important indicators of developing dementia, extra focus should be placed on the development of sensitive, reliable tests that accurately measure small changes in these domains over time.
Decision makers in (government) organizations involved in health care regulations, such as the Dutch Centraal Begeleidingsorgaan (CBO), or similar entities worldwide, could use the results of this thesis to adapt their recommendations about neuropsychological test protocols in dementia diagnostics, placing more emphasis on decline in executive functioning and global cognitive functioning and less on decline in attention/speed.

Products
The main products of this dissertation are the implications that our results have for routine clinical practice in the assessment of cognitive complaints. In the first place, our results have consequences for the use of optimal neuropsychological test batteries that aim to detect dementia at an early stage. Our results indicate that neuropsychological test protocols should be reshaped, not primarily focussing on episodic memory, but giving equal importance to executive functioning and global cognitive functioning, using sensitive and reliable measures. In addition, the main emphasis should not be on attention/speed, since we showed that decline in this domain did not differ between converters to dementia and non-converters.
Besides, we showed that performance and decline on speed-related tests is influenced by the severity of comorbidity. This implicates that a broad assessment of additional medical factors, is important in clinical practice, to take into account other potential causes for cognitive impairment. Further, since (part of) these factors are potentially modifiable, they are also an important target for interventions to ameliorate cognitive performance and in the long-term prevent cognitive decline and conversion to dementia. The importance of the broad

assessment of additional non-cognitive factors in clinical practice is supported by our findings that Health-related Quality of Life is associated with comorbid disease burden and depressive symptoms. Our general findings thus emphasize the importance of a multidisciplinary approach in the diagnostic and treatment possibilities for people with MCI.

Innovation

The results in this dissertation are among the first that are based on a large multicentre clinical cohort of people, meaning that patients included in our study presented themselves with cognitive complaints at a memory clinic. This distinguishes them from cognitively normal subjects from the general population who are most often selected for studies into early stage cognitive decline.
Further, in contrast to what is often done in MCI studies, we explicitly chose to apply broad inclusion criteria, in which most comorbid disorders were not excluded. By this means, we avoided the elimination of these potentially important contributing factors in advance and maximized generalization to the general elderly population, which is characterized by an increased disease burden and multimorbidity.

Valorisation process

Before the results of this dissertation are likely to be applied in clinical practice, several additional steps are required. First, other clinical studies into early stage cognitive decline have to be performed to confirm our results. These studies should also include patients with a variety of comorbidities, since they appear to influence both cognitive decline and Health-related Quality of Life in memory clinic visitors. Further, the inclusion of comorbidities live up to the notion that dementia is a multifactorial disease, with diseases and factors not necessarily located in the brain enhancing underlying neurodegenerative pathologies. As far as we are aware, large-scale studies with comparable broad inclusion criteria like ours have not been conducted yet, so new studies have to be set up.
On the long term, when our results are validated, neuropsychological test protocols should be reshaped, putting more emphasis on executive functioning and global cognition besides episodic memory and attribute less importance to impairments in attention/speed. Tests for these domains are widely available and used in clinical practice, so practical issues do not hinder implementation in this regard, although new, more reliable and sensitive measures might be developed specifically for the purpose of dementia screening. To assure standardization and allow comparison between assessments at different facilities in the Netherlands, agreements should be made about the exact tests that are recommended to measure the indicated domains. To assure generalisation to all hospital and memory clinics the CBO should include these recommendations about the test protocol in the guidelines for dementia diagnostics and treatment. To make sure

that members of the advisory committee of the CBO are aware of the current outcomes, it is important to spread the results within the dementia research community by publication in international journals and presentations on dementia related conferences. Ultimately, when results would be implemented in clinical practice, the health care costs associated with dementia could be reduced. First, by offering support and education and an early stage, by means of which patients are likely to be able to live in their home setting longer, thereby avoiding the costs associated with nursing home placement. Second, if disease-modifying medication becomes available in the future, these patients are likely to not develop the full-blown dementia syndrome and so health care costs associated with severe dementia are no longer applicable in these cases.