

# Meanings and Multiplicity

*Assessing Early Diagnostics for Alzheimer's  
Disease*

Samenstelling beoordelingscommissie:

Prof. dr. Tjard de Cock Buning

Prof. dr. John Grin

Prof. dr. Annette Leibing

Prof. dr. Jeannette Pols

Prof. dr. Tsjalling Swierstra

This research received funding from the Responsible Innovation program of NWO (grant no. 313-99-170), the Dutch science foundation.

ISBN 978-90-9031330-6

Copyright © Y.M. Cuijpers

All rights reserved. No parts of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, without prior written permission of the author.

# Meanings and Multiplicity

## *Assessing Early Diagnostics for Alzheimer's Disease*

**Twijfeltocht door Alzheimerland**

*Betekenenissen van vroegdiagnostiek van de ziekte van Alzheimer*

(met een samenvatting in het Nederlands)

**Proefschrift**

ter verkrijging van de graad van doctor aan de Universiteit Utrecht

op gezag van de rector magnificus, prof. dr. H.R.B.M. Kummeling,

ingevolge het besluit van het college voor promoties

in het openbaar te verdedigen

op woensdag 28 november 2018 des middags te 12.45 uur

door

**Yvonne Maria Cuijpers**

geboren op 6 september 1981 te Gemert

Promotoren:

Prof. dr. E.H.M. Moors

Prof. dr. ir. H. van Lente

# Contents

## INTRODUCTION

<b>Chapter 1 Introduction</b> .....	<b>11</b>
1.1 Multiple meanings of early diagnostics for Alzheimer’s disease .....	11
1.2 Early diagnostics and responsible innovation .....	13
1.3 Research questions and outline of the thesis .....	15

## SETTING THE STAGE

<b>Chapter 2 Thinking about early diagnostics for Alzheimer’s disease: history, diagnosis, ailment</b> .....	<b>21</b>
2.1. A history of Alzheimer’s disease .....	22
2.1.1 The ‘classical’ period: linking symptoms to brains.....	22
2.1.2 The psychosocial turn: dementia as a social problem .....	24
2.1.3 Renaissance of pathology.....	27
2.1.4 A sea change .....	28
2.1.5 Drawbacks of the raising of attention to Alzheimer’s disease .....	32
2.1.6 Renaissance of psychosocial approaches.....	34
2.1.7 Lessons from the history of Alzheimer’s disease .....	35
2.2. Thinking about diagnosis: Early diagnostics for Alzheimer’s disease from a medical point of view .....	37
2.2.1 Disclaimer on the terms ‘early’ and ‘diagnostics’ .....	38
2.2.2 The pathological cascade model.....	39
2.2.3 Promises of early diagnostics for Alzheimer’s disease .....	41
2.2.4 Medical controversy on the promises of early diagnostics.....	48
2.2.5 Lessons from the medical point of view on Alzheimer’s disease.....	50
2.3. Thinking about diagnosis: Early diagnostics for Alzheimer’s disease from a clinical, psychosocial and social science point of view .....	51
2.3.1 Early diagnosis in diagnostic clinical practice.....	52
2.3.2 How persons with dementia experience the diagnosis.....	54
2.3.3 Sociology of diagnosis .....	58
2.3.4 Lessons from a clinical, psychosocial and sociological point of view.....	60
2.4 Thinking about dementia and ailments in general .....	60

2.4.1 Explanatory models of dementia.....	61
2.4.2 Conceptualizing ailment.....	66
2.4.3 Ailment in practice .....	68
2.4.4. Lessons from thinking about dementia and ailments in general.....	69
2.5 Concluding remarks.....	69
<b>Chapter 3 Quandaries of responsible innovation: the case of Alzheimer’s disease.....</b>	<b>71</b>
3.1 Quandary one: technocentric or multi-actor views on innovation .....	72
3.2 Quandary two: singular or multiple futures?.....	74
3.2 Quandary three: identifying with whom? .....	76
3.4 Quandary four: process or outcome? .....	78
3.5 Quandary five: speculation or plausibility.....	80
3.6 Quandary six: responsibility for the future or responsibility for the present .....	81
3.7 Conclusion.....	83
<b>Chapter 4 Research approach: studying the meaning of early diagnosis .....</b>	<b>85</b>
4.1 Three theoretical approaches on the construction of meaning .....	85
4.1.1 Discourse analysis.....	85
4.1.2 Modes of ordering.....	87
4.1.3 Framing analysis .....	89
4.2 Lessons drawn: studying the meaning of early diagnosis .....	90
4.2.1 The networked nature of the construction of meaning.....	91
4.2.2 Patterns in the construction of meaning .....	91
4.2.3 The politics of ordering in a messy, plural world .....	92
4.2.4 Making sense of making sense .....	92
4.3 Research design choices .....	93
4.3.1 The tourist approach .....	94
4.3.2 A focus on language to analyse meaning .....	95
4.3.3 Medium sized constructions of meaning in practice.....	96
4.3.4 Meaning in action.....	98
4.3.5 A modest position.....	99
4.4 Data gathering and analysis .....	99
4.4.1 Selecting settings to study meanings of early diagnostics for Alzheimer’s disease .....	99
4.4.2 Gathering data .....	100

4.4.3 Analysing data.....	103
---------------------------	-----

## STAGING THE SETTING

<b>Chapter 5 The meanings of early diagnostics for Alzheimer's disease in Dutch newspapers - A framing analysis.....</b>	<b>107</b>
--	------------

5.1 Construction of meanings in newspapers.....	107
---	-----

5.2 Method.....	109
-----------------	-----

5.3 Interpretative packages .....	110
-----------------------------------	-----

5.3.1 Apocalyptic demography .....	110
------------------------------------	-----

5.3.2 Scientific progress.....	111
--------------------------------	-----

5.3.3 Complex scientific puzzle .....	111
---------------------------------------	-----

5.3.4 Technological progress.....	112
-----------------------------------	-----

5.3.5 Economic competitiveness .....	112
--------------------------------------	-----

5.3.6 Health care provision .....	113
-----------------------------------	-----

5.3.7 Successful aging.....	113
-----------------------------	-----

5.3.8 Fear, worry, and approaching mischief.....	113
--	-----

5.3.9 Good life and death.....	114
--------------------------------	-----

5.4 Conclusions: multiplicity in 'popularizing' early diagnosis of Alzheimer's disease ....	116
---	-----

<b>Chapter 6 Early diagnostics and Alzheimer's disease: Beyond 'cure' and 'care' .....</b>	<b>119</b>
--	------------

6.1 Introduction: 'cure' or 'care' .....	119
--	-----

6.2 Theory: Alzheimer's and storytelling.....	121
---	-----

6.3 Methods.....	123
------------------	-----

6.4 Results.....	126
------------------	-----

6.4.1 Setting one: health technology assessment .....	126
---	-----

6.4.2 Setting two: Alzheimer Café.....	134
--	-----

6.5 Discussion and conclusions.....	141
-------------------------------------	-----

<b>Chapter 7 Deltaplan Dementia .....</b>	<b>145</b>
---	------------

<b>Part A. Dikes and dementia: How multiple framings of dementia co-exist during the development of a national dementia strategy.....</b>	<b>147</b>
---	------------

7.1 Introduction.....	147
-----------------------	-----

7.2 Theory and methods .....	148
------------------------------	-----

7.3 Results.....	149
------------------	-----

7.3.1 Together we build the dike .....	149
--	-----

7.3.2 Keeping all frogs in the wheelbarrow .....	151
7.3.3 Framing contests becoming public.....	153
7.4 How frames co-exist.....	155
<b>Part B. The dynamic meanings of early diagnostics in the Deltaplan Dementie.....</b>	<b>159</b>
7.5 Introduction .....	159
7.6 Together we build the dike – drawing attention and mobilizing resources.....	160
7.6.1 Disaster rhetoric and early diagnostics .....	160
7.6.2 Early diagnostics and the aging-and-innovation discourse .....	163
7.7 Keeping all the frogs in the wheelbarrow – <i>research program Memorabel</i> .....	164
7.8 Framing contests becoming public – <i>public debate</i> .....	168
7.9 Behind the scenes of the public debate.....	169
7.9.1 A timely diagnosis as a prerequisite for good care.....	170
7.9.2 Early diagnostics and pre-dementia stages.....	171
7.9.3 Early diagnostics and the development of disease modifying treatment.....	172
7.9.4 Medicalization of coping with dementia.....	173
7.10 Discussion and conclusion on the dynamic meanings of early diagnostics in the Deltaplan Dementie.....	175

## DISCUSSION AND CONCLUSIONS

<b>Chapter 8 Discussion and conclusions .....</b>	<b>181</b>
8.1. The meanings of early diagnostics for Alzheimer’s disease .....	182
8.1.1. Setting 1: Dutch newspaper articles.....	183
8.1.2. Setting 2: a Health Technology Assessment .....	184
8.1.3. Setting 3: Alzheimer Cafés .....	185
8.1.4. Setting 4: Deltaplan Dementie.....	187
8.1.5. Subconclusions: meanings of early diagnostics for Alzheimer’s disease .....	189
8.2. Technology assessment ‘in the wild’ .....	193
8.2.1. Acts of assessment .....	193
8.2.2. The scope of implications .....	194
8.2.3. Patterns <i>within</i> settings: Threads of assessment .....	194
8.2.4. Patterns <i>between</i> interpretative packages recurring <i>across</i> settings: Meanings co-exist, but do not accommodate every arrangement .....	197
8.2.5. Subconclusions: technology assessment ‘in the wild’ .....	206

8.3. Responsible innovation .....	207
8.3.1. Understanding implications of early diagnostics for Alzheimer’s disease .....	207
8.3.2. The benefit of the doubt .....	210
8.4 To conclude.....	214
<b>Appendices.....</b>	<b>217</b>
Appendix 1: A non-exhaustive list of explorations in the dementia landscape .....	217
Appendix 2A : Number of articles related to interpretative packages .....	219
Appendix 2B: Search strings used in LexisNexis.....	219
Appendix 2C .....	219
<b>References.....</b>	<b>221</b>
<b>Summary .....</b>	<b>241</b>
<b>Samenvatting.....</b>	<b>251</b>
<b>Dankwoord.....</b>	<b>263</b>



# Chapter 1

## Introduction

The central topic of this thesis is responsible innovation of early diagnostics for Alzheimer's disease. The development of early diagnostics for Alzheimer's disease is approached from a social science perspective, and particularly a Science and Technology Studies (STS) perspective.

To understand the social and cultural implications of early diagnostics for Alzheimer's disease, the meanings of early diagnostics for Alzheimer's disease are traced and analysed in a number of settings. We encountered a kaleidoscopic collection of multiple meanings. To acknowledge and show the complexity of this innovation is in itself a contribution to responsible innovation of early diagnostics for Alzheimer's disease.

The specific approach towards responsible innovation is (1) that it is possible to conduct technology assessment 'in the wild' without using specific TA or foresight tools to mobilize the views of stakeholders; and (2) that the assessment of new and emerging technologies can be empirically studied in the present – in other words, it is not necessary to imagine future situations in order to assess consequences. This study shows how an empirical study of multiple meanings can contribute to responsible (research and) innovation.

This thesis will be of interest to various audiences. First, it is interesting for those who are interested in dementia, Alzheimer's disease, (early) diagnostics for Alzheimer's disease and diagnostic innovation in general. Second, it is interesting for those interested in responsible (research and) innovation. In both cases the group includes academic researchers, policy makers, health care practitioners and other societal actors.

In the first section of this introduction I will argue why the meanings of early diagnostics for Alzheimer's disease deserve critical scrutiny and what this study seeks to contribute to the field of 'dementia sciences' (section 1.1). In the second section of this introduction I argue how this study relates to the ambition of responsible (research and) innovation (section 1.2.). These first explorations will then lead to the research question and a general outline of the thesis (section 1.3).

### **1.1 Multiple meanings of early diagnostics for Alzheimer's disease**

In aging societies such as the Netherlands, due to demographic changes and due to the fact that people live longer and in relatively good health, there is an increasing number of elderly persons who at the same time become older than previous generations. Because age is the most important risk factor for Alzheimer's disease, this is also expected to lead to a growing number of persons with Alzheimer's disease (and other types of dementia for which age is the most important risk factor). The number of persons with Alzheimer's disease is already increasing and is expected to continue to increase in the Netherlands, but also worldwide.

In policy circles there is a growing awareness, not only of the ‘societal challenges’ the aging society poses, but also that public and political attention is needed to deal with the growing number of persons with dementia in society (World Health Organization, 2012). This growing awareness has led to increasing investments in science and innovation to find (partial) solutions to deal with dementia in society (Winblad et al., 2016). One of the innovations in which a lot of hope (and money) is invested are early molecular diagnostic tests for Alzheimer’s disease. Molecular diagnostic tests promise to enable a more reliable and earlier identification of Alzheimer’s disease, at a stage with mild symptoms or even before symptoms occur (Jack et al., 2010).

While these tests have potential to contribute to a more reliable and earlier diagnosis of Alzheimer’s disease, and improve the quality of people’s lives and society, the value and desirability of early diagnostics for Alzheimer’s disease are not uncontested. From within the clinical and medical community, questions are raised on many topics. For example, what is the use of such tests, when medication to cure, arrest or slow down the disease is lacking? What is the use of biomarker tests for the prospects of a person in terms of the development of symptoms, especially since there is no direct relationship between pathological processes in the body and the symptoms a person experiences? Are these tests only interesting for research purposes, or also for clinical practice?

In fields such as medical anthropology and sociology, early diagnostics of Alzheimer’s disease, being a highly medical endeavour, is usually described as part of a biomedical interpretation of dementia, which views dementia as a medical problem and the responsibility of the medical field to deal with it, through understanding the causes, (early) diagnosis and treatment. The medical interpretation of dementia is often considered as (too) dominant and creates the risk of overlooking social, cultural and psychological aspects of the condition (Lyman 1989; Robertson, 1990).

Instead of deciding on the ‘correct’ meaning of Alzheimer’s disease, I decided to take the multiplicity of meanings as the phenomenon under investigation: how do people make sense of this development and what meanings are attached to early diagnostics for Alzheimer’s disease? After all, innovation does not take place in the void of a lab or research centre, but in interaction with society. Technology and society mutually shape each other in a co-evolutionary process (Rip & Kemp, 1998). While early diagnostics for Alzheimer’s disease is a medical innovation, its meaning and success are not confined to a medical context only. The development of early diagnostic instruments takes place within the broader societal landscape with many stakeholders with different goals, interests, values and evaluations of the desirability or acceptability of novel diagnostic instruments. Whether these innovations are considered an improvement of current diagnostic practice and desirable by particular stakeholders, will depend on the meaning of the technology for these stakeholders (Bijker et al., 1989; Bijker, 1995).

Likewise, the scientific knowledge on (diagnosis of) dementia is scattered among many different (sub)disciplines. The contribution of this thesis to ‘dementia studies’ - an overarching term for all scientific research on dementia from a particular angle (Innes, 2009)

- is to take this multiplicity of angles seriously. It makes the complexity of meanings of early diagnostics for Alzheimer's disease explicit and tangible by travelling across the disciplinary boundaries within the dementia field.

With the aim to understand the social and cultural implications of early diagnostics for Alzheimer's disease, this thesis starts by acknowledging the 'kaleidoscope of realities' (Hajer & Laws, 2009, p. 252) and studies empirically how different meanings become manifest. Because there is not one location that can be studied as 'the social world' or 'social reality' to understand social and cultural implications of a new technology, and because meanings are not separately available for study, the meanings of early diagnostics are studied in particular settings where different meanings of early diagnostics for Alzheimer's disease are encountered. These are notably a public media setting, a policy setting, an Alzheimer support group setting, and a health technology assessment setting.

What could this study of multiplicity of meanings imply for responsible innovation of early diagnostics for Alzheimer's disease? Any attempt to govern innovation is surrounded by uncertainties, gaps in knowledge, divergent views, and different values at stake, also known as 'wicked problems' (Hisschemöller & Hoppe, 1995), situations of 'ignorance' (Stirling, 2010) or 'intractable policy controversies' (Schön & Rein, 1995). One response is to try to reduce uncertainties and ambiguities, through knowledge creation or creating consensus. This is, however, often impossible or undesirable as it will suppress crucial differences. Another route is to acknowledge uncertainties and ambiguities (Hajer & Laws, 2009) and to avoid the pressure to come up with one single definitive advice and clear recommendations and to provide plural and conditional policy advice (Stirling, 2010). This enables decision-makers to explore different viewpoints and positions and to increase their understanding of the complexity of an issue. Good policy work, according to Hajer, takes place between two poles: *"one pulling in the direction of clarity and reduction of complexity, the other illuminating precisely that which we do not fully understand."* (Hajer & Laws, 2009, p. 252) Acknowledging diversity, uncertainty and ambiguity creates the possibility for a reflective way of acting in the world. *"The appreciation of ambivalence and the capacity to doubt are arguably essential components of a reflective way of acting in the world."* (p. 252, *ibid.*). While there is a difference between policy processes and innovation processes, because in innovation processes the decision-making is much more informal and distributed, the same argument for a reflective way of acting applies for innovation processes. My study of the multiplicity of meanings of a proclaimed innovation will allow a reflective approach to early diagnostics of Alzheimer's disease.

## **1.2 Early diagnostics and responsible innovation**

Typically, advances in science and technology are both heralded for all good they can bring to society as well as accompanied by debates on potential risks, undesirable side-effects and responsibility. Recently the term 'responsible innovation' (or 'responsible research and innovation' in the context of the EU) emerged as an ambition to address possibly undesirable societal consequences at an early stage of technological development, while maintaining the

desirable outcomes. The concept responsible research and innovation has a rich history and merges, amongst others, the field of technology assessment which aims to prevent undesirable impacts of new technologies, with innovation policy traditions to stimulate positive consequences of science and technology development (Von Schomberg, 2011).

During the work on this thesis the concept of Responsible Innovation became increasingly important within EU policy on science and innovation (European Union, 2018). Likewise, the literature on responsible (research and) innovation expanded and refined what is meant by the term responsible (research and) innovation and reported on initiatives and experiences (Van den Hoven et al., 2014).<sup>1</sup> In 2014 the Journal of Responsible Innovation was launched (Guston et al., 2014). An often-cited definition is from René Von Schomberg and stresses the policy ambition: *“Responsible research and innovation is a transparent, interactive process by which societal actors and innovators become mutually responsive to each other with a view to the (ethical) acceptability, sustainability and societal desirability of the innovation process and its marketable products (in order to allow a proper embedding of scientific and technological advances in our society)”* (Von Schomberg, 2011, p. 47). In contrast, Stilgoe and Owen describe responsible innovation in more general terms as: *“Responsible innovation means taking care of the future through collective stewardship of science and innovation in the present.”* (Stilgoe et al., 2013, p. 1570). They propose a framework in which four dimensions of responsible innovation are integrated: anticipation, reflexivity, inclusion and responsiveness. The four dimensions will not appear separately in this thesis, but collective stewardship of science and innovation in the present is a central concern.

The approach to responsible innovation that is taken in this thesis can largely be defined by two basic insights. Firstly, that it is possible to assess innovations ‘in the wild’ without using specific TA or foresight tools to mobilize the views of stakeholders. Secondly, that it is not necessary to imagine future situations in order to study and assess consequences – a study of present (embedded) meanings is sufficient and maybe superior. I will use the remainder of this section to underpin these insights.

The general goal of TA (or the philosophy of TA) is to assess the potential implications of emerging and future technologies and, by doing so, to reduce the societal costs of trial and error. The idea is to anticipate future developments and accommodate these insights in decision making. The tradition of Technology Assessment has brought a vast array of tools and interventions, like stakeholder workshops, scenario exercises and focus groups. Next to these ‘formal’ assessments also ‘informal’ assessments occur in and through the interactions of the disputing parties which are part of broader societal learning processes (Rip, 1986). In fact, the institutional, professional TA activities to map and assess future technological

---

<sup>1</sup> This study takes place in the context of the NWO research program on Responsible Innovation. This research program has the aim to reflect on and take into account the ethical and social aspects of innovation at an early stage of its development, because *“considering the solutions that technological and scientific know-how is capable to offer to societal issues and problems, it is important to examine their ethical and societal aspects”* (Nederlandse Organisatie voor Wetenschappelijk Onderzoek, 2008).

developments, are always embedded in broader societal processes of technology assessment. So, it is possible to make use of such informal TA by tracing meanings ‘in the wild’, especially when it concerns a hot societal issue such as Alzheimer’s disease and its diagnosis. An additional advantage is that meanings and assessments ‘in the wild’ are situated in real life settings that render them relevant and pertinent, while meanings and assessments that are generated in workshops run the risk of being disconnected from the daily lives of participants and what really matters – and thus being less relevant and pertinent.

The second starting point of this study is that studying and assessing consequences of promising technologies can be rooted in the present and does not necessarily involve predictions or other accounts of the future. Alfred Nordmann argues that you can be prepared for and anticipate what may happen even without knowing the future. For instance, one may anticipate in traffic without knowledge of the future. Even more so, he states that a too large focus on the future diverts our attention from what is happening in the here and now (Nordmann, 2014). He warns against the ‘if and then’ fallacy that invites speculation about future technological possibilities and the concomitant (ethical) speculation of eventual consequences. In his article on speculative ethics of new technologies he elaborates on the risks of “if and then” statements, referring to a ‘foreshortening of the conditional’: *“what looks like an improbable, merely possible future in the first half of the sentence, appears in the second half as something inevitable. And as the hypothetical gets displaced by a supposed actual, an imagined future overwhelms the present.”* (Nordmann, 2007, p.32). Another risk of such speculative ethics is an (illegitimate) mandate for action: when a particular promising future is proclaimed (say, a particular cure) it will become unethical to decline this future. So further investments in the speculative bright future are mandatory (Nordmann, 2007).

An additional argument to focus on the present is drawn from the sociology of expectations. Scientific research and technology development are highly future-oriented activities, in which expectations abound and coordinate developments. When expectations are accessible they can become part of the interactions between actors and shape scientific, technological and societal change (Van Lente, 1993). The sociology of expectations shows that technologies ‘in the making’ already have consequences before they are embedded, because circulating expectations will shape social relations, set agendas and coordinate actions in a specific direction (Borup et al., 2006; Brown & Michael, 2003; Brown et al., 2003; Van Lente, 1993). Thus, the ‘future’ acts in this study as an element of meanings and assessments of early diagnostics of Alzheimer’s disease in the present.

### **1.3 Research questions and outline of the thesis**

Given my interest in an assessment of early diagnostics of Alzheimer’s disease, I will trace the multiple meanings of early diagnostics, reflect on the fruitfulness of this study as studying assessment ‘in the wild’, and explore how such analysis contributes to responsible innovation.

This research is divided into an empirical part and a reflexive part. The empirical part addresses the following question:

1. What are the **meanings** of early diagnostics for Alzheimer's disease **in different settings**?

The reflexive part of the research addresses the following two questions:

2. Does the study of meanings reveal **assessment** of early diagnostics **'in the wild'** and if so, how is early diagnostics for Alzheimer's disease assessed?
3. What does the study of meanings imply for the notion of **responsible innovation**?

To prepare the ground, chapter two provides an overview of literature on Alzheimer's disease and early diagnostics for Alzheimer's disease. Discussions on early diagnosis taking place can be better understood when being aware of different ways to understand Alzheimer's disease as such. The first part of this chapter provides a historical reconstruction of dealing with Alzheimer's disease in western societies. The second part is devoted to understanding early diagnostics for Alzheimer's disease and diagnosis in general. The third part provides an overview of understandings of Alzheimer's disease that circulate in the present and a variety of ways to think about diseases in general.

The third chapter presents an ex ante reflection on the concept of responsible innovation, based on the results of a first empirical exploration of the field of Alzheimer's disease and early diagnostics for Alzheimer's disease. This chapter summarizes the fundamental questions about responsible innovation in terms of six 'quandaries': problematic, difficult and ambiguous conditions that somehow require fundamental and practical decisions. This explorative chapter provides a critical introduction to the concept of responsible innovation and provides additional arguments to study the multiplicity of meanings of early diagnostics for Alzheimer's disease in particular settings.

Chapter four designs the methodology for the empirical work. It draws on different theoretical approaches that study how meaning is (socially) constructed. To be able to study the meanings of early diagnostics, an understanding of what meaning is, how meaning is constructed and how meaning can be studied is essential. Lessons are drawn from three traditions, i.e. discourse analysis, framing analysis and modes of ordering on how meaning is constructed and how it can be studied. Finally the choices made in the research design, as well as the methods for data gathering and analysis are described.

Chapters five to seven are the empirical chapters, in which the meanings of early diagnostics for Alzheimer's disease are analyzed in four different settings: public media (Chapter 5), Alzheimer Cafés and a health technology assessment (Chapter 6), and the development of a national dementia strategy (Chapter 7).

Chapter eight, discussion and conclusions, returns to the research questions. It brings together the findings of the empirical chapters and concludes on the meanings of early diagnostics for Alzheimer's disease. It will discuss the implications of this study for

responsible innovation in the field of early diagnostics for Alzheimer's disease and reflects on the implications of this study for the concept responsible innovation.



# **SETTING THE STAGE**



## **Chapter 2**

# **Thinking about early diagnostics for Alzheimer's disease: history, diagnosis, ailment**

This chapter positions early diagnostics for Alzheimer's disease within thinking about diagnosing Alzheimer's disease and diagnosis in general, as well as in thinking about Alzheimer's disease and disease in general. Knowledge on dementia, Alzheimer's disease and its diagnosis is scattered among many different scientific (sub)disciplines, which all address this topic from their specific angle. Chapter one already mentioned a number of the questions on early diagnostics for Alzheimer's disease that are raised by these (sub)disciplines.

The literature presented in this chapter has been collected throughout the research: partly before, partly during, and partly after the empirical research. The literature also addresses issues encountered during the empirical work. For practical reasons the reader receives this overview up front to provide a backdrop to the observations in the empirical chapters, and it provides a background of the themes in the literature, which are complementary to the myriad of meanings delineated from the messiness of actual practices.

The first section of this chapter (section 2.1.) provides background on the history of the concept of Alzheimer's disease and describes different ways of understanding Alzheimer's disease. Alzheimer's disease is not a straightforward disease concept and throughout history different understandings of this condition have circulated. Section 2.1 is quite elaborate on the history of the concept, not only because it is interesting as such, but also because it has facilitated to understand that innovation, such as early diagnostics for Alzheimer's disease, is a novel development, yet at the same time a continuation of a development that has been going on for decades. The discussions arising on early diagnosis of Alzheimer's disease play out in the present, yet have their historical roots in a long tradition of similar discussions. The second part of the chapter (section 2.2) explores the thinking about early diagnostics for Alzheimer's disease and diagnosis in general. Since this thesis started from a collaboration between social scientists and philosophers with LeARN, a medical research program, section 2.2. aims to articulate the medical logic driving these developments and the issues discussed within the medical domain. Section 2.3 then presents an exploration of literature addressing clinical and psychosocial perspectives on (early) diagnosis of Alzheimer's disease. Based on the sociology of diagnosis, I introduce the image of the diagnosis of Alzheimer's disease as a node in a network, functioning as an ordering device in a multitude of domains. Section 2.4 subsequently addresses thinking about dementia and ailment in general. The chapter ends with concluding remarks (section 2.5)

## **2.1. A history of Alzheimer's disease**

A number of authors have reconstructed a history of Alzheimer's disease (e.g. Ballenger, 2006; Fox, 2000; Fox, 1989; George & Whitehouse, 2009; Lock, 2013; Neuvel, 2014). These authors share the observation that the history of the concept 'Alzheimer's disease' has been a turbulent one, with twists and turns in the interpretation and use of the concept, steering the way society deals with elderly with this condition in different directions. These changes were influenced by many scientific, technological and social developments. Being acquainted with this history helps to understand where we have arrived today regarding Alzheimer's disease, and enables learning from the past. Throughout this thesis we will encounter some issues that come up today concerning early diagnosis, that have been persistent and recurring in the history of Alzheimer's disease, and could continue to be topics of discussion in the future. An understanding of the history helps to be sensitive to these issues.

### **2.1.1 The 'classical' period: linking symptoms to brains**

Even though there have always been writings about old age and the ailments of old age, I start this history around the year 1900, right before the term Alzheimer's disease was coined by Emil Kraepelin.

At that time, age was an important category to think about disease. Certain conditions occurred at certain ages, and senile dementia occurred at old age and was considered to belong to the aging process. Aging itself was understood in terms of a 'decline-and-loss paradigm' (Holstein, 2000, p. 162), or as the Dutch say 'ouderdom komt met gebreken' (age comes with defects). Senility and decline of functioning shaped the expectations of old age. Every person was considered to have a finite amount of vitality, which should be distributed over life. Towards the end of life, persons run out of life energy. While this is inevitable, it may be postponed by spending your energy wisely during life. In this reasoning it was implicitly assumed that the process of aging caused senile dementia, and physicians and psychiatrist showed little interest in this process that was considered to be normal. Old age itself and the ailments that came with that were not an important topic for medical or biological research, and were treated mainly palliative, rather than curative (Holstein, 2000). When the term Alzheimer's disease was coined it referred to dementia occurring in younger persons. It was restricted to what we now call early onset Alzheimer's disease, which is a very rare condition. The actual diagnostic label 'Alzheimer's disease' was hardly ever given to a patient. This would remain to be the case for 60 years, until the 1970s (Ballenger, 2006).

Alois Alzheimer was a physician-scientist working in the beginning of the 20th century in Germany. It was a time with a drive towards a more precise ordering of psychiatric conditions within psychiatry. A biologic psychiatry was practiced (next to Freudian psychoanalysis), aiming to relate symptoms of a patient to changes in the brain (Dillmann, 2000; Neuvel, 2014). Alois Alzheimer showed a great interest in both patients and science. He was highly skilled in the newest techniques and methods to study the brains of diseased persons, using new methods to preserve the brain and to process tissue with a silver staining technique so that microscopic examination could be conducted. Alzheimer, as a child of his time, wanted

to “*help the field of psychiatry on its way with the assistance of the microscope*” (Braak & Braak, 2000, p. 59). His name was given to the condition that he initially described in a patient called Auguste Deter. He followed this patient from 1902 until her death in 1906, when she was 51 years old. Dr. Alzheimer was interested in this patient, because she developed many symptoms that he could not relate to a known condition. After she died, he examined her brain (with a then new technique using silver staining and microscope) and found that in her brain there were depositions of plaques between the neurons, and accumulation of fibrils (now known as ‘tangles’) inside of the neurons, leading to a loss of those neurons. This showed that her psychiatric condition was also visible in her brain. Her brains resembled the brains of persons with senile dementia, however, at an unusual early age (Förstl, 2000). He presented her ‘case’ at a meeting for psychiatrists in 1906, and this lecture was published in 1907.

On the suggestion of Alois Alzheimer, a handful of other cases with comparable symptoms and brain changes after autopsy were described in the following two years. Alois Alzheimer’s boss, Emil Kraepelin (known as the Linnaeus of psychiatry) decided to include this condition in the *Handbook of Psychiatry* in 1911, and referred to it as ‘*Alzheimer’s disease*’ (See Maurer, Volk, & Gerbaldo, 2000 for details on the August D. case and Dr. Alzheimer’s life and work). This was the birth of Alzheimer’s disease as a disease category. However, this birth was not without some hesitation. The hesitation lay in the difficulties to draw a line between pre-senile dementia and senile dementia. In the *Handbook* Kraepelin added: “*At present the clinical importance of Alzheimer’s disease is still unclear. While the anatomical findings would suggest that it represents a particularly severe form of senile dementia, the fact that it may start in the 40s argues against that view. One would have to assume at least a senium praecox, if it was not perhaps a more or less age-independent disease process of its own.*” ((Kraepelin, 1910, p. 627) in (Förstl, 2000, p. 74)). And actually, in the same year that Emil Kraepelin created the disease category ‘Alzheimer’s disease’ in the *Handbook of Psychiatry*, Alois Alzheimer also expressed his doubt about the disease category. He wrote an article in which he discussed to what extent the cases he found differed from other pre-senile conditions, or from senile dementia, and came to a different conclusion than Kraepelin did. He argued that “*all elements are altered in the same manner and direction as in senile dementia*” (Möller & Graeber, 2000, p. 40) and “*similar cases of disease obviously occur in the late old age*” (ibid, p. 41). For Alois Alzheimer there was “*no tenable reason to consider these cases as caused by a specific disease process. They are senile psychosis, atypical forms of senile dementia. Nevertheless, they do assume a certain separate position, so that one has to know of their existence (...) to avoid misdiagnosis.*” (Möller & Graeber, 2000, p. 41). Alois Alzheimer was not convinced that “Alzheimer’s disease” differed from senile dementia in old age, except for the age of onset, and did not consider it as a distinct disease category per sé. He did, however, consider it useful for physicians to know that senility can occur at a younger age (See Möller & Graeber, 2000 for an extended description of this discussion).

The birth of ‘Alzheimer’s disease’ was a small event, of creating a disease category for a rare condition. The term Alzheimer’s disease was restricted to younger persons, who had similar complaints as persons with senile dementia, but at an earlier stage in life where this was not

to be expected. And (as Kraepelin put it) the causes of this condition at younger age may be different from the causes at old age.

### **2.1.2 The psychosocial turn: dementia as a social problem**

From the 1930s onwards, things started to change in the thinking about senile dementia. There was a heightened awareness and interest in dementia in old age and aging in general, due to demographic shifts (Ballenger, 2000). The assumption that decline with old age was inevitable was challenged. The problems of aging were studied physically, but also within the social context. It was argued that the problems of senility with old age may not only occur from bodily aging, but also because of the societal context in which the aging person was situated. Social and economic conditions of elderly, as well as personal aspects were associated with physical and mental problems of aging. Transforming the negative image of aging, and economic and social conditions were advocated as a way to remedy ailments of old age (Holstein, 2000). A convergence of different developments contributed to these changes: the dominance in psychiatry of psychodynamic and psychoanalytic models, demographic changes and the rise of a gerontological movement. This psychosocial turn, however, then turned on itself and led back to a more biological psychiatry, and a strive from physician-researchers to create better diagnostic categories.<sup>2</sup> In the period between the 1920s and 1950s there was a rise in interest in senile dementia in US psychiatry – not because psychiatrists thought senile dementia was a fascinating research topic but because they were faced with increasing numbers of persons with senile dementia in state mental hospitals. Due to regulatory changes more and more persons with senile dementia were admitted to mental hospitals, rather than almshouses or private old age homes. Psychiatrists were not happy with this increasing group of incurable old persons who they had to provide care for. Their response was twofold. They tried to change the policy to relocate the care for these persons, and while they were faced with these patients, they started studying the condition as a (possibly treatable) mental illness. In line with Alois Alzheimer's findings, these psychiatrists found the etiology of senile dementia to be similar to Alzheimer's disease. The distinction between the term senile dementia and Alzheimer's disease was kept for practical purposes. During this period research into senile dementia faced additional anomalies: (1) the plaques and tangles that were found in the brains of persons suffering from senile dementia, were also found in persons suffering from very different conditions and (2) these plaques and tangles were also found in the brains of elderly who had not shown any signs of dementia during their life, and (3) a discrepancy was noted between the presence and degree of symptoms of dementia in living patients and the presence and degree of pathology found in autopsy. What to make of this? (Ballenger, 2000) Some psychiatrists continued working on a strict organic approach to dementia and argued that because the overwhelming majority of patients suffering from dementia did show large amount of plaques and tangles during autopsy, the link between these pathological signs and the symptoms was definitely

---

<sup>2</sup> For the description of the gerontological movement I mainly rely on the work of Ballenger, which is restricted to US history.

there ((Neumann & Cohn, 1953) in (Ballenger, 2000)). Other psychiatrists faced with these anomalies sought for other explanations, which sparked the rise of psychodynamic models.

The leading figure in this move to a psychodynamic model was the American psychiatrist David Rothschild. He was struggling with explaining the lack of correlation between damage in the brain and the presence of dementia in persons. Why do some old persons become demented, while others remain functioning well, when they show the same damage in the brain? Can the plaques and tangles be the cause of senile dementia if they were also found in other conditions, and in fit elderly? An explanation was missing. Where Alois Alzheimer and scientists had turned to the microscope to help psychiatry forward, Rothschild, puzzled by the pathological findings, looked up from the microscope and argued that *“too exclusive preoccupation with the cerebral pathology led to a tendency to forget that the changes are occurring in living, mentally functioning persons who may react to a given situation, including an organic one, in various ways.”* ((Rothschild & Sharp, 1941, p. 49) in (Ballenger, 2000, p. 90). With this widened gaze he argued that pathological changes were important, but did not inevitably lead to mental illness, as brain research had shown, and to explain this he included ‘factors of a more personal nature’ (Rothschild & Sharp, 1941). Individuals differed in the ability to compensate for the organic damage in their brain. A problem is that some persons are not well equipped to deal with aging, with the lack of work employment, loss of friends, physical and mental deterioration and so on. He ascribes the development of dementia to this failed adaption to changing circumstances in life. The ability to compensate for changes with aging, including an aging brain, may be decreased by personality traits, but also due to stress or life crises. Rothschild’s explanation was in line with the attitude in psychiatry between 1920 and 1960 in the US, which was dominated by psychodynamic theory in which mental phenomena were conceived as *“a dialectic interplay between biological, social and psychological forces”* ((Holstein, 1996) in (Ballenger, 2000, p. 90)).

Between the 1920s and the 1950s, Rothschild’s approach to senile dementia, emphasizing the psychosocial factors contributing to the etiology of Alzheimer’s disease over the neuropathology, became dominant. And rather than looking at dementia as the inevitable outcome of (brain) aging, dementia became understood through a dialectical model in which the aging person was influenced by both biological processes and the social context. Factors of importance for explaining dementia were besides the plaques and tangles, also the personality, emotions, family support and social in- or exclusion. These developments changed the understanding of senile dementia, and other ailments of old age. Where they were first attributed to aging, they were more and more understood in terms of diseases, socio-cultural effects and personality factors (Ballenger, 2006).

The dominance of the psychodynamic approach over a strict organic approach ties in with social developments after the Second World War. Social developments included a gradual increase in the proportion of persons over 65 since the 1920s, (Fox, 2000) mandatory retirement, disintegration of traditional family ties, and social isolation of elderly. Aging was accompanied with negative stereotypes, and elderly were not regarded as full members of society. This so-called ‘social pathology’ was characteristic of modern (US) society *“in our present social set-up, with its loosening of family ties, unsettled living conditions and fast*

*economic pace, there are many hazards for individuals who are growing old.*" ((Rothschild, 1947, p. 125) in (Ballenger, 2000, p. 94)). Dementia in the psychodynamic model was not only due to brain pathology, but also to social pathology. *"Bereft of any meaningful social role, the demented elderly did not so much lose their mind as lose their places in the world. (...) it was society that stripped elderly people of the roles that had sustained meaning to their lives."* (Ballenger, 2000, p. 93). This argument of social pathology was used by more psychiatrists, ranging from statements such as *"pathology of senility is found not only in the tissue of the body, but also in the concepts of the individual and the attitude of society"* ((Wilson, 1955, p. 905) in (Ballenger, 2000, p. 95)), up to the extreme position that social pathology actually was the cause of brain pathology. An impoverishment of social relations, an exclusion from society, induces an impoverishment of the brain. If the brain is not maintained, it will slowly decay. Use it or lose it (Ballenger, 2006; Neuvel, 2014).

Emphasizing the social character rather than the biological character of senile dementia, the psychodynamic model opened up a whole new array of possible therapeutic inventions for persons with senile dementia. It also led to a search to differentiate between irreversible and reversible conditions influencing the development of senile dementia. Treatment of dementia was not only a task of physicians anymore. If social relations are pathological, than societal changes can prevent person from becoming demented. According to the psychodynamic model, addressing the material, social and psychological needs of elderly should result in lower occurrence of dementia. Failing to accommodate these needs would lead to a catastrophic increase in persons with senility, becoming a burden for society. Social and recreational programs were set up to provide elderly with activity and a sense of meaning, which would at the same time prevent senility and lower its occurrence. In terms of finances, there programs were a bargain compared to the high costs of institutional care for demented elderly. However, this also changed the view on senile dementia as 'part of old age' to something that can be prevented. Furthermore, if senile dementia is partly due to impoverishment of a person's life, the task of a person is to find a meaning in life, to lead an active and fulfilling life, also at a higher age. The task of the aging individual is to find a balance in the changing personal and social circumstances. Preventing dementia had become not only a societal but also a personal responsibility (Ballenger, 2006).

This development was aligned with the emergence of gerontology after the Second World War. Gerontology advocates aimed for improvement of societal circumstances for elderly. This was done in different ways, such as social and recreational programs, increasing pensions, abolishing mandatory retirement, but also by replacing the stereotype of fear of growing old, with positive images, and an optimistic attitude towards old age. It also lead to distinctions between the 'young old' labelled as persons in their third age, and the more fragile 'old old' said to be in their fourth age (Laslett, 1987). And in the end of the 1980s when much of this program was accomplished, ideas on the 'third age' or the 'young old' had found firm ground. This led to ideas about 'successful aging'. With the rise of an optimistic view on aging, dementia became a much feared condition, and an increasing need was felt to distinguish 'normal aging' from 'pathological aging'. Dementia was no longer accepted as an

inevitable consequence of aging, and as the opposite of successful aging, it was more and more considered a disease that should be eradicated (Ballenger, 2006).

### **2.1.3 Renaissance of pathology<sup>3</sup>**

This strive to distinguish 'normal' from 'abnormal aging' is present in the efforts undertaken by physician-researchers from the 1950s onwards, aiming for more diagnostic rigor in mental disorders occurring in late life. The term 'senile' was too often used to not take complaints of elderly seriously, and senile dementia, or 'organic brain syndrome' as it was called in the DSM-II (Diagnostic and Statistical Manual of Mental Disorders-II) in 1978, was considered a poorly defined catch-all term. A more careful biomedical diagnosis of dementia was needed. This acted as a double edged sword. It served to better address complaints of elderly and not discard them as belonging to senility when they might be treatable, just because persons had reached a certain age. And it served to protect the elderly of the third age from the prospect of deterioration during the fourth. Physician-researchers became public advocates striving to change the conceptions of old age. (Holstein, 2000) Robert Butler (who I will come back to later) was one of these advocates.

The modern era of Alzheimer research took off during the 1960s with the first successful electron microscopic studies of the Alzheimer brain in both the US as the UK. Here again we see that the regained emphasis on brain pathology was fed by new possibilities to study the brain, this time enabled by electron microscopy. In the 1960s research on brain tissue of persons with Alzheimer's disease (pre-senile) identified the core of plaques to be the protein amyloid. And shortly after it was proven that the same held for the plaques in the brains of persons with senile dementia. Further studies on elderly persons with senile dementia in 1965 showed that the majority of cases of so-called senile dementia showed two kinds of pathological changes in the brain, one was called arteriosclerotic dementia (based on cerebral infarcts) and the second showed the same changes as Alzheimer's disease, but occurring later in life. Clinicians, however, remained to consider Alzheimer's disease and senile dementia as distinct disease categories. This changed during a congress on Alzheimer's disease in 1968 in London, when it was acknowledged that Alzheimer's disease was found in elderly subjects as well and that defining Alzheimer's disease as a pre-senile condition was not correct. However, considering Alzheimer's disease as the cause of the majority of senile dementia was not accepted as a necessary consequence. Although the pathological changes may look the same, the clinical symptoms differed in their intensity and localization. Alzheimer's disease in younger persons showed to be more severe (Katzman & Bick, 2000). Looking back it is important to realize that the discussion on Alzheimer's disease had drastically changed from the time that Kraepelin coined the term Alzheimer's disease, from whether Alzheimer's disease wasn't actually an atypical form of senile dementia, to whether senile dementia wasn't actually Alzheimer's disease.

---

<sup>3</sup> Better well-stolen, than badly invented. Title is literally taken from Ballenger (2006), chapter 4 "The Renaissance of Pathology".

#### **2.1.4 A sea change<sup>4</sup>**

In 1974, the National Institute of Aging (NIA) was established within the National Institute of Health (NIH) in the US to promote and conduct research on different aspects of aging, such as biological, medical, psychological, social, educational, and economical aspects. The first director of the NIA was Robert Butler. Robert Butler wanted to counter the misconceptions of senility, and in particular counter the public perception of elderly as being functionally and cognitively disabled persons (Fox, 2000). He framed this as a fight against 'ageism', aiming to change the former negative stereotypes of aging with counter-images to repositions aging persons in society (Holstein, 2000). He emphasized that just because some illnesses mostly occur at higher age, does not mean that they are part of the normal process of aging.

At the same time, Katzman worked as a neurologist at a medical center in New York on senile dementia and Alzheimer's disease. When it was acknowledged that considering Alzheimer's disease as a pre-senile condition was not correct, and the majority of persons with senile dementia had the pathology of Alzheimer's disease but occurring at later life, he argued that this means that most persons with senile dementia, actually suffer from Alzheimer's disease. This reframing of senile dementia, changed Alzheimer's disease from a very rare disorder into a very common disorder. Katzman drew these conclusions in an editorial in the *Archives of Neurology* in 1976 (Katzman, 1976). If between 48 and 59 percent of the persons with senile dementia in late life have the pathology of Alzheimer's disease, that means that in the US alone between 880.000 and 1.200.000 persons were suffering from Alzheimer's disease, adding up to 60.000 to 90.000 deaths per year. This made Alzheimer's disease the 4<sup>th</sup> or 5<sup>th</sup> most common cause of death in the US (Katzman & Bick, 2000).

The NIA was established but still needed to prove its legitimacy, because its establishment was not without critical voices from within the NIH and from the US Congress. Other institutes of the NIH had been successful in doing this by adopting a disease-specific approach. Alzheimer's disease seemed to be a very good candidate for that, and it would be even better if this was supported by a community based movement. Katzman had already put effort into organizing a lay organization on Alzheimer's disease and both Katzman and Butler were aware of lay organizations on dementia across the US. Some of these were started by researchers (like Katzman) and others were grassroots organizations started by family members whose relatives had Alzheimer's disease or other types of chronic brain conditions and experienced difficulties in getting emotional, financial, social and medical support. The idea to form a national organization was supported by these local groups. In 1979 the national Alzheimer's disease and Related Disorders Association (ADRDA) was established. The involvement of the NIA served as a catalyst to bring these groups together to form a national organization. And Butler of course had the aim to put Alzheimer's disease

---

<sup>4</sup> A 'sea change' is an expression in English, often used to denote a metamorphosis or alternation. The expression is used in similar ways as the words paradigm shift, or a communities zeitgeist. A sea change refers to a change of perspective of society, a community, or a group on a particular issue.

on the research and public agenda and to be supported in this by a social movement which could help to create legitimacy and mobilize resources for his new institute (Fox, 2000).

These different technological, scientific, social and political developments merged into what can be considered a social movement targeting Alzheimer's disease. With the growing emphasis on Alzheimer's disease, and the activities to increase public awareness by the ADRDA, the term Alzheimer's disease was starting to replace the term senility, not only in field of research, but also in politics, and the general public. Personal stories about the problems of caring for someone with this condition were starting to appear in newspapers, leading to an increasing growth of local self-help family support groups. The NIA was successful in gaining research funding for Alzheimer's disease related projects, and their legitimacy and credibility was growing. Throughout the '80s the ADRDA and the NIA were working closely together and collaborated in drawing public attention to the 'disease of the century', and the mobilization of resources for the 'fight against Alzheimer's disease'. The ADRDA for example kept on disseminating human-interest stories in the media, increasing public consciousness and recruiting new allies. This was strengthened by Ronald Reagan, Rita Hayworth and her daughter Yasmin Aga Khan as public flagships (Fox, 2000).

While this description of the history of Alzheimer's disease is due to available literature mainly situated in the United States of America, in the Netherlands similar processes occurred. To describe this I rely on the work of journalist Koos Neuvel who wrote a 'biography of Alzheimer's disease' in the Netherlands (Neuvel, 2014).

Also in the Netherlands there was a rapid sea change from senile dementia being viewed as a bad adjustment to changing personal or societal circumstances, towards a disease called Alzheimer's disease. This can be understood through scientific, demographic and social changes and efforts from scientists, patient organizations and journalists to increase awareness for Alzheimer's disease as a disease that is problematic for individuals and family members faced with this condition, as well as for society at large.

The scientific ground to view senile dementia as a 'real' disease was internationally prepared by the developments of whom Roth, Katzman and Butler were the leading persons. In the Netherlands Frans Stam and Piet Eikelenboom were pioneering researchers in the Valeriuskliniek, an observation clinic for elderly persons before they were moved to a nursing home. Both were working in the line of Roth, studying dementia as a disease, and finding ways to reliably determine Alzheimer's disease in the brain. However, the Dutch field got quickly divided with the entrance of neurologist Dick Swaab, who, after studying brain pathology of Alzheimer's disease, came to a different standpoint. He did see a general decay of brains in elderly persons, but did not find a sharp deviation between aging brains that could be a boundary between normal and abnormal aging (Alzheimer's disease) that was in line with the symptoms persons developed. So, as a neurologist he did not agree with the distinction between normal and abnormal aging. Swaab held the position that there is no clear distinction, but rather a gradual transition. He, however, did not disagree with calling senile dementia a disease, if that was helpful for persons suffering from symptoms that were related to this type of brain aging. So he had a less strong definition of Alzheimer's disease

as a 'disease'. This difference is mainly visible in the expectations regarding a 'cure'. With the strong disease definition, a cure might be possible. Swaab, viewing dementia as a gradual transition, argued that one may try to slow down aging processes, but eventually it is inevitable. So with the start of the sea change, this fundamental scientific controversy, which is still hotly debated, (see for example Richard et al., 2012), immediately got embodied in the different scientists working on it. However, in line with their Dutch polder-nature, their different standpoints did not prevent them from working together, or shift positions (Neuvel, 2014).

Because Swaab considered the Alzheimer-brain a very interesting object for research, he continued in this line of work. He did encounter one problem: he could not find brains to study, while there were thousands of people suffering from the condition. This was mainly because persons with Alzheimer's disease do not die in academic hospitals but in nursing homes. Swaab decided to erect the Brain Bank (in Dutch: 'Nederlandse Hersenbank'), that would cooperate with nursing homes to gather brains for research. This, however, appeared to be problematic. In nursing homes nobody was aware of the existence of Alzheimer's disease. They would call it senile dementia, psychogeriatric patients, persons who are 'childing' (*verkindsen* in Dutch), or in whom the light goes out. However, they did not consider them as having a disease and did not see the necessity of asking permission to donate their brains after death for autopsy. This made Swaab decide that it was time to create more public awareness of Alzheimer's disease. This public awareness was necessary because Alzheimer's disease was expected to become a huge societal problem that was not getting the attention it deserved, to educate the public on scientific advances made with public funding, but also to recruit donors for the erected brain bank. Swaab became a public figure educating the public about Alzheimer's disease (Neuvel 2014) and he still is (e.g. Swaab 2010).

Contrary to the US, mandatory retirement, which was introduced after the Second World War was applauded in the Netherlands and seen as one of the first fundamentals of the welfare state. Yet also in the Netherlands the aging population got dissatisfied with the position of elderly in society, with old persons being envisioned as less capable than young persons. In the Netherlands this came with a movement against elderly discrimination. Elderly discrimination is the Dutch variant of what was called 'ageism' in the US. This development was fed by elderly going on 'early retirement', quitting work around their 60s, and still having a long life ahead of them. These are persons of whom gerontologists would say, are in their 'third age': elderly persons who are far from fragile (the 'fourth age'). These elderly started an emancipatory movement. The desire to free the persons in their third age from the negative stereotypes of the fourth age, strengthened the need for a medical delineation between elderly that are vital and fit and elderly that are fragile and ill. Furthermore, there was a need to view 'elderly complaints' as symptoms of disease, rather than the consequences of normal aging. So also in the Netherlands there was a societal eagerness to embrace the concept of "Alzheimer's disease" for aging persons (Neuvel 2014).

The Alzheimer Stichting (currently Alzheimer Nederland) played an important role in this sea change. The Alzheimer Stichting in the Netherlands started differently from the Alzheimer Association in the US. This organization started with Henk and Vera ter Haar. Henk ter Haar

was a physician and director of a nursing home in the north of the Netherlands. When talking with a government inspector for mental health care, they spoke about Alzheimer's associations that had popped up in other countries, but did not yet exist in the Netherlands, and Henk ter Haar was asked by the inspector if he could set up an Alzheimer association in the Netherlands. Henk ter Haar agreed with the aim of these associations to increase public awareness of Alzheimer's disease and the message that dementia is a real disease and not just part of normal aging. So he agreed to take on this task. What would be a good strategy to create more public awareness? They started from their home, but decided after talking with the Canadian Alzheimer Association that it would be best to have local networks spread across the country that people can contact easily. Local departments of the Alzheimer Stichting spread across the Netherlands. One of the main messages of the Alzheimer Stichting was that Alzheimer's disease should not be a taboo anymore. 'Taboo' and getting rid of 'taboos' is also very Dutch and in line with the cultural movements in the 70s and 80s in the Netherlands. There was a desire for shaking off fear, shame, and not talking about subjects like sex, abortion, euthanasia, or suicide. These issues should no longer be forbidden, ignored or oppressed. Dementia was aligned with this movement by the Alzheimer Stichting. It was important that Alzheimer's disease became a topic of conversation, and by doing that, it could become a more accepted condition. However, it did differ from other topics of the anti-taboo movement, in the sense that dementia was already an accepted condition, almost ordinary even. The taboo to be broken here was the attitude of indifference, and the shame of telling other people of the problems in your household when your partner develops dementia. Persons with dementia should not be tucked away and forgotten, but they deserve care, attention and treatment and their wives or husbands should be supported in the difficulties they face (Neuvel 2014).

The Alzheimer Stichting got an unexpected ally in the form of journalist Magda Berman, who wrote an article on the new view on dementia as Alzheimer's disease and suggested it as a topic to a television presenter, Koos Postema for his popular tv show. After that tv show in 1984 they had a phone line in case persons had questions or felt the need to talk with somebody. Over 20.000 persons called after the show to share their feelings. This was unheard of and a sign that there was a large unmet need to talk about dementia. This happened around the same time that Henk ter Haar was founding the Alzheimer Stichting. Magda Berman felt that she needed to do something to support the persons caring for persons with dementia and decided to join the Stichting as a board member, for which she wrote many educational material on Alzheimer's disease. She also brought Alzheimer's disease into public attention, and decided to do so with big, dramatic wording to create optimal public involvement. In line with the strategy of the NIA in the US, she wrote articles with titles as 'the epidemic of the future' and presenting it as something that could happen to anybody and that everybody could be a potential victim of this tragic fate. Because journalists follow other journalists, and because of the large number of reactions on the tv show, in 1985 a small media hype occurred on Alzheimer's disease, with more tv shows and media articles. The way Alzheimer's disease was presented as a disease that causes severe suffering, especially for the informal caretakers was in line with the strategy of the Alzheimer Stichting, which viewed itself as an organization supporting relatives of persons with

dementia and as a funding organization for research. Through providing information and support to the relatives they aimed to help the persons with dementia as well (Neuvel, 2014).

The rise of Alzheimer's disease in the Netherlands was the consequence of different developments coming together. There were demographic and social changes drawing attention to increasing numbers of vital and less vital elderly. Scientists were aiming to advance research on Alzheimer's disease, and creating awareness on this condition. The public attention for Alzheimer's disease had brought out the voices of relatives of persons with dementia, made the struggles and suffering that had been going on inside of households visible, and made it a topic of conversation and changing it from a private to a public issue. This fed into the desire to support relatives of persons with Alzheimer's disease (Neuvel 2014).

The understanding of Alzheimer's disease had shifted in the relatively short period between the 1970s and mid-1980s, from a normal condition of elderly to a 'real disease' to be distinguished from normal aging. The increasing awareness of and interest in Alzheimer's disease led to an eagerness to do something about it. This particularly took the shape of a "*crusade to eradicate this seemingly new disease*" (Ballenger 2006, p. 114). Funding of biomedical research became a very important strategy to solve the problem of dementia and there was a huge increase in investments in Alzheimer's disease. In the US, for example, investments in biomedical research on Alzheimer's disease increased from less than 1 million in 1976, to 11 million in 1983, more than 300 million in 1994 up to 700 million dollar in 2005 (Ballenger 2006).

### **2.1.5 Drawbacks of the raising of attention to Alzheimer's disease**

The creation of political, societal and scientific awareness for Alzheimer's disease was accompanied by a typical kind of discourse, also referred to as the 'health politics of anguish' (Fox, 2000) a term coined by Robert Butler, emphasizing a disease-specific approach to Alzheimer's disease rather than seeing it as a part of aging and thus part of basic research. Within this health politics of anguish, the search for a cure for Alzheimer's disease became a moral imperative, but was less able to provide support and relief to persons with dementia and their informal caregivers. Another (unintended) consequence of the increased awareness and sense of urgency mobilized by this 'politics of anguish' was that it increased the fear and stigma associated with Alzheimer's disease. I will go into in some more detail now.

With the aim to draw attention and funding for Alzheimer's disease, Alzheimer's advocates emphasized the devastating burden this condition would pose on the aging society, both socially and economically in terms of health care costs, which would become even worse when the baby boom generation aged. Critics have called this discourse 'apocalyptic demography' (Robertson, 1990). These arguments have remained central in putting Alzheimer's disease on the public agenda (Ballenger, 2006).

The US strategy to call Alzheimer's disease the 'disease of the century' (first coined by Thomas (1981)), was used to argue that Alzheimer's disease was not just another disease-of-the-month for which attention was raised. By calling it the disease of the century the

increasing societal costs of this condition and the devastating impact this will have on an aging society, was easily linked with a strategy to conduct biomedical research to cure this condition (Fox, 1989; Ballenger, 2006). However, the link with policy initiatives to address the needs of caregivers became less evident. *“Alzheimer’s disease advocates emphasized the tremendous economic burden the disease placed on society such as nursing home care – costs that would dramatically increase if a treatment or cure for the disease was not found. In so doing, they also underscored the degree to which policy changes that would substantially benefit caregivers would be prohibitively expensive.”* (Ballenger, 2006, p. 119). Although, the ADRDRA has always formulated two policy goals: increased scientific funding and relieve the burden of caregivers, due to the discourse discussed above *“caregiving is positioned as an unfortunate and unnecessary burden – the price we pay for our failure to commit enough resources to cure.”* (Ballenger, 2006, p. 120). Reducing the number of persons afflicted by this condition either through cure or prevention seemed the only ‘real solution’ in this way of reasoning (Ballenger, 2006).

During the 1980s and 1990s ‘medical triumphalism’, that is the assumption that biomedical research would eventually find a solution to Alzheimer’s disease if enough money would be invested, stood strong. Not only in the US, but also in other countries such as the Netherlands. A medical breakthrough on treating Alzheimer’s disease would occur sooner or later. The funding for biomedical research on Alzheimer’s disease was seen as a short term investment, which would pay itself back easily, once a cure was found. Ballenger shows in reports from congressional hearings in the US from 1980 to 1990, that a number of medical experts were being quite nuanced and stated that there is no guarantee that finding a cure will succeed. Yet, the other option to deal with this apocalyptic demography would be to financially support the informal caregivers and provide care through the health care system, which would bankrupt the system (Ballenger, 2006). Within this reasoning, investing in biomedical research would be a relatively easy and inexpensive option for the US congress to deal with Alzheimer’s disease. Some cautioning did occur in these discussions, warning for arousal of unrealistic expectations, yet this was countered by stressing that highlighting all the difficulties was not getting the situation further, and encouraging the determination to find a medical solution is much more constructive. Also those stressing the need for increased support for caregivers would show confidence in an ultimate medical solution. They would argue that while no cure for Alzheimer’s disease is available, -and it is not clear *when* it will be-, in the meantime more has to be done for caregivers (Ballenger, 2006).

Another part of the ‘health politics of anguish’ (Fox, 2000), next to the urge to cope with the social and economic burden of Alzheimer’s disease, was the representation of the human suffering involved in this condition. Biomedical research was intended to save lives and save the dignity of millions of people suffering from this condition and their families. Through testimonies of caregivers of dementia, professionals and the ADRDA advocates, the new stereotype of persons with dementia became the *“victim of dread disease”* (Ballenger, 2006, p. 129). What made Alzheimer’s disease such a dread disease, was its’ representation as a disease that struck people, all people, not only the very old, but also persons in the prime of their life.

Alzheimer's disease advocates proclaimed that the stigma on senility would be lower by calling it a real disease, namely Alzheimer's disease. By calling senile dementia a real disease, unsettling behavior could be seen as a symptom of the disease, for which the persons should not be held accountable. However, others stressed that this is exactly what made Alzheimer's disease so frightening: To lose self-control, to lose awareness, and to lose personal responsibility is exactly that what is feared most in our modern hypercognitive, individualized culture. The symptom that made Alzheimer's disease such a terrifying condition was not the pain or symptoms, but the fear to lose your memory, your language and your essence of selfhood, a coherent self. Persons with Alzheimer's disease became represented as non-persons, the living death, the failures, not really there, persons who lose their 'self', and Alzheimer's disease as a condition consuming someone from the inside, leaving an empty shell (Behuniak, 2011). This 'loss of self' image of Alzheimer's disease stood in contrast with the aim to reduce the stigma on dementia and to retain the humanity of persons with dementia (Ballenger, 2006).

This image of Alzheimer's disease is not much different from what was earlier considered senile dementia. Yet, Ballenger stressed that it is different in one significant aspect: Alzheimer's disease as a form of senile dementia was not considered to be part of normal aging processes anymore. When senile dementia was considered to be part of old age, this meant that young and middle aged persons would be free from it. Reconceptualizing elderly complaints from being a part of aging to symptoms of diseases, enabled the idea that also later stages in life could be free from deterioration. On the backside *"Alzheimer's disease generated such intense fear in part because many people could now expect an old age that was relatively free of physical, social, and economic deprivation."* (Ballenger, 2006, p. 144). Persons with dementia thus became that part of the population that failed to age well, and became victim of this horrible disease (Ballenger, 2006).

This is in line with the expectations of life after retirement, successful aging and vital elderly. After having worked hard all your life and finally having the time to enjoy it, Alzheimer's disease spoils this and replaces this rosy prospect of aging with quite a different prospect. This makes Alzheimer's disease not only a horrible condition, but also a thief of life, and an unfair fate, which robs a person from the leisure and enjoyment of life after retirement (Ballenger, 2006).

### **2.1.6 Renaissance of psychosocial approaches**

Alzheimer's disease has been brought under public attention as a huge social issue and a condition causing a lot of suffering. Putting Alzheimer's disease on the agenda as a real disease and urging public attention for this condition has had a number of 'side-effects' on the cultural conceptualization of dementia. Alzheimer's disease has eventually become the, or one of the, most dreaded disease(s) in western societies. Alzheimer's disease became surrounded by a zombie-rhetoric: Alzheimer's disease takes everything that we call human, or ourselves, from us (Behuniak, 2011).

With the attention focused on dementia, being positioned as an organic condition where the mind declines while the body continues to live, and the research on causes of and possible

treatments for 'the disease of the century' in full swing, another approach to dementia came up. Interests, again, moved to how socio-cultural factors mediate the experience and responses to dementia (Downs, 2000; Milne, 2010; Whitehouse & George, 2008).

One of the main issues at stake in the fear for dementia and the metaphors used to describe persons with dementia is the notion of 'self' and what this entails. Different models of selfhood can be distinguished. In the US, Sabat (Sabat & Harré, 1992) argued that the 'self' is not lost when a person has Alzheimer's disease. This model of selfhood is based on "*cognitive mastery of the social world: a person is a self because he/she knows, in very concrete terms, who, where he/she is in the social world.*" (Ballenger 2006, p. 173). In the UK, Kitwood argued that the person is still there (Kitwood, 1990, 1997). His model of self is "*rooted in the inter-subjectivity of the social; a person is a self when he is connected to a world that will accept him no matter how grave his failings, no matter how confused and forgetful he may be about the particulars of who, what and where he is.*" (Ballenger 2006, p. 173). In the Netherlands, amongst others Rosemarie Droës argued that persons with dementia use similar 'stress-appraisal-coping' strategies as other persons with severe chronic illnesses. She emphasized that persons with dementia are not different than other persons in the way they cope with the troubling situation they are in (Dröes, 2007). What these 'models of self' revolve around is the question to what extent persons with dementia are different from 'normal people' and whether this difference also reduces them to being less human. These notions led to approaches such as 'person-centered care' (Kitwood, 1990, 1997; Kitwood & Bredin, 1992; Vermeiren, 2012).

The emphasis of these researchers shifted again from the brain to the person and society. In a sense this is a revitalizing of the ideas of Rothschild, but slightly different. The organic basis of Alzheimer's disease is not contested, but the suffering related to this condition is not only caused by this organic condition, but also because of what Kitwood calls 'malignant social psychology' (Kitwood, 1997). By considering Alzheimer's disease as a neuropathological condition, this came along with a pure medical approach looking at all symptoms as an expression of the disease. These researchers argue again that not everything a person with dementia experiences or does is to be related to the changes in the brain.

### **2.1.7 Lessons from the history of Alzheimer's disease**

This turbulent history shows that how dementia is approached is the outcome of an interplay between cultural, social, demographic, political, technological and scientific developments. To conclude, five (recurring) dynamics found in this history of Alzheimer's disease will be highlighted.

The first dynamic highlighted is the oscillation of conceptualizations of dementia, between dementia as part of normal aging and as a pathological condition. The view on senile dementia as 'a real disease' has appeared to be fairly recent. Dementia at old age has been re-conceptualized from a process that is an inevitable part of normal aging processes, to a distinct pathological condition that should be treated or prevented, and back again. Changes in how dementia is approached are not reducible to progress in scientific knowledge.

Actually, whether Alzheimer's disease can be distinguished from normal aging processes is a constant topic of scientific debate (Dillmann, 2000; Lock, 2013).

Secondly, the reconceptualization of senile dementia as Alzheimer's disease was the consequence of a strategic political move. This move changed Alzheimer's disease from a rare condition to the 'disease of the century' (Fox, 1989). This move enabled senile dementia to emancipate problems related to dementia and dementia care from family issues to be dealt with inside of the homes into issues deserving public attention. This move has led to an impressive increase in the investments in research on Alzheimer's disease, as well as to better support for persons dealing with the condition.

Thirdly, throughout the history there has been a constant shift in emphasis from the biological to the personal and societal factors that contribute to the development of dementia. And likewise the ways to deal with dementia has ranged from biological interventions, interpersonal interventions, and societal changes.

Fourthly, the emphasis on the underlying biological causes of dementia seems to go hand in hand with new medical (imaging) technologies. First, by the turn in psychiatry to the study of the brain using microscope and staining techniques, and second by the rise of imaging technologies such as electron microscopy, MRI, PET and so on, as well as the genetic revolution. This knowledge and techniques created the opportunity to study elements that could not be studied before, drawing attention to where the microscope is pointing.

The fifth dynamic highlighted, is a paradoxical relation between drawing attention to the goal to avoid ageism and to help informal caretakers and people with dementia, and increasing public fear for this condition. While one of the drivers for this reconceptualization is to avert ageism, and to re-position elderly as full citizens in societies, it also resulted in Alzheimer's disease being tightly connected to the other elements of the 'health politics of anguish' emphasizing that it is a terrible condition. With the rising expectations of later life, with the rise of ideals, such as successful aging, the fear of failure increases.

These dynamics that have been present in the history of Alzheimer's disease are relevant for a study on the social and cultural implications of early diagnosis for Alzheimer's disease, because the development of early diagnostics for Alzheimer's disease can now be positioned within a certain school-of-thought within history. This is the school of thought that treats Alzheimer's disease as a 'real disease' and that aims to distinguish Alzheimer's disease strictly from other conditions and normal aging processes, by tracing the biological changes in the brain. This has been referred to as the localization theory or a reductionist theory, emphasizing the biological factors contributing to the development of the condition (Dillmann, 2000; Lock, 2013). From this history one can learn that this involves the risk of medicalizing aging populations and neglecting the psychosocial components.

Furthermore the dynamics occurring in the past, clearly show that early diagnosis is positioned in a field where different approaches to dementia exist. Because of the complex field of Alzheimer's disease, it will probably not only gain meaning within this fragment of the *Alzheimer's disease kaleidoscope* (chapter 5), but will be mobilized or related to in

different ways as well. Early diagnostics thus gains meaning not only in the localization or reductionist theory, but it may contribute equally to and can be understood from a sort of 'entanglement theory' (Lock 2013) where an interaction of environment, aging processes, life events, personality, lifestyle and mind bring about pathological changes, or more societal approaches towards dementia.

Finally, the initial aim of this thesis is to understand the social and cultural implications of the emergent development of early molecular diagnostics for Alzheimer's disease. The historical account showed that changes in the past in the conceptualizations of Alzheimer's disease and the way to deal with it have been an interplay between different developments that became aligned to enable change. Progress in the scientific or technological realm does not have the power to define the meaning of Alzheimer's disease and how to deal with it, nor is it the only place from which changes in meaning and dealing with Alzheimer's disease initiate. Looking at this history, it is more plausible to assume that early molecular diagnostics of Alzheimer's disease will probably only lead to societal implications when it is aligned with other developments. However, at the same time, we did see (and thus can be sensitive to) the dynamic that new medical (imaging) technologies go hand in hand with an increased emphasis on the underlying biological causes of dementia.

## **2.2. Thinking about diagnosis: Early diagnostics for Alzheimer's disease from a medical point of view**

Early diagnosis of Alzheimer's disease has a strong presence in medical research so a reflection on how it currently features in this literature is appropriate. Moreover, the research of this thesis is conducted within a research team on responsible diagnostics for Alzheimer's disease. As a team we collaborated with a Dutch biomedical research consortium, called LeARN (Leiden – Alzheimer Research Nederland), which aimed to develop new instruments with which Alzheimer's disease can be determined earlier and more reliably. Between 2009 and 2015, LeARN aimed to develop and evaluate new instruments, based on molecular markers. These instruments were expected to contribute to an early diagnosis of Alzheimer's disease and to the speeding up of evaluations of novel treatments. Within the LeARN consortium, three types of diagnostic instruments were developed to identify and trace biomarkers for Alzheimer's disease: PET scans, MRI scans and CSF analysis respectively. PET (Positron Emission Tomography) and MRI (Magnetic Resonance Imaging) are medical imaging techniques that are used in LeARN to visualize changes in the proteins in the brain that might identify and trace the development of Alzheimer's disease. CSF (CerebroSpinal Fluid) analysis is the chemical analysis of proteins in the cerebrospinal fluid, that is applied in learn to trace proteins that are related to the onset and development of Alzheimer's disease. The LeARN consortium also investigated which (combination of) these tests would be able to detect Alzheimer's disease in a sufficiently reliable way and assessed the clinical and economic value of these tests (LeARN, 2010). Our collaboration with LeARN provided a starting point and entrance in the field of early diagnostics for Alzheimer's disease.

LeARN is a Dutch consortium. The Netherlands, of course, is not the only country where this type of research is conducted. With entering the LeARN consortium I did not only enter a Dutch research programme, but a worldwide effort to identify and validate biomarkers for Alzheimer's disease. These researchers across the globe, aim to identify and trace pathological changes related to Alzheimer's disease occurring before a person experiences (all) the symptoms of dementia.

In this section I introduce the medical understanding of early diagnostics for Alzheimer's disease. What is early diagnostics and why is it considered an important development from a biomedical point of view? This section does not provide a complete review of medical literature on early diagnostics of Alzheimer's disease, but rather a 'tour' along important models, concepts and promises. I hope to provide an understanding of what is at stake according to medical researchers working on early diagnostics of Alzheimer's disease.

In section 2.2.1. the different uses of the terms 'early' and 'diagnostics' in practice are described. This is important because while it may seem that everybody speaks about the same topic, actually the terms can be used refer to different 'early's' and different 'diagnostics'. Paragraph 2.2.2 describes the pathological cascade model, the medical hypothetical model underlying the development of early diagnostic instruments. This is followed by an explication of why early diagnostics for Alzheimer's disease has gained such interest. It explicates the different goals for which early diagnostic instruments for Alzheimer's disease are mobilized as important means in section 2.2.3. In section 2.2.4. controversies in the medical field related to early diagnostics are discussed. Finally a summary of the medical thinking about early diagnostics for Alzheimer's disease is provided in section 2.2.5.

### **2.2.1 Disclaimer on the terms 'early' and 'diagnostics'**

Before continuing the 'tour', I would like to start with a disclaimer on what *early diagnostics* for Alzheimer's disease could mean. It is not always straightforward what is exactly referred to with the words 'early' and 'diagnostics'. This disclaimer unravels the uses of both the terms 'early' and 'diagnostics'.

#### ***'Diagnostics' in early diagnostics for Alzheimer's disease***

The term *diagnostics in 'early diagnostics for Alzheimer's disease'* can refer to (1) biomarker tests and novel imaging techniques; (2) (early) signs and symptoms of the condition; and (3) enabling an earlier diagnosis of Alzheimer's disease. All this is covered by the term 'diagnostics'. This is inherent to the term 'diagnostics' in general – it can be used to refer to the practice of diagnosing (early diagnostics as providing an early diagnosis), the tools used to do so (early diagnostics as advanced medical imaging techniques), and the signs and symptoms that accompany a condition (early diagnostics as identifying the biomarkers that indicate the development of Alzheimer's disease).

Table 2.1: Uses of the term ‘diagnostics’, descriptions and examples

Use of the term ‘diagnostics’	Description	Examples
Sign / symptom / feature	Supporting evidence in a diagnostic process	Plaques, tangles, white matter, cognitive problems, changing behaviour
Device / instrument/ technique	Instruments/techniques analysing or detecting the signs/ symptoms or features serving as supporting evidence in a diagnosis	CSF analysis, MRI scans, PET scans, neurocognitive tests
Art or practice of diagnosing	Diagnosing diseases based on pathological hallmarks of that condition	The use of biomarkers as evidence in diagnostic practice.

### *The ‘early’ in early diagnostics for Alzheimer’s disease*

When referring to early diagnostics for Alzheimer’s disease, the word ‘early’ can refer to different phases in the development of Alzheimer's disease (De Vugt & Verhey, 2013):

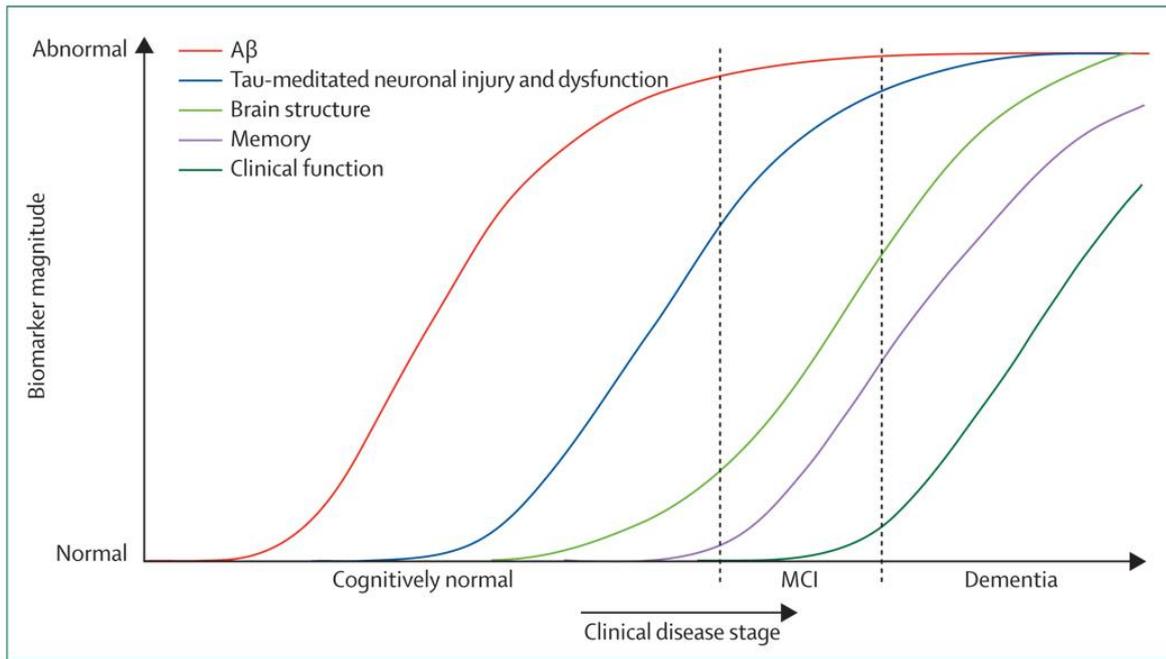
1. A diagnosis of dementia, meaning that the clusters of signs and symptoms of dementia are recognized at an early stage of the dementia rather than at an advanced stage. This is also referred to as a ‘timely diagnosis’.
2. A diagnosis of the pathology of Alzheimer’s disease in a pre-dementia stage: when there are complaints, but these are not severe enough to be labelled dementia.
3. A diagnosis of Alzheimer’s disease before any symptoms are present at all, at an a-symptomatic stage, based on biomarkers only. <sup>5</sup>

### **2.2.2 The pathological cascade model**

To understand why early diagnostics for Alzheimer’s disease are considered important in the medical world, the first site of the tour is the pathological cascade model. This hypothetical model, described by Jack et al. (Jack et al., 2013; Jack et al., 2010), is often referred to in biomarker research for Alzheimer’s disease (Figure 2.1). This model is used by medical professionals to describe how Alzheimer’s disease develops. It also explains the importance of early diagnostics within this understanding of Alzheimer’s disease.

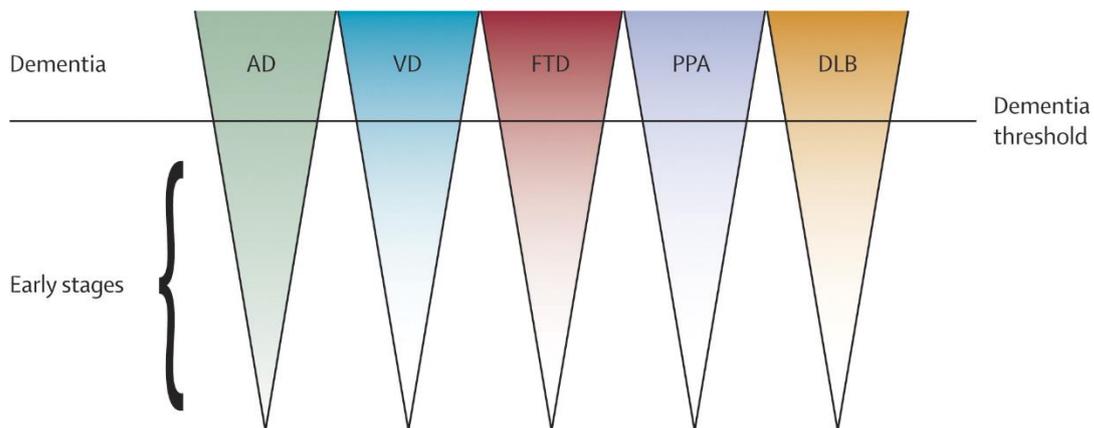
---

<sup>5</sup> The distinction in disease stages is not specific to Alzheimer’s disease but a general distinction used in preventative health care, which is similar to the distinctions made by terms, such as primary prevention, secondary prevention and tertiary prevention. (Gordon, 1983)



**Figure 2.1** Dynamic biomarkers of the Alzheimer's pathological cascade (Jack et al. 2010)

Alzheimer's disease is explained as having a subtle onset, and a slow and gradual progression - hence the 'cascade' metaphor. The expression of symptoms are preceded by gradual changes occurring in the body that can be signalled through changes in biomarkers and brain structure. The cascade model proposes a view on the development of dementia as a condition with a gradual onset. In terms of symptoms, a person slides from normal cognitive functioning, to MCI (Mild Cognitive Impairment) towards the first stages of dementia. After a person has passed the 'dementia threshold' (see Figure 2.2 Dubois et al., 2007) the condition is labelled 'Alzheimer's disease'.



**Figure 2.2** Alzheimer's disease starts and should be identified before the occurrence of full-blown dementia (as for other dementing conditions) (Dubois, 2007)

*AD=Alzheimer's disease; VD=vascular dementia; FTD=frontotemporal dementia; PPA=primary progressive aphasia; DLB=Lewy Body Dementia*

This threshold is based on clinical symptoms, yet these are preceded by milder symptoms and pathological changes. As can be seen in the hypothetical model (figure 2.1), these changes in biomarkers are thought to precede the manifestations of symptoms of dementia in a person. Following this model the development of the pathological changes related to Alzheimer's disease should be detectable before the onset of symptoms of dementia or even before signs of Mild Cognitive Impairment. The detection of these pathological changes is what the LeARN consortium is after. The aim of biomarker research is thus to predict which persons with mild complaints or forgetfulness or even with normal functioning will progress to dementia and which persons will not (Humpel, 2011; Van Rossum, Vos, Handels, & Visser, 2010).<sup>6</sup>

### **2.2.3 Promises of early diagnostics for Alzheimer's disease**

Relating back to the disclaimer on 'diagnostics' (paragraph 2.2.1.), biomarker research on Alzheimer's disease concerns the measurement or visualization of *signs* of pathological processes related to Alzheimer's disease, through the developments of *instruments* to measure these. Yet biomarker research to track the progression of pathological processes related to Alzheimer's disease is not solely, or maybe not even primarily, conducted for the purpose of enabling an earlier clinical diagnostic *practice*.

#### ***Different interests***

The early signalling of biomarkers of Alzheimer's disease is considered to be beneficial to many domains. The interest for identifying and evaluating biomarkers for Alzheimer's disease is explained to be (at least) threefold and these three goals are interrelated (LeARN, 2010). These goals are the following:

1. improving clinical trials to speed up the development of disease modifying treatment,
2. furthering research on the disease mechanisms of Alzheimer's disease, to understand the causes of Alzheimer's disease, and
3. enabling an earlier diagnosis, with the aim to:
  - a) provide certainty to patients on whether they will be developing Alzheimer's disease or not;
  - b) provide information, care and support to patients from an early stage of the development of Alzheimer's disease;
  - c) reduce the financial burden to society through enabling persons with dementia to stay at home longer.

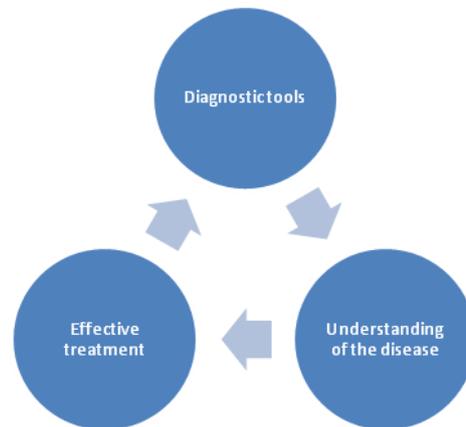
These goals show that the LeARN consortium aims to service at least the processes of drug development (cure), basic biomedical research (cause), and of health care provision (care).

---

<sup>6</sup> For more in depth discussion on the difficulties surrounding the categories MCI, see for example Beard & Neary, 2013; Corner & Bond, 2006; George & Whitehouse, 2009; Moreira et al. 2009; Moreira et al., 2008; Petersen et al., 2014.

### ***Medical vicious circle***

A crucial role is ascribed to biomarkers in the medical quest to understand, diagnose and treat Alzheimer's disease. Biomarker research is described as key to force a breakthrough from what is considered to be a vicious circle of Alzheimer's disease (figure 2.3), which medical disciplines are confronted with. (LeARN, 2010)



**Figure 2.3. Vicious circle of understanding, diagnosing and treating Alzheimer's disease**

The vicious circle is described as follows: For effective treatment it is necessary to understand the disease. To understand the disease it is necessary to diagnose patients at an early stage of the disease. However, early diagnosis of the disease is only useful when there is also treatment available. (Ent, 2006; Hengel, 2007) By identifying biomarkers that 'mark' AD in an individual at an early stage of disease progression, the research program promises to turn the vicious circle around and enable earlier and more reliable diagnosis of Alzheimer's disease, contribute to finding leads for drug development, and enable monitoring of drug response.

### ***Changing diagnostic guidelines***

In clinical practice a diagnosis of Alzheimer's disease is mainly a *syndromal* diagnosis. The term syndrome refers to a set of symptoms and signs that appear together. A diagnosis Alzheimer's disease can be conducted, by for example a general practitioner, based on clinical observations of signs and symptoms, that together form a certain *dementia-syndrome*. Researchers on early diagnostics look at something different. They look for example at brain scans and results of chemical analyses of spinal fluids, in order to find markers, which are indicators for pathological processes that are thought to cause the symptoms to occur. They aim to make a diagnosis based on the *underlying disease mechanisms* that result in certain symptoms and signs to occur. This is called a *nosological* diagnosis.

Up to 2007 (Dubois et al., 2007) the most important international clinical guideline to establish a diagnosis Alzheimer's disease has been the NINCDS-ADRDA criteria<sup>7</sup>, stemming from 1984 (McKhann et al., 1984). The definition of these criteria in 1984 was a demarcation point in the history of Alzheimer's disease, in the sense that it relabelled senile dementia, which was previously considered as the result of normal aging processes, to Alzheimer's disease, which is the result of pathological processes (see also 2.1. A history of Alzheimer's disease).

In these guidelines (McKhann et al., 1984) Alzheimer's disease was conceptualized as a 'dual clinicopathological condition'. The diagnosis was given on the basis of both symptoms and underlying pathological processes. This meant that to diagnose Alzheimer's disease, two sets of requirements had to be met. The first set of requirements was the presence of symptoms including memory impairment, impairment in at least one other cognitive domain, and problems in the activities in daily life (the so-called clinical phenotype). The second set of requirements dealt with the presence of specific neuropathological changes in the brain including neurofibrillary tangles and senile plaques, often accompanied by synaptic loss (dying neurons). The investigation of the pathology in the brain could, until recently, not be done during life, but only through autopsy. The diagnosis that was established by medical professionals was done on a clinical basis: on the basis of symptoms. MRI scans were conducted, but with the purpose of excluding other possible causes for the complaints. This is also why the diagnosis formally was labelled 'probable Alzheimer's Disease', and the label 'definite Alzheimer's Disease' could according to these guidelines only be given after death through autopsy.

The relation between the two sets of requirements has been complicated and highly discussed since then. The problem remained that there were people diagnosed with Alzheimer's disease during life, who did not necessarily show the typical pathological hallmarks of Alzheimer's disease after death. Likewise, some people who did not show any symptoms or signs of Alzheimer's disease during life appeared to have brains cluttered with plaques (Snowdon, 1997).

The emergence of improved imaging techniques and biomarker tests makes enables the tracing of pathological processes in the brain during life. One does not have to wait until after death to look inside of the brain. These new possibilities opened up research opportunities, and clinical possibilities, but also asked for a new lexicon to redefine Alzheimer's disease (Dubois et al., 2010) and novel diagnostic guidelines (Boenink, 2017; Dubois et al., 2007; George et al., 2013; George et al., 2011; Hyman et al., 2012).

---

<sup>7</sup> The abbreviation NINCDS-ADRDA is short for the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (now Alzheimer's Association), who collaboratively proposed these criteria for the diagnosis of Alzheimer's disease.

First diagnostic criteria were revised for research purposes. The revised *research* criteria of the NINCDS-ADRDA (Dubois et al., 2007) include biomarkers and changes made visible through novel imaging techniques as supporting feature for a diagnosis 'probable AD'. The *new lexicon* (Dubois et al., 2010) to serve the research community distinguishes between Alzheimer's disease dementia, prodromal Alzheimer's disease, also called the pre-dementia stage, and a preclinical state of Alzheimer's disease, which includes an asymptomatic at-risk state and a presymptomatic state. The progression of Alzheimer's disease in both symptoms and pathology is now captured in a new terminology to talk about the condition. Biomarkers and imaging techniques have obtained a large role in diagnosing Alzheimer's disease. The pathological hallmarks have become inclusive diagnostic criteria during life, instead of a way to exclude other causes like it was in the past.

Soon after the NINCDS-ADRDA, the NIA/AA<sup>8</sup> also proposed new criteria for the *clinical* diagnosis Alzheimer's disease (Jack et al., 2011). These criteria also include biomarkers of the underlying pathology. The NIA/AA criteria distinguish between on the one hand pathophysiological processes related to Alzheimer's disease, and the clinically observable syndrome. They formalized three stages of disease progression: AD dementia, MCI due to AD, and preclinical AD (which is only meant for research purposes). (Albert et al., 2011; McKhann et al., 2011; Sperling et al., 2011)

Although in these guidelines it is stressed that biomarkers for Alzheimer's disease are not (yet) good enough to be taken up in clinical diagnostic practice, they do reconceptualise Alzheimer's disease in such a way that biomarkers can easily be included in the future. (Boenink, 2017)

### ***Enabling an earlier and more reliable diagnosis to improve patient care***

One of the promises of early diagnostics for Alzheimer's disease concerns the enabling of an earlier and more reliable clinical diagnosis. The main question, relating to this promise, is whether a person is experiencing normal age-related forgetfulness or the early stages of Alzheimer's disease. Not only the pathology, but also the symptoms of dementia due to Alzheimer's disease develop gradually. Different phases in terms of experiencing symptoms are delineated ranging from pre-dementia to very severe dementia, such as for example (Jonker et al., 2009):

- Pre-dementia (starting stage): Different small signs occur that something is not right , such as being tired, difficulty with activities which are outside of the daily routine, being a bit anxious, less spontaneous or withdrawn.
- Mild dementia (stage of support): Increasing cognitive complaints and experiencing problems in the activities of daily life.

---

<sup>8</sup> NIA/AA is short for National Institute on Aging at the National Institute of Health and the Alzheimer's Association.

- Moderate dementia (stage of care): Patient is more and more dependent on support in many aspects of daily life and behavioural problems increasingly occur.
- Severe dementia (nursing stage): Basic functions such as dressing, eating, going to the toilet become more and more difficult. Basic personal hygiene cannot be conducted independently anymore and the person is fully depending on care and support. At this stage a move to a nursing home can be necessary.

So the symptoms of Alzheimer's disease develop gradually. Persons do not move from having no complaints one day to having Alzheimer's disease the next. There is a gradual change from normal functioning up to a full-blown dementia. So all persons who have Alzheimer's disease in the early stages, have had mild complaints at earlier moments in time. However, not everybody who has mild complaints also develops Alzheimer's disease dementia.

The first symptoms of Alzheimer's disease are often (but not necessarily) memory complaints. Research on early diagnosis of Alzheimer's disease is conducted to determine whether these cognitive complaints which are not severe enough to be labelled dementia, are a precursor of Alzheimer's disease and the complaints of this person will become more severe, or not. This stage of Mild Cognitive Impairment (Petersen et al., 2014) is considered a grey area in medical terms, in which more clarity is desirable for patients. An earlier and more reliable diagnosis of Alzheimer's disease would provide more clarity in this grey area. This is the argumentation with which research on early diagnostics is legitimized with regard to improving care for patients. At the same time early diagnostics for Alzheimer's disease would increase economic efficiency of the health care system, provide more clarity for adequate medical interventions and organization of health care, as well as for development of disease modifying treatment (see next part).

### ***Speeding up the development of disease modifying treatment***

The provision of more clarity to persons in uncertainty on whether their complaints are a precursor of dementia or are due to another reason, is not the only driving force behind research on early diagnostics for Alzheimer's disease. The strive to develop disease modifying treatment may be an even more important driver.

While the Dutch LeARN consortium places a relatively high emphasis on the need for early diagnostic instruments to provide clarity to persons with mild complaints, the main goal of, for example, the US Alzheimer's Disease Neuroimaging Initiative (ADNI) was to improve clinical trials for disease modifying treatment (Miller, 2010; Mueller et al., 2005). The ADNI is another example of a research program to identify and validate biomarkers for Alzheimer's disease. In the pursuit to improve clinical trials that evaluate the efficacy of disease modifying treatments (medication) for Alzheimer's disease, advancing biomarker research is considered the most important 'next step'. As said earlier in this chapter 'diagnostics' refers to three aspects at once: signs, instruments and devices, and diagnostic practice. In this case

the signs and devices of early diagnostics are not developed for improving *diagnostic* practice, but for improving the practice of *clinical trials for drug development* (Blennow, 2010a; Hampel et al., 2010).

While there are several drugs to treat symptoms of dementia, there is currently no treatment that can slow down the underlying neurodegeneration. Hope was put on biomarkers to track the progression of Alzheimer's disease "*more faithfully than do the cognitive and clinical measures now used in treatment trials*" (Miller, 2010 p. 386). By measuring the signs of brain atrophy in a scan or changing proteins in CSF (CerebroSpinal Fluid), the underlying disease process rather than the symptoms could be used as an outcome measure in clinical trials (Lyketsos, et al., 2008). This would speed up research, because there is no need to wait for a long time to see whether the disease symptoms occur later.

One of the important hypothesis on which research on early diagnostics for Alzheimer's disease (in LeARN and other consortia), as well as the development of disease modifying treatments were based was the 'amyloid cascade hypothesis'. Amyloid was considered to be the cause of Alzheimer's disease, and the disease modifying drugs tested targeted substances related to the amyloid hypothesis<sup>9</sup>. The importance of biomarker research increased when in 2010 all clinical trials on new disease modifying drugs, using the amyloid cascade hypothesis failed. It was a huge disappointment for the research on disease modifying treatment for Alzheimer's disease, where a lot of hope, effort and money was vested in this hypothesis. Three explanations for the disappointing results emerged (Blennow, 2010b):

1. The amyloid cascade hypothesis is wrong. New or other hypothesis are needed to further advancement in disease modifying treatment for Alzheimer's disease.
2. The trials were conducted with persons who had Alzheimer's disease *dementia*. In these persons the disease has progressed already to such an advanced stage that these drugs were no longer effective. The neurodegeneration in the brains of the persons enrolled in trials was too advanced for the treatment to work. The drugs would be "*most efficacious early on in the disease process, before severe plaque pathology is present*" (Blennow, 2010b, p. 1219). This means that in future trials persons with a less advanced pathology should be enrolled.
3. The subjects in the trials were too heterogeneous to show results, because the diagnostic procedure to include them in the trial was not specific enough.

All three explanations point to an increasing importance of biomarker research on Alzheimer's disease for the development of disease modifying treatment. This created a range of promises of and goals for biomarker tests to improve the clinical trials on treatments

---

<sup>9</sup> There are more hypothesis on the causal mechanisms of Alzheimer's disease. I will not go into these specific medical discussions on disease mechanisms in this thesis. If interested in this please see Lock (2013) for persons with a non-medical background or for a medical overview for example Winblad et al. (2016).

for Alzheimer's disease: (a) to identify pathological mechanisms related to Alzheimer's disease, (b) to exclude people from trials who actually do not have Alzheimer's disease and to include persons with very mild Alzheimer's disease pathology in the trials, and (c) to monitor the effect of the treatment under investigation.

There is a problem in the identification of pathological mechanisms related to Alzheimer's disease, and some authors discuss that these mechanisms should be approached with caution. If there are changes in the body or brain related to Alzheimer's disease, it is not clear whether these so-called pathological changes actually are pathological. They could also be reactive or maybe even protective. Currently, there are numerous underlying 'disease pathways' that are possibly related to the eventual development of Alzheimer's disease. Yet there is no clear single linear chain of events from cause to consequence. What triggers the disease is still unknown, and it is even argued that the development of the characteristic plaques and tangles found in Alzheimer-brains are minor factors or even protective factors, and some other age related process may be a trigger for the disease (Querfurth & Laferla, 2010; Quinn, 2013).

The challenge becomes to identify persons with Mild Cognitive Impairment (MCI) who actually will develop Alzheimer's disease. Of the persons with these mild complaints only a number<sup>10</sup> develops Alzheimer's disease, whereas the rest has these complaints due to other reasons. If biomarkers can be used to identify persons with mild complaints who will develop Alzheimer's disease (Buckholtz, 2011; Koch & Iliffe, 2010), this would create the possibility to include a more homogeneous group of subjects at an earlier stage of disease progression in clinical trials. *"Thus biomarkers will be key tools for enrichment of clinical trials with true prodromal Alzheimer's disease cases."* (Blennow, 2010b, p. 1219).

Next to including 'the right' persons in clinical trials, biomarkers could also be used in clinical trials to prove the efficacy of the treatment that is tested. Clinical and cognitive scales were used for that. But a problem with clinical and cognitive scales is that these measures *"go up and down for who knows what reason because people just have good days and bad days"* (Miller, 2010, p. 388). Biomarkers could improve the measuring of the efficacy of treatment by supplying 'surrogate markers' in clinical trials based on biomarkers, like *"blood pressure and cholesterol level have been used to approve drugs for heart disease"* (Miller, 2010, p. 388). These markers should not only track progression of the disease, but also the response to the treatment at trial in a way that mirrors actual clinical improvements that would only be observable at a later point in time (Miller, 2010, p. 389).

### ***Biomarkers as a shortcut***

Research on biomarkers for Alzheimer's disease promises to solve two discussions at the same time, as argued by Boenink (2017). Biomarkers could provide a clue to distinguish which

---

<sup>10</sup> Percentages differ since the definitions of MCI are not uniform.

particular persons experiencing mild complaints will be developing Alzheimer’s disease on the long run. And they could provide a link between early and late pathological findings. And even more beautiful: they could provide a ‘shortcut’ between early pathological findings and later clinical symptoms of Alzheimer’s disease (Table 2.2).

**Table 2.2: Different observations associated with AD and the possible short-cut promised by biomarkers (Boenink, 2017)**

	Early	Later
<b>Clinical observations</b>	Subjective memory complaints; Mild Cognitive Impairment	Severe memory loss, behavioural & personality changes, interference with daily functioning
<b>Pathological observations</b>	Biological changes in the brain, the cerebral/spinal fluid (CSF) or blood (A $\beta$ -accumulation, tauopathy, synaptic dysfunction, neuronal injury, changed brain structure)	Plaques and tangles (post mortem)

### 2.2.4 Medical controversy on the promises of early diagnostics

The importance and need of a quest for early diagnostic biomarkers is not shared by all medical researchers. Most literature on early diagnostics is from the researchers working on the topic. Those researchers who do not think that early diagnostics is *the* way to proceed in medical research, tend to write on the topics that they find more worthwhile.

The difference in position towards the importance of biomarkers for Alzheimer’s disease is part of a hot issue within the medical domain of Alzheimer’s disease. This hot issue is the fact that despite tremendous efforts and enormous amounts of research money, no disease modifying treatment for Alzheimer’s disease is found (see also section 2.2.3.). Why is no disease modifying treatment found and what lessons to draw from that? This issue is part of fierce debate in research on Alzheimer’s disease. (Ballenger et al., 2009; Brayne, 2007; Richards & Brayne, 2010; Selkoe, 2012; Whitehouse & George, 2008)

The debate centres on the key question whether late onset Alzheimer’s disease is a disease of which the pathological mechanisms can be unravelled and treated, or an accumulation of many processes throughout life, resulting eventually in the same kind of symptoms. There are a number of issues related to this key question. One example is the issue that has haunted Alzheimer’s disease since the birth of the term (see also the historical overview in section

2.1.), namely whether early onset Alzheimer’s disease and late onset Alzheimer’s disease are the same ailment. This boils down to the question to what extent research conducted on persons with early onset Alzheimer’s disease is relevant for late onset Alzheimer’s disease (Richard et al., 2012). A related issue is that while a search for biomarkers aims to pinpoint the pathological mechanisms underlying Alzheimer’s disease, many persons with late onset Alzheimer’s disease might have more heterogeneous pathology than assumed, and most persons do not only have Alzheimer pathology, but a mix of multiple pathologies. (Kapasi et al., 2017; Schneider et al., 2007) Margareth Lock has written a meticulous account on the efforts to slow down or halt Alzheimer’s disease, and the assumptions driving these developments (Lock, 2013). The differences in understanding of the phenomenon referred to as Alzheimer’s disease, also lead to different strategies to deal with Alzheimer’s disease: should one strive for disease modifying treatments, or adhere to a more pragmatic approach of providing the best possible care and a focus on prevention?

The controversy remains to play out, and is reheated continuously. There are different interpretations, conclusions and directions drawn from the same research findings, depending on the understanding of Alzheimer’s disease. It is not always a matter of fully disagreeing, or complete controversy, but a matter of interpretations, belief and prioritizing. The quotes of different positions towards early diagnostics for Alzheimer’s disease in two articles of leading Alzheimer’s disease scientists, i.e. Richards and Brayne (2010) and Selkoe (2012), in Table 2.3, illustrate the content and morality of this debate in scientific literature.

**Table 2.3: Quotes of different positions towards early diagnostics for Alzheimer’s disease**

<b>Richards and Brayne, 2010</b>	<b>Selkoe, 2012</b>
<i>“If Alzheimer’s disease is a diffuse clinical syndrome, there is unlikely to be a therapeutic silver bullet, notwithstanding the dominant research endeavor towards finding effective drug treatments.” (p. 866)</i>	<i>“we will learn more about the natural history of the disease and any partial therapeutic responses from detailed analysis of recent trial results. This process will likely position the field for success, but only with much greater investment in all aspects of Alzheimer research and with careful design of future trials.” (p. 1488)</i>
<i>“the large volume of research on its pathophysiology has not led to any effective preventive breakthrough in the population, unlike cardiovascular disease and stroke.” (p. 865)</i>	<i>“Attempts to treat complex, chronic diseases such as AIDS or certain forms of cancer have been marked by major failures before tangible success emerged. One hopes that this will be the case in AD.” (p. 1491)</i>
<i>“No straightforward correspondence exists between higher mental function and the burden of lesions in the ageing brain. If this shifts the focus away from detailed diagnostic classification made on the basis of assumed clinical-pathological correlation and towards a global pragmatic approach to the needs of patients and cares, and to modifiable lifetime risk factors, then the apparent loss of scientific precision is a gain to clinical practice.” (p. 866)</i>	<i>“changes in lifestyle are unlikely to be sufficient to stave off the development of AD, particularly if these changes are instituted close to the time of clinical onset.” (p. 1491)</i>  <i>“Our patients and their families should remind us of Churchill’s exhortation: “... never, never, ever quit!” (p. 1491)</i>

The promises of early diagnostics for Alzheimer's disease are not equally shared by all medical researchers. Particularly biomarkers that only mark the traditional Alzheimer pathology, that is markers related to plaques and tangles, are considered to be too 'clean', and thus poor markers for dementia in older persons. This leads to a school of thought that does not see an urgent need for more scientific precision in detailed clinical classifications, and that argues for a pragmatic approach to address the needs of patients and caregivers and to reduce risk factors throughout life.

### **2.2.5 Lessons from the medical point of view on Alzheimer's disease**

In this section (2.2) we explored early diagnostics for Alzheimer's disease from a medical point of view. In the medical realm early diagnostics for Alzheimer's disease is considered an important and promising issue, however, the terms 'early' and 'diagnostics' have multiple definitions and meanings, and can thus refer to different situations, applications and research practices. (section 2.2.1.) It is important to realise this, since the terms are often used, but can point to many different situations without this being completely clear for participants in interactions.

The cascade model (section 2.2.2.) was introduced as a model to understand what biomarker research aiming for early diagnostics for Alzheimer's disease entails and why this is considered an important development. Alzheimer's disease is seen as a disease with a gradual onset and an accumulation through time, where pathological changes precede the symptoms. This is why biomarker research can enable an earlier diagnosis of Alzheimer pathology, and may predict which persons with mild complaints or forgetfulness or even with normal functioning will progress to dementia and which persons will not.

Alzheimer's disease is considered a dual clinico-pathological condition, meaning that the diagnostic guidelines include two sets of requirements: (1) the presence of specific symptoms and (2) the presence of specific pathology. Since until recently pathology could only be examined after death, the clinical diagnosis was restricted to the presence of symptoms. This has changed with the rise of imaging techniques and biomarker analysis, and has led to changes in diagnostic guidelines.

The promises of the development of reliable biomarkers (section 2.2.3) would create a shortcut to predict which persons with early pathological changes will progress to develop the symptoms of Alzheimer's disease. The promises of biomarker and imaging research to improve patient care include the provision of clarity to persons who are in uncertainty on whether the changes they experience in their functioning, are an indication of Alzheimer's disease or not. But the promises of biomarker research and imaging techniques are not limited to conduct an earlier diagnosis. There are more interests in Alzheimer biomarker research, including speeding up the development of disease modifying treatment, and furthering basic medical research.

This vision on the importance of research on early diagnostics for Alzheimer's disease through biomarker analysis and imaging techniques is not shared by all medical researchers in the field. There is a controversy between scientists interpreting research results through a disease model aiming to trace and treat the causes of the condition, and scientists adhering to a model of Alzheimer's disease as an accumulation of risk factors throughout the span of life, to be dealt with through prevention over the life span and provision of good care and support (section 2.2.4.).

For this thesis it is important to realize that the development of early diagnostics for Alzheimer's disease is not uncontested in the medical realm, and that there are multiple stakes involved. While it might be possible that early diagnostics is a double edged sword, it can also be the case that some interests are better served than other interests. And it might not always be crystal clear whose interests are served.

### **2.3. Thinking about diagnosis: Early diagnostics for Alzheimer's disease from a clinical, psychosocial and social science point of view**

The history of Alzheimer's disease (section 2.1. A history of Alzheimer's disease) showed that the understanding of Alzheimer's disease and how it is dealt with has shifted throughout time. This sense of history creates a sensitivity to what may be at stake when it comes to changes in dealing with Alzheimer's disease in the present. The pendulous movement between emphasis on pathological explanations and medical interventions, and psychosocial explanations and social interventions, is one of the dynamics highlighted in the history section. The image used was that of looking into a microscope (by looking at the biological details) and of looking up from the microscope to see that brain cells are part of a body, of a person, with a personal history, living in a family in a society.

Research on early diagnosis lies in the tradition of understanding Alzheimer's disease 'through the microscope'. Section 2.2. is based on literature, mainly from the enactors (Garud & Ahlstrom, 1997), professionals that develop and advocate early diagnostics. The general image emerging from section 2.2. is, that persons experiencing cognitive (or other) problems that might be a foretoken of dementia, should be provided with clarity on whether or not they are on a 'dementia lane'. Furthermore to advance research on the causes of dementia and to test disease modifying treatment, an early identification of research subjects that will actually develop dementia, and reliable biomarkers to measure disease progression, are desirable. Guidelines are adjusted to understand Alzheimer's disease as a gradually developing condition in which the pathological signs precede the expression of symptoms in a person. At the same time that these promises are raised and medical researchers are working on fulfilling these promises, there are also researchers aim to understand what early diagnostics means for persons, health care provision and society at large.

This section addresses current literature, looking up from the microscope, studying the psychological, social and cultural aspect of early diagnostics. I will start with issues that are

discussed in the context of diagnostic clinical practice (section 2.3.1), moving to issues concerning the (psychosocial) experience of a person and their family with Alzheimer's disease (section 2.3.2), into the sociology of diagnosis (section 2.3.3). I will zoom in on the changes that (may) occur with the rise of early diagnostics of Alzheimer's disease. I will end with lessons learned from a clinical, psychosocial and sociological point of view on diagnosing Alzheimer's disease (section 2.3.4).

### **2.3.1 Early diagnosis in diagnostic clinical practice**

When it comes to a diagnosis Alzheimer's disease, probably one of the most discussed issues is the question 'to diagnose or not to diagnose?'. For medical professionals the question comes in the form of 'should you disclose the diagnosis?' and for possible patients as 'would you like to know?' (Bortolotti & Widdows, 2011; Carpenter & Dave, 2004; Cornett & Hall, 2008; Fisk et al., 2007). These questions become even more salient with the strive towards early diagnostics for Alzheimer's disease (Comer, 2008; Iliffe et al., 2003).

The answers to the question 'to diagnose or not to diagnose' have shifted from the 1980s up to now<sup>11</sup>. Before the 1980s, when dementia was not dealt with as a medical condition (see history section in chapter 2.1.), the general stance towards a diagnosis dementia used to be that of non-disclosure. This became a topic of debate during the 1980s.<sup>12</sup> With a growing cultural emphasis on dementia as a 'real disease', growing importance of personal autonomy and especially with the arrival of some treatments for Alzheimer's disease on the market, the balance shifted from non-disclosure to disclosure of the diagnosis, unless the affected person waives it. Currently, in the Netherlands, disclosure of the diagnosis Alzheimer's disease is a basic psychosocial intervention in dementia care and an important element in the provision of health care for persons with dementia. A diagnosis at an early stage of the condition is advised, because of the progressive loss of competency over time. (Derksen, 2011; Derksen et al., 2005; Gauthier et al., 2013; Vernooij-Dassen, 2006)

The diagnosis Alzheimer's disease is currently mainly presented as a valuable psychosocial intervention. It is deemed important for improved coping with the changing situation by the individual with Alzheimer's disease and for their relatives and friends (Carpenter et al., 2008; De Vugt & Verhey, 2013; Derksen et al., 2005; Pratt & Wilkinson, 2003; Robinson et al., 2015; Samsi et al., 2013; Vernooij-Dassen, 2006). At the same time the provision of the diagnostic label 'Alzheimer's disease' impacts individuals and their caregivers. Literature mentions a long list of consequences that persons diagnosed with Alzheimer's disease face. The development of dementia involves being faced with a process of loss, changing social

---

<sup>11</sup> This is generally the case in the western world, but is not necessarily in each country, or culture the case.

<sup>12</sup> Arguments in favour of disclosure included respect for patient autonomy, an active role of patients in the planning of their own care, the opportunity to formulate advanced directives, make financial arrangements, settle personal affairs, organize health care, or decide to participate in research. Arguments against disclosure of a diagnosis range from the inability of a person to understand the diagnosis in the later stages of dementia; the (perceived) wish of patient to not be told in earlier stages; the diagnostic uncertainty and imperfect prognostics; the absence of effective treatments; evading potential adverse reactions like anxiety, depression and catastrophic thinking; and risk of social stigmatization (Derksen, 2011).

relationships, asking and receiving support from family, friends and professionals, and it influences a person's self-esteem and self-value. Emotional consequences involve feelings of anxiety, confusion, loss and grief, for both the person with dementia and their family. The loss involves loss of autonomy, but also loss of joy and companionship. Feelings of loneliness and social isolation can be a risk for persons with dementia, or even a risk factor indicating the onset of dementia (Holwerda et al., 2014), while friendships may also provide richness to the lives of persons with dementia and their friends (Phyllis et al., 2012). The relationship between partners changes (ongoing from the diagnosis) to a patient-carer relationship. Furthermore, a diagnosis can lead to a mutual concern of persons with dementia and their family members for each other (Vernooij-Dassen, 2006). Practical consequences include a re-evaluation of a person's lifestyle in the light of the new situation, such as moving to another house, making financial arrangements, or getting married. This longlist shows that a diagnosis dementia is much more than a medical label, leading to medical interventions. Dementia involves a process of loss of competencies for a person and changing social relationships. A diagnosis could help the patient and family to make sense of the new situation and prepare for a constant adjustment and active coping with the issues addressed above.

While a diagnosis Alzheimer's disease is currently mainly presented as a valuable psychosocial intervention, a number of authors outlined conditions that should be met when a diagnosis is conducted (Iliffe et al., 2003; Manthorpe et al., 2003; Mattson et al., 2010; Vernooij-Dassen, 2006). These conditions include for example determining if a person wishes to know the diagnosis; assessing their coping style and psychological profile before a diagnosis in order to provide information during and after a diagnosis suited to the individual and the concerns of the family; and the availability of support after the diagnosis. Support after a diagnosis preferably includes psycho-education. Within psycho-education particular emphasis is put on providing support to families to draw attention away from 'covering up' what is going on, to enable maintenance of a valued social identity for the person with dementia and access to support from friends and families. Furthermore it matters a lot *how* a diagnosis is disclosed, including what the physician actually says, how it is said, which information is given, and references to other professionals or places for further information and support (Carpenter & Dave, 2004; Vann, 2011)

Despite a diagnosis generally being considered a basic intervention, it remains a topic of discussion, particularly in the case of early diagnosis (see for example Claassen, 2011; Grundmeijer, 2011). General practitioners do not all share the position that a diagnosis dementia should be a basic intervention. (Hansen et al., 2008; Iliffe et al., 2003; Koch & Iliffe, 2010, 2011; Perry et al., 2008; Renshaw et al., 2001; Vernooij-Dassen et al., 2005). Different reasons are mentioned for the hesitance of general practitioners: the fear doing more harm than good, suicidal ideation and co-morbid depression after the diagnosis are concerns, the feeling of general practitioners that they have nothing to offer to patients, and that a diagnosis Alzheimer's disease is an uncertain diagnosis. Since a diagnosis is considered a basic intervention in dementia care, efforts are taken to educate general practitioners to change

their attitude towards a diagnosis Alzheimer's disease or dementia. (e.g. Van den Dungen et al., 2012; Koch & Iliffe, 2011; Perry et al., 2008; Renshaw, Scurfield, Cloke, & Orrell, 2001).

With the shift in diagnostic categories (see section 2.2.) from the stage of dementia to diagnosing MCI patients or even diagnosing the pre-symptomatic stages of AD, the question whether or not to disclose the diagnosis Alzheimer's disease is again topic of debate (Pernecky & Kurz, 2012, Leuzy & Gauthier 2012, and see section 2.2.). This time the question is raised whether or not to disclose the outcome of biomarker tests to persons with no or minimal symptoms and full insight. This question is even more difficult in the light of the uncertainty of early diagnostic labels, the uncertainty of test results in terms of prognosis, and in terms of the relation between pathology and symptoms.

The discussion on biomarker tests mainly plays out in research settings. While the clinical utility associated with biomarker tests are not yet established (Mattsson et al., 2010), these tests are already used in for example clinical studies on persons without symptoms of dementia (Kutschenko, 2012; Leuzy & Gauthier, 2012). Ideally, the predictive power of biomarker 'signatures' should be high. But while this is not the case, the question becomes whether or not to disclose test results to subjects in clinical trials. Different strategies have been applied to deal with the disclosure of biomarker information, such as non-disclosure (Karlavish, 2011; Shulman et al., 2013), and running a sub-study on the consequences associated to the knowledge of one's amyloid status (Miller, 2012).

Finally, there are speculations about the acceptability of early diagnostic tests as screening tools in clinical practice when there will be effective disease modifying treatment available. Mattson argues that the acceptability of early diagnostic tests as screening test would depend on the efficacy of tests and the safety and costs of treatment (Mattson et al., 2010).

The question whether a diagnosis should be disclosed is a (still) debated issue amongst medical and health care professionals. One of the issues at stake is the well-being of the person with dementia and their relatives. The balance between the potential harm done and the potential benefits of a diagnosis has shifted more and more towards the potential benefits. Where previously the diagnosis was withheld, currently mainly the advantages of disclosing a diagnosis are stressed: to understand what is going on, to plan future care, access to drug treatments, to obtain advice and support. This discussion, however, was mainly held among health care professionals. The persons with dementia are mainly spoken about, and studied as subjects. During the last decades the lived experience of persons with dementia themselves became a topic of study.

### **2.3.2 How persons with dementia experience the diagnosis**

In the previous sections, we have seen how an (early) diagnosis of dementia is perceived by medical professionals in the light of psychosocial interventions. Yet from the 1990s onward a new line of literature emerged studying the subjective, lived experience of persons who have been diagnosed with dementia. This kind of research can be positioned in the tradition of Kitwood (Kitwood, 1990), who emphasized that the way in which people with dementia are treated highly influences the subjective experience of living with dementia. I will discuss

some of the articles addressing the subjective experience of dementia and its diagnosis of persons with dementia.

### ***The voice of persons who received the label Alzheimer's disease***

It is an interesting observation that the experience of the persons actually being diagnosed and living with the condition are largely spoken for in second hand accounts, and not that much is known about what persons with dementia experience, or how they experience the dementia (Mast, 2009). Beard provides various explanations of why this might be the case (Beard, 2004). Firstly, the biomedicalization of aging has created a conceptualization of Alzheimer's disease based on the biomedical model, in which the body is object of the diagnosis. This model neglects the sociocultural context of illness experience. Secondly, a separation is made dividing research in the physical, psychological and cultural dimensions to different research specialisations. So where in the biomedical research specialties the psychological and sociocultural aspects of Alzheimer's disease are neglected, in gerontological accounts for example the 'body' is lacking. Thirdly, the dominant story of dementia involves an irreversible loss of the very things that define our humanness. This lead to the assumption that interaction with persons with dementia is no longer of interest. This kind of discourse she states "*leaves little room for the subjective reality of the person with memory loss and discounts, if not silences, the most 'deeply forgetful' (Post, 1995) among us.*" (Beard, 2004, p. 418). The 'loss of self' rhetoric related to dementia thus increases the risk of dehumanizing persons with dementia (Behuniak, 2011). Finally, by labelling persons with dementia a rhetorical division is made between 'us' and 'them'. As if 'they' have crossed an invisible line (Ballenger, 2006) after which 'they' are different from 'us'.

Boer et al. argue that including the voices of those living with dementia is important, because the actual experience of dementia by persons with dementia often deviates - in a positive sense - from the perception that elderly without dementia have on living with dementia (Boer, et al., 2010).

Because with new knowledge, technology and guidelines the diagnosis Alzheimer's disease can be given with more certainty at increasingly earlier stages of the disease trajectory, this makes the inclusion of the voice of persons with dementia easier. At an early stage of Alzheimer's disease the cognitive abilities of the persons diagnosed as such are still substantially intact. This trend towards an increasingly early diagnosis of Alzheimer's disease might contribute to an emancipation of persons with dementia.

### ***Coping with the disease label and the condition***

A diagnosis Alzheimer's disease can be understood as a defining moment in a person's life and for their perception of self. From a social point of view it can be seen as a 'status passage' from where a person receives an 'illness identity'. This identity functions both as a resource and as a point of resistance for a person with this diagnosis (Beard & Fox, 2008, p. 1518).

With an increasingly early diagnosis of Alzheimer's disease, and with biomarker research on early diagnostics, problems that were related to normal aging before are now part of Alzheimer's disease and diagnosed as such. Persons are given a disease label at an earlier

stage. Beard argues that regardless of the accuracy of such an early diagnosis, and regardless of discussions on the lack of correlation between the pathology and the development of symptoms of dementia, creating the risk of rendering normal aging phenomena into a disease, the so-labelled experience themselves within this disease context (Downs, 2000). Which means that persons diagnosed with Alzheimer's disease at a very early stage will also deal with the issues that come with receiving an illness identity.

A number of studies address the subjective experience of persons with dementia. The emphasis on these studies is that *"people with dementia are just like the rest of us, their lives continue to have meaning."* (Beard 2004, p. 426). These studies show persons who are faced with a new reality and are *"struggling with and adapting to the changes a diagnosis Alzheimer's disease brings along, while attempting to maintain a fulfilling life"* (Harman & Clare, 2006, p. 485).

Harman and Clare, for example, show that after receiving a diagnosis, the so-labelled persons need to deal with several things at the same time. Firstly, they need to deal with the development of symptoms and the impact these have on daily life. Persons deal with their changing competences through normalizing change, adapting and accepting, withdrawing from activities, or struggling to maintain a pre-illness way of life. Secondly, persons need to deal with the knowledge that one has this condition, the emotional response to this information and the changing identity or notion of self. This involves a re-evaluation of core assumptions and expectations of life and self. Harman and Clare show how persons diagnosed with dementia juggle the tension between the prognosis and the desire to remain a sense of identity. A person diagnosed with Alzheimer's disease also needs to deal with the reactions of others (family, friends, health professionals, anybody), and the cultural ladenness of a diagnosis dementia. While dealing with all this would be though for anybody, a person with dementia needs to deal with all that while being cognitively impaired to a certain extent – which makes it even harder (Harman & Clare, 2006).

Another good example is the study of Lee (2014) on mechanisms of coping and adapting. This study shows the process persons go through after a diagnosis Alzheimer's disease, which is understood as a grief cycle, and then continue their lives. The initial reaction involves shock and distress, followed after a couple of months by coping mechanisms: functional coping mechanisms to deal with functional limitations, emotional coping mechanisms to regulate distress and meaning-making coping through appraising the diagnosis in a meaningful way and normalizing their condition. Acknowledging grief is also at the core of the Dutch Alzheimer Cafés, supporting persons with dementia and their informal caregivers (Miesen, 2002).

Steeman et al. (2013) studied the experience of persons living with early stage dementia in which a major theme was their struggle to be valued. They state that during time the value that is upheld shifts from 'being valued for what you do' to 'being valued for who you are'. They see this as a way in which persons with early stage dementia adjust to the unavoidsabilities in life and maintain a sense of identity and self.

These studies on the experience of persons with dementia mainly focussed on the experience of persons with *early stage* Alzheimer's disease. This seems logical because the earlier the diagnosis is given, the easier it becomes to include the voices of persons diagnosed with (early stage) Alzheimer's disease. All authors argue that it is possible to actively include the voice of persons with Alzheimer's disease, instead of relying on caregiver accounts, and that there is no more justification to not include their voices. While this is an important step, these studies still leave the persons with more advanced stages of Alzheimer's disease without a voice.

### **Stigma**

One issue that is ever-present in literature on the social and cultural implications of an (early) diagnosis Alzheimer's disease, is stigma. Alzheimer's disease is generally considered to be a stigmatizing label (Behuniak, 2011; Kitwood, 1997). Stigma can be defined as an attribute that is deeply discrediting (Goffmann, 1963). People who are in possession of such an attribute come to be viewed as inherently defective, and therefore less valued than other 'normal' people. Stigma involves processes such as stereotyping, loss of status and discrimination (Goffmann, 1963). Since Alzheimer's disease is often framed in terms of tragedy, loss of humanity, and loss of self, stigma of persons with Alzheimer's disease is generally considered well-established. Post considers this an effect of our hypercognitive society, which places a disproportional emphasis on rational thinking as human quality, and as a result Alzheimer's disease takes synonymy with the status of a non-person (Post, 2000), which is described by others as social death (Sweeting & Gilhooly, 2008).

This stigma associated with Alzheimer's disease is becoming even more troublesome when the diagnosis Alzheimer's disease is established at an increasingly early stage, with persons who have moderate complaints, or even no symptoms at all. People with early stage dementia feel stigmatized by others as well in personal relationships with friends and family (Batsch & Mittelman, 2012). In the study of Beard and Neary (Beard & Neary, 2013) on stigma associated with MCI, a self-stigmatization is seen, where people internalize the predominant negative public perception of Alzheimer's disease as a death sentence, the loss of everything. Also efforts are undertaken to prevent discrimination through institutions when a person is early diagnosed with Alzheimer's disease. Persons with early stages of Alzheimer's disease are often confined in their possibilities via information from insurance, pharmaceutical or medical records (Karlavish, 2011). Summarizing, the move towards an earlier diagnosis brings along the risk of increased stigma and discrimination.

Effort is put in the reduction of stigma associated to Alzheimer's disease, mainly by supplanting the discourse of loss of self with another kind of discourse (Basting 2009, Beard 2009, Harris 2008), emphasizing "*a more compassionate, hopeful and realistic perspective*" (Gauthier et al., 2013, p. 110); "*highlighting that individuals with AD can lead lives marked by meaning and productivity*" (Gauthier et al., 2013, p. 110) which should result in "*evocation of compassionate attitudes and increased caregiving if public awareness were to increase along less distorted lines*" (Gauthier et al., 2013, p. 110). In the last decade this

compassionate discourse has gained foothold, leading to a dichotomy between the tragedy and the living-well discourses (McParland, Kelly, & Innes, 2017).

### **2.3.3 Sociology of diagnosis**

The previous sections explored and presented the thinking about (early) diagnostics for Alzheimer's disease from medical (section 2.2.), clinical (section 2.3.1) and psychosocial (2.3.2) perspectives. All these domains present different narratives on what is at stake when it comes to a diagnosis Alzheimer's disease, and highlight different consequences of a diagnosis Alzheimer's disease. When a condition is attributed a diagnostic status, this status creates order in many different domains. This phenomenon is at the core of 'sociology of diagnosis'. (Brown, 1995; Jutel, 2009; Jutel, 2011; Jutel & Nettleton, 2011)

Within this (small) strand of literature a diagnostic category is considered as a social agreement that a condition should be given a diagnostic status. The sociology of diagnosis studies how these social agreements on what is considered to be in need of a diagnostic label and what not come to be. Alzheimer's disease is one of these diagnostic labels with many twists and turns in its history (see section 2.1 of this chapter) and used in one of the founding articles of the sociology of diagnosis to illustrate through which dynamics new diagnostic labels emerge to frame a condition as a disease (Jutel, 2009). A second strand in the sociology of diagnosis is the study of the social ordering through diagnostic labels. When a condition is attributed a diagnostic status, this status creates order in many different domains. These domains include the medical profession, the structuring of medical knowledge, building the body of knowledge, the doctor's practice, the experience of a person, and what society is willing to accept as normal and what is considered deviant. This phenomenon of a diagnosis influencing many domains is thus not particular to Alzheimer's disease, but is a characteristic of diagnosis in general. This paragraphs briefly describes the ordering work of a diagnosis within these different domains.

Diagnostic categories offer a structure delineating and organising the medical profession. Diagnosis for example defines the authority of the medical profession, because only medical professionals have the authority to construct a diagnosis from complaints of a patient and physical or biological findings. This sets medical professionals apart from lay persons. Diagnostic categories subsequently structure relations between medical professionals as to who should take responsibility for which disorders and who has authority over which disorders. These discussions are quite alive, and there is a competition on different medical disciplines as to who is to claim authority over the condition Alzheimer's disease: psychiatry, neurology, geriatrics, or another discipline (see for example Verhey, 2002; Olde Rikkert et al. 2011).

Diagnostic labels structure medical knowledge, because each diagnosis is a category in a classification system, such as for example the DSM. The classification system is based on a taxonomy in which medical knowledge is organized. This structure serves as a pre-existing set of categories, agreed upon by professionals, in which professionals and others fit their observations.

This classification system serves as a vehicle for building the body of medical knowledge. Yet a diagnosis is also a name given to a condition of a person. It is essential to understand the difference between the disease concept in the classification and the natural entity it refers to (Dehue, 2008; Dillmann, 2000). There is a person who experiences some changes and changes may be seen in physical examination. The 'natural entity' consists of a number of phenomena: symptoms, complaints, physical or biological changes. When a disease category is established for such conditions, the disease concept functions as an impetus to assume that changes in functioning of a person are the result of that particular disease. The disease concept is accepted as a 'given' in order to investigate changes *as if* they were the expression of this disease. The patient becomes a 'case' within that disease category and studying such a case can contribute to the body of knowledge on that condition (Dillmann, 2000).

This classification system provides a tool for doctors to attribute a condition of a person to a category in the classification system. When a patient visits a doctor with a number of complaints and symptoms, the classification system helps the doctor to understand and interpret these as belonging to a certain disease category.

When a doctor assigns the signs, symptoms and complaints of a person as belonging to a certain disease category, the diagnosis then organises the management of medical care for this patient. The diagnosis provides explanations of the complaints, a prognosis, and possible courses of treatment. Furthermore a diagnostic label serves as an 'entrance ticket', because a diagnosis enables access to health care services, insurance reimbursements, access to medication, and entitlement to sick leave or membership of a support group.

A diagnosis also organises the experience of a persons with a specific condition. When a constellation of complaints is labelled as a specific disease, a disease label is an acknowledgement and acceptance of that deviance. Rather than being blamed for a deviance, a person is treated and cared for and provided with an explanation for this deviance. It gives the person the permission to be ill and persons who are provided with a disease label are authorized to sickness privileges. A diagnosis can also provide personal and emotional control by knowing what is going on. On the other hand, it can set a person apart as abnormal or sick, in a negative and stigmatizing manner, which is often illustrated by the example of homosexuality being diagnosed as a mental disorder and treated as such for a long time. The literature on the role of a diagnosis on the ordering of the (psychosocial) experience of a person with Alzheimer's disease has been addressed in paragraph 2.3.2.

Finally, a diagnosis is a cultural expression and a form of social control. Some conditions become medically labelled and some don't. A diagnosis is a social agreement at a particular moment in time, that a condition should be given a diagnostic status. Diagnostic categories are an expression of what a society is prepared to accept as normal and what is set aside as deviant. As we saw in the history of Alzheimer's disease, senile dementia changed from a normal condition belonging to old age, to becoming a 'real disease' by re-labelling it as Alzheimer's disease. The demarcation of 'deviant' through a diagnosis can societally be explained as acknowledging that a person functions differently and is provided with support, but it can also be explained as disqualifying.

What the sociology of diagnosis shows is the politics behind diagnostic labels, the social processes feeding into it and the ordering work conducted through this one shared label across many domains.

#### **2.3.4 Lessons from a clinical, psychosocial and sociological point of view**

This section on thinking about diagnosis, showed that early diagnostics for Alzheimer's disease is not a development that takes place in the confined isolation of a laboratory. From a medical point of view (section 2.2.), early diagnosis was considered important to speed up the development of disease modifying treatment of Alzheimer's, to further research on the causes of Alzheimer's disease, to provide certainty, and proper health care to patients, as well as to reduce societies' health care costs. While most discussions on early diagnostics of Alzheimer's disease tend to narrow down to the medical domain and the context of (evidence based) health care provision (Milne, 2010), we have passed amongst others medical, clinical, psychosocial and sociological literature in which next to the laboratory, early diagnostics was understood in the context of the clinical practice, the person diagnosed with AD, the informal caregivers and society at large.

In this section (2.3) we have further unpacked (early) diagnosis of Alzheimer's disease with clinical, psychosocial and sociological literature. One of the first questions that comes up when it comes to an (early) diagnosis Alzheimer's disease is whether a diagnosis is a desirable intervention for a patient and at which moment in time. Furthermore we have seen that the value of a diagnosis and the type of consequences of a diagnosis are addressed from many different positions, ranging from how to provide best health care, how it fits a person's life, how a person copes with it, how friends and family deal with the condition, the cultural images related to dementia, the perceived consciousness and competence of persons with dementia, to the role of a diagnosis in the building of medical knowledge. The social implications of (early) diagnosis of Alzheimer's disease include many different social realities, such as basic biomedical research, clinical trials, diagnostic practice by health care providers, the lives of persons with dementia and their family and cultural representation of aging and dementia.

The image emerging from literature on (early) diagnosis of Alzheimer's disease is that a diagnosis serves as an ordering device in many domains at once. It appears as a node connecting different domains and doing ordering work in these domains. From the sociology of diagnosis we learned that this social ordering is not restricted to a diagnosis of Alzheimer's disease in particular and is a characteristic of diagnosis in general.

#### **2.4 Thinking about dementia and ailments<sup>13</sup> in general**

Throughout history dementia has been understood in different ways, in terms of its causes and in practices on dealing with (persons with) dementia (section 2.1). In our current time,

---

<sup>13</sup> The word ailment is used, because in this paragraph the word disease will be used in relation to a particular way of understanding dementia.

the legacy of all these ways of understanding dementia are still present. The different strands of literature on diagnosis (section 2.2. and 2.3) also showed different understandings of Alzheimer's disease and dementia.

Knowledge about dementia comes from multiple sources with different starting points and interests. Innes and Manthorpe (2012) observe that *"curiously, dementia attracts little overlapping multi-disciplinary and multi-professional interest, with the result that underlying assumptions around dementia care practices are often implicit and blurred."* (Innes & Manthorpe, 2012, p. 683) Depending on the context, some understandings of dementia will be more foregrounded than others. Being aware of the multitude of understandings of dementia that are present today is important because *"(h)ow we approach dementia, what our starting point is, whether this is professionally and/or academically oriented or as policy makers, will impact how we see the 'problem'; how we might try to approach it; and how we might try and respond to look for a solution"* (Innes & Manthorpe, 2012, p. 689). How dementia is approached, will also affect how early diagnosis for Alzheimer's disease is approached and responded to.

Section 2.4.1. addresses different explanatory models of dementia. These are analytical models that will hardly ever exist in the pure form in which they are described. Section 2.4.2. addresses different conceptualizations of ailment in general. And section 2.4.3. provides an approach on ailments in practice.

### **2.4.1 Explanatory models of dementia**

For this section I draw on the explanatory models delineated by Murna Downs et al. (2006) and the so-called 'webs of understanding' delineated by Anthea Innes and Jill Manthorpe (2012). Downs et al. (2006) delineates four explanatory models: dementia as normal aging, as a neuropsychiatric condition, as a spiritual experience and as a dialectic process involving an interplay between biological, psychological and social components. Innes and Manthorpe (2012) delineate three broad theoretical models: a biomedical, a (bio)psychosocial and a social gerontological model for dementia. Since the models of Downs et al. and Innes and Manthorpe partly overlap, instead of addressing them separately I have fused them under the following five headings: dementia as normal aging, dementia as a biomedical or neuropsychiatric condition, dementia as a (bio)psychosocial process, dementia from a social gerontological perspective and spiritual explanations for dementia. I will describe the view of dementia as expressed in the different models and the subsequent way to deal with dementia. When specifically mentioned, I will also discuss the meaning of (early) diagnosis of dementia within these approaches.

#### ***Dementia as normal aging***

In this model dementia is viewed as an impairment that comes with age (Downs et al. 2006). This was the western view up to the 1970s and due to the difficulty to neuro-biologically distinguish between normal aging and dementia, it continues to be an explanatory model today. In this view the difference between normal aging and dementia is a matter of degree

and a social construct (Scodellaro & Pin, 2013). If dementia is part of normal aging, it should be accepted as part of life (Downs et al. 2006).<sup>14</sup>

### ***Dementia as a biomedical or neuropsychiatric condition***

Dementia is viewed as a pathological condition, which is the result of an underlying progressive brain disease: 'a real disease' (neuropsychiatric model - Downs et al., 2006; biomedical understanding - Innes & Manthorpe, 2012). This neurodegenerative disease is the cause of symptoms such as cognitive and behavioral changes. Dementia, like any disease, is classified through diagnosis, which should lead to a prognosis and (development of) medical interventions. This model proposes a biological cause and changes in behavior, cognition and psychotic symptoms are attributed to neurological impairment. Viewing dementia as a neuropsychiatric condition puts it in the realm of medical specialists, and creates the moral obligation to deal with this condition in terms of diagnosis, prescription of cognitive enhancers and management of behavioral symptoms.

Especially in this model (a timely<sup>15</sup>) diagnosis has a central position. Diagnosis is a key service provided by medical professionals. Dementia and the stages of progression are defined using an array of information: brain scans, psychological tests, physical tests, anamnesis and hetero-anamnesis. A diagnosis and prognosis enables patients and their families to come to terms with the diagnosis, adjust their life to this progressive condition and organize care and support. Furthermore a diagnosis is of importance for the subsequent prescription of possible medication. A timely diagnosis is desirable because it enables support from skilled professionals, the timely prescription of possible medication and enough time for patients and caregivers to come to terms with the prospects of dementia. (Downs et al., 2006; Innes & Manthorpe, 2012)

### ***Dementia as a (bio)psychosocial process***

The (bio)psychosocial model (Innes and Manthorpe, 2012) or dialectic model (Downs et al. 2006) puts the person central. The manifestation of dementia in an individual should be understood as an "*interplay of neurological impairment, physical health, personality and agency, past experience, social psychology and social resources.*" (Downs et al., 2006, p. 246) Persons with dementia are viewed as active agents "*seeking meaning, responding and attempting to act on their world*" (Downs et al., 2006, p. 244) Challenging behavior, for example, in this view is not considered as merely a symptom of a brain condition, but as an attempt to express oneself, to express needs, or to communicate. Furthermore, in this model, the environment of a person has as much effect on the person's abilities as the brain has. The disabling effect of dementia, is not primarily due to the functional impairment, but

---

<sup>14</sup> If Alzheimer's disease is considered to be part of aging, another strategy is to make the process of senescence the object of biomedical interventions. There is an increasing trend to see senescence as the object of biomedical intervention (Grey & Rae, 2013; Schermer, 2013; Schermer & Pinxten, 2013).

<sup>15</sup> With the word 'timely' referring to a diagnosis of dementia, meaning that the clusters of signs and symptoms of dementia are recognized at an early stage of the dementia rather than at an advanced stage (De Vugt & Verhey, 2013). See paragraph 2.2.1.

also stems from the interactions with other people, which is described in the negative sense by Kitwood as a 'malignant social psychology' (Kitwood, 1997). While not much can be done to arrest the underlying brain pathology, a lot can be done to promote health and well-being and maintaining quality of life. This approach focusses on maintaining and enhancing quality of life, rather than managing and controlling symptoms. The interventions range from support for active coping, at the individual level by helping persons to adapt and cope with the new situation, and at societal level by reducing stigma and negative stereotypes, and provision of an enriched social environment by providing person-centered care, and relationship-centered care, and by reducing malignant social psychology, to the promotion of rehabilitative approaches to reduce functional disability. This approach has led to studies on the experiences of persons with dementia themselves and giving voice to them by for example involvement in advocacy activities. The challenge for carers is to renegotiate the relationship with the person with dementia, and to deal with the person with dementia to preserve and enhance their personhood (Downs et al., 2006).

### ***Dementia from a social gerontological perspective***

The social gerontological perspective stresses that social and structural factors shape the individual's experience of dementia. *"Dementia is seen as an experience and disability located within particular social, environmental and structural contexts."* (Innes & Manthorpe, 2012, p. 691). Different authors have positioned the meaning and experience of Alzheimer's disease within specific cultural situations (Cohen, 1995; Leibing, 2002; Post, 2000). While in western societies dementia is mainly framed as having to do with memory, Cohen for example showed that an angry voice is an important sign of dementia in Banararas in India (Cohen, 1995). In Brazil dementia is related to the lack of capacity to deal with life's stress and strain in a creative and flexible way (Leibing, 2002). Post (2000) positions Alzheimer's disease as a symptom of the western hypercognitive society.

At the heart of the agenda of western social gerontology, lies a strive towards social inclusion of persons with dementia and a dementia-friendly society. A barrier for this is the current stigma and image of decline and loss that accompanies dementia. In order to create a dementia-friendly society, rather than a dementia averse society, more positive conceptualizations are needed for persons with dementia for them to remain resilient and even to age successfully with dementia (e.g. Harris & Keady, 2008). Public images and attitudes on dementia contribute to the fear of dementia and can lead to a reluctance to obtain a diagnosis. (Innes & Manthorpe, 2012)

### ***Spiritual explanations for dementia***

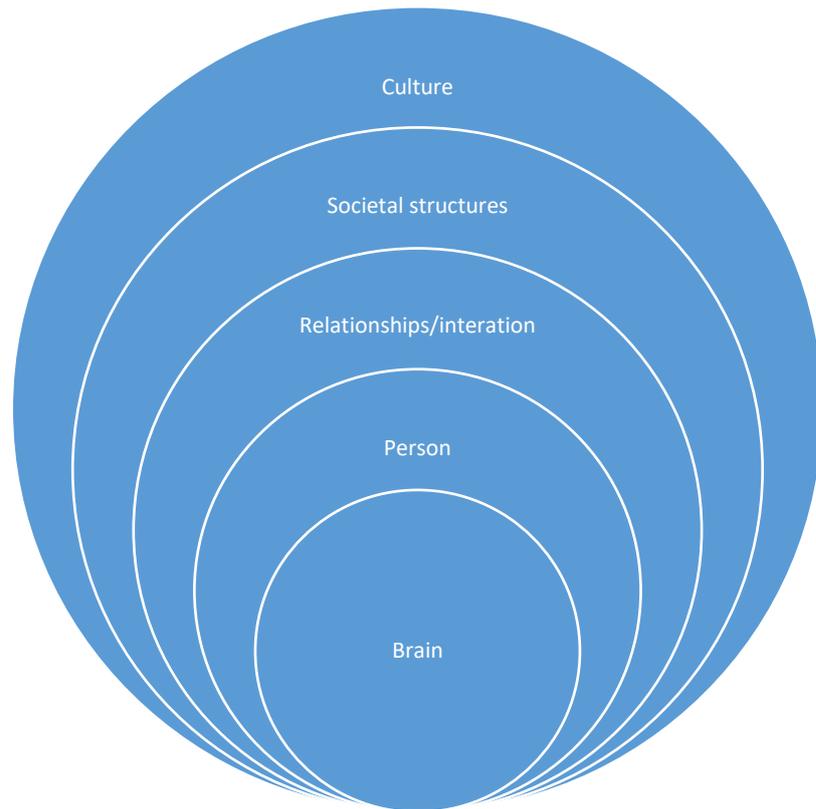
In some cultures dementia is viewed as a consequence of forces of good or evil (Downs et al. 2006). Examples of this explanation are witchcraft, the retribution for family wrong-doing or sins of ancestors, a disturbance between yin and yang, possession by evil spirits, or a negative force or spell cast on a person. The implications for people with dementia and their families can go two ways. The first is that a person with dementia can easily become stigmatized or an outcast, should be feared, avoided or isolated from the community. The way to deal with dementia in this approach are for example prayer to provide salvation, go to a folk healer,

music, dancing, or even exorcism. The second is that a person with dementia can be considered as 'chosen by God', or 'especially spiritually rich', or in 'close communion with the spiritual side of life' (Downs et al. 2006, p. 236).

While this explanatory model may sound exotic, and may be deemed irrelevant in western societies, I would like to keep it here as a relevant model for understanding. The notion that Alzheimer's disease is a matter of fate is present in western societies as well. Dementia understood as a retribution for wrong doing may revive with the current move towards healthy aging, lifestyle influences and prevention of diseases in late life. Dementia could change from a tragic fate to something that closely resembles the notion of penance for earlier bad lifestyle choices. Furthermore there are some voices stressing that persons with dementia have something to give, that they provide us with a way of being in the world that brings us back to our sensitive self, and a being-in-the-world beyond our rationality. Furthermore spiritual or religious guidance might be needed by persons in the process of coming to terms with a diagnosis Alzheimer's disease, and the need to rethink life and the expectations on life. This understanding also relates to cultural notions of what it means to be human. Looking at western society, this has changed considerably in the past centuries. Witches that were prosecuted in the Middle Ages, may have actually been persons with dementia (Berchtold & Cotman, 1998). Up to the late 19<sup>th</sup> century persons with dementia would not lose their role in society, because religion played a large role, and persons with dementia often still relate to God (Ballenger, 2006). While Post argues that in modern society, with a strong emphasis on humans as rational beings, persons with dementia do lose their humaneness. (Post, 2000), Downs et al. (2006) describe this explanatory model mainly in terms of non-western cultures, I would like to emphasize that matters of fate, faith and existential, spiritual or religious interpretations of (life with) dementia are possibly more present in western societies, than Downs description of this model suggests.

### ***Reflecting on these explanatory models***

The explanatory models differ in focus on what causes or contributes to dementia and where to intervene (see Figure 2.4). These analytical understandings of dementia exist side by side, and are drawn upon in different practices. There are few efforts to integrate these perspectives, and not all actors dealing with Alzheimer's disease are aware of the multiple perspectives shaping dementia practices, or one's own position within these understandings.



**Figure 2.4 Focus of explanatory models on dementia**

There is a tendency to critique models based on their theoretical origins, on possible negative consequences they have had in the past, or on the interests that are involved in upholding these models. If dementia should for example be accepted as normal part of life, too much acceptance could lead to a passive attitude and the risk that there is no felt need for specialist therapeutic effort, or provision of additional health and social services. It may also lead to ideas that no medical intervention is needed, while it might be possible. The biomedical model and the diagnosis of a persons with dementia, are critiqued for reducing a person with dementia to a brain condition, with all expressions of a person being attributed to this label. In its extreme form this has led to the 'loss of self' rhetoric, experiences of disenfranchisement of persons with dementia, and cultural stigma. There is especially a tendency to contest the biomedical model, because it has been the most 'dominant' model and much of the money and power is concentrated around this approach, mainly targeting the large interests and power plays of medical researchers, and the pharmaceutical industry, favoring investments in 'cure' over 'care'. A personhood approach puts the person with dementia at the center stage, but has been critiqued for putting too much responsibility on the caregivers and their achievement or failure to enable personhood. A social gerontological model while aiming to reduce ageism and move away from negative images of persons with dementia as being a burden for society, is critiqued for drawing on the increasing numbers of persons with dementia and the increasing societal costs, thus possibly contributing to the stigmatization of persons with dementia, to make dementia a public priority (Innes & Manthorpe, 2012). Innes and Manthorpe stress that while these critiques are legitimate and it is important to be aware of possible interests, or negative consequences

of models, they do not dismiss the insights that each approach provide on the issue. Every perspective has its strengths and weaknesses (Innes & Manthorpe, 2012).

An interesting observation for this thesis on the meaning of early diagnosis of Alzheimer's disease is that both Innes and Manthorpe (2012) and Downs et al. (2006) only refer to (early) diagnosis relating to the model of dementia as a biomedical or neuropsychiatric condition. (Early) diagnosis has a central place in these models and is not particularly mentioned in the other approaches to dementia.

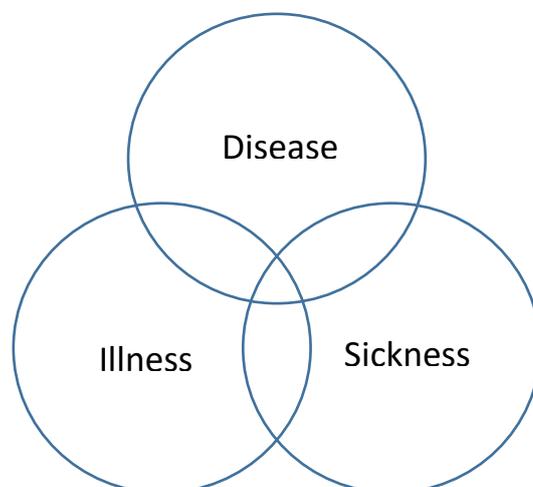
The meaning of early diagnosis of Alzheimer's disease will be differently constructed within these different modes of understanding. Early diagnostics is positioned mainly within the biomedical understanding of dementia. Criticism on the biomedical understanding often includes that too much attention goes to biomedical research and that the promises for a cure of Alzheimer's disease are highly disputed if not impossible (Lock, 2013; Whitehouse et al., 2005; Whitehouse & George, 2008). Often these critiques end with the plea to abandon the biomedical quest in favor of one of the other understandings of dementia. While it could be argued that too much emphasis is put on a medical solution for Alzheimer's disease, this does not mean that the development of early diagnostics for Alzheimer's disease cannot be desirable for the other understandings of Alzheimer's disease.

#### **2.4.2 Conceptualizing ailment**

The different models to understand dementia addressed in the section before, and particularly the division in biomedical, psychosocial and social gerontological models shows high resemblance with conceptualization of disease in general in terms of 'disease', 'illness' and 'sickness'.

##### *Disease, illness and sickness*

The different 'webs of understanding' and explanatory models addressed in the previous section show resemblance to the triad disease-illness-sickness that is often used in sociology, anthropology and philosophy to analyze controversies over forms of un-health or ailment (Hofmann, 2002).



**Figure 2.5 Triad disease-illness-sickness**

While Innes and Manthorpe (2012) urged for a more explicit reflection on the underlying understandings of dementia to benefit from the insights of these different ‘webs of understanding’, the triad as shown in Figure 2.5 is useful to explain discussions and controversies that surround ailments. Ailments in which disease (biological deviation), leads to illness (experience of symptoms) and results in sickness (social identity) will not cause much discussion. Controversies occur when an ailment does not cover all three aspects at the same time, or these aspects do not apply at the same time in a particular situation. It is mainly in controversial cases that this triad is useful, because it helps to make the distinction between the three concepts, rather than merge all aspects and theories on ailments under one word (such as disease). These three concepts are defined as follows:

*Disease “is a health problem that consists of a physiological malfunction that results in actual or potential reduction in physical capacities and/or a reduced life expectancy.”* (Twaddle, 1994 p.8 in Hofmann, 2002, p. 652) Disease refers to an organic phenomenon, which is considered to be independent of subjective experience and social conventions and can be known through objective means.

*Illness “is a subjective interpreted undesirable state of health. It consists of subjective feelings states (e.g. pain, weakness), perceptions of inadequacy of bodily functioning, and/or feeling of incompetence.”* (Twaddle, 1994, p. 10 in Hofmann, 2002, p. 653). Illness refers to a subjective state of the individual, often referred to as symptoms. This state can be directly observed by the subject and indirectly accessed through the individuals’ report.

*Sickness “is a social identity. It is poor health or the health problem(s) of an individual defined by others with reference to the social activity of that individual.”* (Twaddle, 1994, p. 11 in Hofmann, p. 653). It is a social phenomenon constituting a new set of rights and duties and sickness is defined by the (partial) inability to participate in the social system. Epistemically it can be accessed by measuring levels of performance with reference to expected social activities when these levels fail to meet social standards.

According to the triad, these three aspects are involved in all ailments. Yet, often approaches to ailments<sup>16</sup> implicitly privilege one of the three aspects of the triad to have the power to define. Looking at Alzheimer’s disease through the triad, shows that Alzheimer’s disease is a quite controversial kind of ailment and discussions are to be expected. While Alzheimer’s disease is used as a ‘disease’-category, this is also contested because of the difficulty to delineate it from normal aging, or other conditions. The biological causes of Alzheimer’s disease (the ‘disease’) are still largely unknown and factors contributing to the problem persons experience when having Alzheimer’s disease are sought in the biological, psychosocial as well as the societal domain.

Early diagnosis of Alzheimer’s disease moves into the realm of tracing the ‘disease’ Alzheimer’s that might explain mild cognitive problems as early symptoms (illness experience) and providing persons with a ‘sickness’ status. When early diagnosis is even

---

<sup>16</sup> This triad is why I started to use the word ailment, since disease, illness and sickness all have a particular connotation in this triad.

possible in a pre-symptomatic stage, it moves to the situation where a disease is diagnosed and a sickness identity is created in the absence of illness.

### 2.4.3 Ailment in practice

The analytical approaches delineating different conceptualizations of (Alzheimer's) disease are helpful to understand how Alzheimer's disease can be understood. They provide different (theoretical) perspectives on the same phenomenon. The assumption is often that there is one object (Alzheimer's disease) that is looked upon from different perspectives.

Annemarie Mol, in her book *The Body Multiple: Ontology in Medical Practice* (2005) takes another approach. She does not study how a disease can be *looked upon*, but how it is *done* in practice. "*If practices are foregrounded there is no longer a single passive object in the middle, waiting to be seen from the point of view of seemingly endless series of perspectives. Instead, objects come into being – and disappear – with the practices in which they are manipulated. And since the object tends to differ from one practice to the other, reality multiplies.*" (Mol 2005, p. 5) Mol teases out how a disease like arthrosclerosis is 'done' in multiple ways in one hospital. Her work shows a disease that does not have an essence that can be known, but takes different shapes depending on the way it is enacted. Arthrosclerosis is shaped and re-shaped through practices. Phenomena like diseases thus differ from one practice to another, because they are enacted differently.

Alzheimer's disease is also enacted in many ways as can already be understood from the review of literature found in this chapter. Alzheimer's disease as sought for in the results of a CSF<sup>17</sup> analysis, is not the same entity as the problems a person with Alzheimer's disease encounters in daily life, or Alzheimer's disease to be dealt with by the economic and health care system - even though the same word is used. The question is not which enactment is most accurate, but how these different enactments are coordinated.

In line with Mol, Ingunn Moser (2008) has studied how Alzheimer's disease and dementia are being done, or made a *matter of concern*. Particularly she argues against science-centrism: the idea that science is the location where reality is produced. She has explored different locations in which Alzheimer's disease is made to matter, including an Alzheimer's disease patient movement, a medical textbook, a research laboratory, a care practice, an advertisement, at a general practitioner, in parliamentary politics and on a conference on dementia. In this study she shows how Alzheimer's disease is crafted as a matter of concern in these different locations. She shows that there is not one single origin to Alzheimer's disease as a matter of concern. There are multiple 'worlds-in-progress' – or rather 'Alzheimer's-diseases-in-progress' which interfere with one another. Different locations either include or exclude some version of Alzheimer's disease as a matter of concern (Moser, 2008).

In an anthropological study on a nursing home, Moser (2011) urges STS researchers to not only focus on scientific practices, but also on the performativity of different *knowledge regimes* in daily practices. She again argues that biomedical science is not the only place

---

<sup>17</sup> CerebroSpinal Fluid

where realities become defined. On the nursing ward dementia is known, and enacted in at least two different 'modes of ordering' (she uses the term of Law, 1994): a somatizing, biomedically oriented ordering and a relational ordering. She also shows that these two modes of ordering do not just co-exist, but interfere with each other. Moser (2011) draws attention to the way a somatizing mode of ordering overshadows a relational mode of ordering. Contrary to the relational mode of ordering, the somatizing mode of ordering is not only present, but also made explicit, reinforced and circulated through reporting, medical inspection, embedded in educational programs, regulatory practices, and so on. She states that these modes of ordering are more than mere different interpretations, or perspectives – through their enactment they shape not only practices, but also the ways of living (and dying) with dementia on a nursing ward (Moser, 2011).

#### **2.4.4. Lessons from thinking about dementia and ailments in general**

This section on thinking about dementia and ailment in general, showed different ways in which dementia and ailment in general can be understood. Section 2.4.1. showed different explanatory models or webs of understanding on dementia. These are narratives on causes, effects and possible interventions which have an internal logic and stem from different professional disciplines. These explanatory models or webs of understanding differ in focus on what causes or contributes to dementia and where to intervene. They are analytical models and hardly ever occur in such a clean way as described in this section. They appear as separate ways of understanding dementia, which are implicitly present in many practices, often without the actors in these practices being aware of it. Furthermore they are hardly ever integrated. Early diagnostics mainly figures as an important development in the biomedical model of Alzheimer's disease. In section 2.4.2. the disease-illness-sickness triad is described in which the different models of dementia described in section 2.4.1. are recognizable. The disease-illness-sickness triad, however, stresses the interrelatedness between three aspects of ailment (physiological malfunctioning, subjective experience, and social identity) and the way these are intertwined. The model helps to understand discussions occurring when shifts on either of the three domains occur, such as is the case with early molecular diagnostics for Alzheimer's disease. Section 2.4.3 describes an anthropological way of thinking about dementia and ailment, with an emphasis on how ailments are enacted or made to matter in practices.

### **2.5 Concluding remarks**

This chapter provided an impressionistic sketch of the literature landscape on Alzheimer's disease and early diagnostics for Alzheimer's disease, which was related to thinking about disease and diagnosis in general. It resulted in a fragmented picture, and become more of a Picasso-like painting of early diagnostics for Alzheimer's disease from different perspectives and positions, zooming in at the molecular level and zooming out to changing socio-cultural representations and the zeitgeist. The fragmentedness of the image provided in this chapter is mainly due to the many different scientific disciplines working on this topic, building on their own specific body of knowledge.

Without pretending to be complete on the full literature on the topic, I traced the thinking and multiple meanings about diagnostics for Alzheimer's disease throughout many strands of literature. This resulted in different stories of what a diagnosis Alzheimer's disease is and what is at stake when early diagnostics for Alzheimer's disease emerged.

Again, with this chapter I aimed to provide a background for the empirical chapters and further reflection of the thesis, and to explore some roots of the multiple ways of thinking and judging about Alzheimer's disease and its diagnosis. The histories and strands of research of this chapter already point to the complexity of the field of the issues at stake in early diagnostics for Alzheimer's disease. In the empirical chapters (chapter 5 to 7) we will study how the meaning making continues in four different settings in which Alzheimer's disease and its diagnosis gains meaning in practice.

# Chapter 3

## Quandaries of responsible innovation: the case of Alzheimer's disease

*This chapter has been published as Cuijpers, Y.M., Van Lente, H., Boenink, M., and Moors, E.H.M., chapter 13 Quandaries of Responsible Innovation: The Case of Alzheimer's Disease p. 239-255, in the book Responsible Innovation 1, Innovative Solutions for Global Issues, edited by Jeroen van den Hoven, Neelke Doorn, Tsjalling Swierstra, Bert-Jaap Koops, Henny Romijn, Springer, Dordrecht (2014)*

In recent years, the notion of 'responsible innovation' has become fashionable amongst policy makers, firms and researchers. Based on the insight that technologies are not neutral and that innovation may have serious side effects, the ambition is proposed to include concerns about the social, economic and moral consequences of new technologies and their embedding in society. The European Commission, for instance, urges researchers to investigate the possibilities of responsible innovation, defined as “[...] *a transparent, interactive process in which societal actors and innovators become mutually responsive to each other with a view on the (ethical) acceptability, sustainability and societal desirability of the innovation process and its marketable products (in order to allow a proper embedding of scientific and technological advances in our society).*” (Von Schomberg, 2013, p. 19).

Likewise, the Dutch research foundation NWO has launched a program to explore and support 'responsible innovation', which, in their definition “[...] *concerns research, development and design and reflects social values, interests, needs, rights and welfare.*” (Nederlandse Organisatie voor Wetenschappelijk Onderzoek 2008a).

Unsurprisingly, the ambition of responsible innovation is not straightforward. It entails important challenges for policy makers, technology developers and social science researchers that seek to unravel the possibilities and limits of responsible innovation. We are involved in a project on responsible innovation in the case of new molecular early diagnostics for Alzheimer's disease (AD). We collaborate with Leiden Alzheimer Research Netherlands (LeARN), a public-private partnership of several Dutch academic medical centres, universities and companies (i.e. Organon and Philips), funded by the Dutch Centre for Translational Molecular Medicine (CTMM). LeARN develops a number of novel technologies for in vivo early diagnosis of AD, by identifying and testing new molecular biomarkers made visible by PET-, MRI scans and/or CerebroSpinal Fluid (CSF)-analysis. Such biomarkers are promising tools to enable earlier and more reliable diagnosis of AD, to identify leads for drug development, and to enable monitoring of disease development and/or drug response. In

our project, we study scientific and clinical uncertainties in technology development, analyse the social and cultural as well as the moral implications of existing and alternative ways to deal with them. Eventually, we hope to design strategies for responsible uncertainty reduction in innovation of AD diagnostics.

When we started our study on the possibilities of responsible innovation in the case of new molecular early diagnostics for AD two years ago, we came across various basic questions concerning the ambition, assumptions and approaches of responsible innovation. In this chapter we summarize our findings and struggles in terms of what we have labelled as ‘quandaries’: problematic, difficult and ambiguous conditions that somehow require fundamental and practical decisions. We think that this reflection is of general interest for researchers, technology developers and policy makers.

### **3.1 Quandary one: technocentric or multi-actor views on innovation**

Responsible innovation, in a basic sense, points to the integration of viewpoints. By explicitly coupling research, development and design, and social values, interests, needs, rights and welfare, responsible innovation stresses the alignment of the social landscape, and research and innovation within this landscape. This, however, raises questions about *where to start* any thinking about responsible innovation. One could, for example, start in the context of ongoing technological and scientific developments, including potential controversial ones, because: *“Considering the solutions that technological and scientific know-how is capable to offer to societal issues and problems, it is important to examine their ethical and societal aspects.”* (Nederlandse Organisatie voor Wetenschappelijk Onderzoek 2008b). Another starting point is the articulation of societal needs and ‘grand’ challenges, because: *“When it comes to solving global problems (...), people have great expectations from technology and science.”* (Nederlandse Organisatie voor Wetenschappelijk Onderzoek 2008b).

Clearly, the development of early diagnostics of Alzheimer’s disease is highly intertwined with the societal challenges posed by an aging society. The fact that the population is aging confronts public health systems, social care as well as the economic system as a whole with tough questions, requiring innovators and policy makers to rethink current practices. Against this backdrop, research programs aim to develop a more reliable and earlier diagnosis of AD based on biomarkers, working towards a future in which, hopefully, prevention and personalized treatment of AD will be available. Scientific and clinical efforts, as well as public funding are being invested in this type of research. Where should thinking about responsible innovation start, in the first place?

A technocentric perspective on responsible innovation would focus on the promises of early diagnostics and investigate questions like: How to responsibly embed this technology in society? What will be the social, cultural, ethical consequences of such techniques and how can we deal with them? In that case thinking about responsible innovation starts with the innovative development itself.

This, however, is not the only option. One may also start with for example the aging population and the care for the elderly, which concerns many actors and their viewpoints. Such a starting point would employ a multi-actor perspective on responsible innovation. It would focus on a societal problem or need, in which many actors are involved. In this case, different technological and non-technological options may be expected to provide some sort of solution, a means to deal with the problem or to fulfil the need.

Both the technocentric and the multi-actor perspectives have a history and their drawbacks have been reported in various ways. The technocentric perspective has been accused of a deterministic bias. It puts the expectations and promises of technology developers centre stage, while other stakeholders only enter the scene when they react to these expectations. The focus is on reducing negative side effects of an innovation in order to improve the acceptance of technology. Moreover, by closely collaborating with persons who have a strong interest in a particular technology, there is a risk of being co-opted and becoming less critical (Johnson, 2007). Being co-opted brings along the risk of neglecting questions concerning the *need* for the development of these technologies in the first place. It thus tends to ignore questions such as: How will this technology solve social problems? How will research address the social problems? Is this technology a response to these needs or issues? Who will benefit from this development? Should we invest our scarce sources in this development? What are alternative ways to deal with a specific societal issue?

A multi-actor perspective, on the other hand, does not take the promising development as a starting point, but starts with a social problem and the various ways in which this is voiced. Hence, it does not privilege the perspective of technology developers but emphasizes that technological developments are social developments. In this view "*emerging technologies are emerging social arrangements, social relationships and meanings*" (Johnson, 2007, p. 27). And since sociotechnical developments embody values, the multi-actor view highlights how values are infused in social practices, social arrangements, systems of meaning, as well as in the technological artefacts themselves (Johnson 2007). Likewise, the need for and the development of an early diagnosis (including the social institutions, mindsets and values), are being constructed, ignored, or destructed in multiple places simultaneously. According to the multi-actor perspective, it is relevant that these processes are all constitutive for early diagnosis and they can all be useful starting points. So, the fear of getting demented, ideas of successful aging, social workers wanting to prevent crisis situations, visits to a doctor when there is a suspicion of dementia, support and care for elderly when getting the diagnosis AD, changing diagnostic criteria and protocols, TV programmes for elderly practicing memorizing shopping lists - all these developments may be seen as parts of the distributed construction of early diagnostics for AD. In this perspective, responsible innovation appears as a task to acknowledge this richness and to shape innovation accordingly. Yet, the same richness and multi-directionality of the perspective may paralyze the whole endeavour. Where to start? With the current instruments? With the patients? The clinical practices? The public perception of AD? Arguably, all these starting points are justified, yet they cannot be followed at the same time.

### 3.2 Quandary two: singular or multiple futures?

Any inquiry for responsible innovation will entail sketches of a future, or futures. The question, then, is whether one should assume a sketch of a singular future, or prefer the ambivalence of multiple futures. This, then, is the second quandary for responsible innovation, which relates to the *goal* of the exercise: singular or multiple futures?

In research conducive to early diagnostic instruments for AD a strong, singular, future is being sketched. Research on biomarkers and advances in imaging techniques, as the dominant argument goes, will enable an earlier and more reliable diagnosis of AD, which will have two advantages. An early diagnosis is valuable for patients because it reduces uncertainty about their health status and it enables them to prepare for dementia and to organize care and support. Second, the diagnosis of AD at an early stage enables biomedical research to study the early development of the disease and to monitor the treatment through biomarkers at an early stage of the disease, at which it is expected to have most effect. Within this future image, AD will be diagnosed early and treated with disease modifying drugs. And while disease modifying drugs are not yet available, an early diagnosis will provide support and care for patients and informal caregivers.

This future of early diagnostic instruments entails a chain of research stages, starting with hypotheses about the most important mechanisms in the brain causing AD and moving onwards to the identification of biomarkers which allow to signal (or mark) these processes. Then, these biomarkers will be visualized through dedicated MRI or PET scans, or measured with chemical analysis of the cerebrospinal fluid. If these tests offer proof of sufficient sensitivity and specificity they can be implemented in the diagnostic process, providing more certainty to patients and the possibility to organize care and support. These tests could then be used to speed up research into drug development. The final promise is that this leads to an earlier diagnosis and treatment of AD. See Figure 3.1.

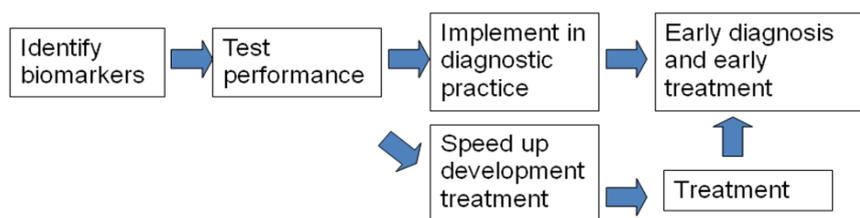


Figure 3.1. The singular future of early diagnosis of AD

These expectations are articulated in the Dutch research program LeARN (LeARN ), which is working on these developments, and are embedded in broader expectations about molecular medicine that guide the research center CTMM which co-funds the research of LeARN (Center for Translational Molecular Medicine, 2006). The vision of CTMM is as follows:

*“The practice of medicine in the 21st century will be very different from how it is today. We are on the brink of a paradigm shift both in medical technology and in its therapeutic applications and effects. New technologies will enable clinicians to take great strides forward in addressing the main obstacles to effective healthcare: (too) late diagnosis of disease, medication that is ineffective or has serious side effects, and delays in translating therapeutic innovations from the lab to clinical practice. The impact of the most common lethal and debilitating diseases, such as cancer, cardiovascular diseases, and neurodegenerative diseases like Alzheimer’s will be significantly reduced, and people who must live with disease will enjoy an improved quality of life. Mere stargazing? It need not be. Molecular Medicine holds the promise to realize this paradigm shift”*

These promises are indeed held to be more than mere stargazing and have already led to proposals for new diagnostic guidelines for AD, which include molecular imaging techniques and chemical analysis of biomarkers, both in the research and the clinical context. *“Expansion of the conceptual framework for thinking about Alzheimer’s disease to include a “preclinical” stage characterized by signature biological changes [i.e. biomarkers] that occur years before any disruptions in memory, thinking or behaviour can be detected. The new guidelines [...] propose a research agenda that builds on promising preliminary data emerging from recent studies”* (Clifford et al. 2011).

This stipulated future of AD, thus, is underpinned by results, but is contested as well. It is uncertain whether such research eventually will lead to these particular futures. The uncertainties are also fuelled by disputes about definitions (What is the distinction between normal and pathological aging?); about limits of the current knowledge on AD (What is the relation between specific changes in the brain and the symptoms of dementia?); about moral questions (What is the value of early diagnosis when treatment is lacking?); about strategic issues (Should we not spend the money and effort on better care?); about the innovation trajectory (Will the research trajectories of PET, MRI, CSF succeed in developing diagnostic instruments?); about the future implementation/embedding (Who will be offered early molecular diagnosis for AD?) and about visions on ‘good diagnosis’ (How early do we want to diagnose AD?).

The promises of early diagnostic instruments measuring biomarkers are based on the expected future availability of disease modifying treatments. Yet, if one considers the development, or the possible effectiveness of disease modifying treatment under development, as uncertain, and when an earlier identification of the disease merely serves to organize the best care and support available, there are more possible routes to provide early care and support and to achieve an earlier diagnosis, besides imaging or measuring biomarkers. And when there are many possible routes to innovate the diagnosis of AD, the question of responsible innovation also multiplies.

Instead of investigating the singular future and its particular uncertainties, we decided to explore the multiple futures at stake. As an example we will describe alternative futures that were prominent during our observations in so-called Alzheimer Cafés. Alzheimer Cafés are

monthly events in The Netherlands where patients, family, and local professionals in the field of dementia meet to exchange experiences, ask informally for advice and discuss a specific theme.

The futures of AD that circulated here were diverse. For instance, the problem of dementia was not so much considered as a medical problem, but as a care problem. Also in this future image the identification of dementia at an early stage is important. It refers to 'early signalling' of dementia by care professionals, general practitioners, as well as the general public. This may avoid crisis situations, misunderstandings and may provide persons timely with needed care and help. This is perceived as better than the present situation in which often persons go to see a general practitioner very late in the development of the disease, when they are already running into a lot of problems. Signalling problems at an early stage and receiving a diagnosis, thus, is not seen as a stepping stone to 'cure', but provides the possibility of timely organizing the care, support and guidance a person needs.

To provide good care for persons with dementia, the disease modifying treatments were not put central, but the main concern was the development of customized, patient centred care arrangements, and the 'tinkering' needed to achieve the best care in that specific situation (Mol et al., 2010). In this future image, the differences between the development of the disease in individuals, as well as the coping strategies of patients and their partners is acknowledged. Since the problem is not singular, there will never be one solution to strive for, but always a careful balancing of options.

Other future images we encountered concerned the development of Alzheimer's disease from a societal perspective. For instance, our society is facing a growing aging population with a growing number of persons with AD. Ageing baby boomers will increasingly put pressure on the health care system and the economic system. Another desired future development concerned the social status of persons with Alzheimer's disease. The Alzheimer Cafés aim to improve the position of patients and their relatives by reducing the stigma and taboo on AD, and emancipate AD patients and their families in order to better deal with the condition. To conclude, efforts for responsible innovation may be predicated on a particular future, or may embrace the plurality of futures. Depending of the problem definition and the perspective, responsible innovation of early diagnosis of Alzheimer's disease is likely to take a different shape.

### **3.2 Quandary three: identifying with whom?**

Questions about what constitutes responsible innovation are often triggered by new technological developments, like the rise of genomics, nanotechnology or synthetic biology. The funding for research on responsible innovation may even be closely linked to the funding of technological development itself, as in the case of genomics and nanotechnology in both the USA and Europe. Moreover, it is now quite common for researchers in the field of responsible innovation to use methods in which they collaborate or engage with technology developers (Guston and Sarewitz, 2002; Fisher and Mahajan, 2006). As a result, it is easy for researchers in responsible innovation to identify with the scientists and engineers working

on a specific innovation. As noted above, a close collaboration with actors who have a strong interest in bringing about a particular technology, brings the risk of 'going native' and thus to become less critical (Johnson, 2007).

To avoid such lock-in, one should go beyond the perspective of the technology developers, as was already stipulated in the first quandary. The third quandary points to another difficulty of identifying with the ideas of the developers: the moral question of whose interest to pursue. In general, one may argue that one of the conditions that makes innovation responsible is that it is aligned with important social needs and moral values. Some work in the field of Science & Technology Studies seems to be implicitly driven by the desire to support groups or views that tend to be marginalized in political, public or professional debates. However, it does not suffice simply to side with the perspective of more marginalized stakeholders either. Yes, highlighting what is less visible or not taken seriously is a valuable contribution to making innovation more responsible. However, an ethical interpretation of responsible innovation requires that *all* relevant stakeholders and their views and interests are taken into account, including the dominant ones.

The question with whom to identify relates to the issue of users in the innovation process. Users often develop new functions for technologies, solve unforeseen problems and propose or even develop innovative solutions. Therefore, users are recognized as important sources or even co-developers of innovations, and can have an impact on the direction of technological developments and innovations, especially in early stages of technology development (e.g. (Von Hippel, 1976; Oudshoorn and Pinch, 2003; Lüthje et al., 2005). Smits and Boon (2008) summarized the reasons for user involvement as follows: (1) users can address market failures and suggest ways to overcome them; (2) they contribute to adoption of innovations by articulating their creative potential in the form of wishes and experiential knowledge; (3) they can support the boundary conditions of innovation processes and by this are instrumental to processes; (4) they can 'champion' innovations and by this form a counterforce to potential (ethical) objections; (5) and they have the moral and democratic right to co-decide on and co-produce innovations that have a great impact on their lives.

Likewise, multi-actor involvement can contribute to more responsible innovations. Research in responsible innovation thus should investigate how this inclusive form of deliberation can be facilitated. (Gutman and Thompson, 1996) Ultimately, this means that research in responsible innovation should engage with all stakeholders but identify with no one in particular. This aim does not presuppose a view from nowhere (Nagel, 1989), a detached moral point of view. It does, however, require the researcher to continuously compare and mutually assess all possible viewpoints and considerations.

This is easier said than done. In the case of innovating technologies for diagnosing AD, for example, many actors may be potentially affected by this development. An earlier diagnosis addresses governments and all citizens by promises to reduce public health care costs, by providing timely home care allowing persons to live at home longer. It influences the future prospects of persons suffering from AD. And there actors who for several reasons do not use, or are against the use of these innovations (Henwood et al., 2003; Katz et al., 2002). In the

case of AD, for example, often patients do not want to get diagnosed due to a fear of the prognosis of AD itself (denial), or a self-chosen and conscious 'blissed ignorance'. For insurance companies early diagnosis might be a way to assess the risks of a person to develop AD. For researchers it provides new possibilities for research on the causes of AD and interventions. Other stakeholders involved are municipalities, nursing homes, home care institutions, welfare organizations, all elderly people (or even all healthy people who may be at risk – which means everyone), neighbours, industry, housing corporations, and more. To include all these stakeholders in deliberation on the desirability of emerging diagnostic technologies for AD is an immense task. In practice, then, one has to focus on some stakeholders and leave others aside, due to limitations of time and funding. How to make a well-considered selection?

To identify with all stakeholders, thus, is a complicated route, to say the least. An additional complicating factor is that different stakeholders will have different meanings of 'Alzheimer's Disease'. AD is an existential problem for patients and caregivers, for biomedical researchers it appears as processes in the brain, and policy makers have to approach it as a societal issue. While one may consider all these meanings as valid, it is not easy to acknowledge them at the same time. Any practical effort of deliberation will imply a choice. The quandary, thus, is: identifying with whom?

### **3.4 Quandary four: process or outcome?**

The ambition of responsible innovation, in principle, entails two possible questions: 'How to innovate in a responsible way?', and 'What kind of innovation (as a result of an innovation process) is responsible?' In other words, does responsible innovation refer to the process or the outcome of a process? This basic distinction leads to very different kinds of questions and activities.

When responsible innovation refers to the *outcome* – the innovative product and the societal embedding of this product - a researcher on responsible innovation should assess the products and systems as envisioned and might advise on conditions in which this innovation may be responsible. In the case of early diagnostics for AD there are many different kinds of outcomes envisioned. Generally three scenarios are mentioned by the researchers in the field: (1) the use of these instruments as an add-on in current diagnostic practice; (2) the use of these instruments to distinguish between patients with mild memory complaints (Mild Cognitive Impairment) who will develop Alzheimer's Disease, and those who will not; or (3) a pre-symptomatic diagnosis of Alzheimer's Disease, even before any symptoms are present (which is then positioned far in the future). We could try to analyse possible and plausible outcomes of this innovation and the conditions in which early diagnostics for AD would be responsible.

(Mattson et al., 2010) and (Gertz & Kurz, 2011) pursued this approach. Mattson reviews possible clinical consequences of early diagnosis of AD. The issues that should be anticipated include (a) the risks of erroneous tests, misdiagnosis and wrong treatment; (b) the consequences of an early diagnosis for a patient and for the relatives, including the role of

stigmatization, feelings of despair and hopelessness; (c) the attitude of doctors bringing the bad news. A big advantage of an early diagnosis is that patients can prepare at an early stage of the disease, and get the help they need at a later stage, when they will be too demented to decide on this. An ethical problem in this case is whether a patient at the early stages of the disease might misjudge his or her future self's best interest. There is a problem in making decisions about a future self when developing such a thoroughly life changing disease, such as AD. All these issues could already be discussed or decided upon.

Gertz & Kurz (2011) discuss the improvements of diagnostic methods to enable a very early diagnosis of AD, while there is no such progress in the development of disease-modifying treatments. They emphasize the need to change the current practice of diagnosing AD, to more actively include the patient in the decision to undergo an early diagnosis, and to make very clear to this patient that there will be a lack of therapeutic options when the diagnosis is positive.

These two articles discuss conditions under which such an early diagnosis could be responsible and the measures that should be taken, or discussed in order to decrease the undesirable consequences of this development for the patients involved. By focusing on the outcome of the innovation process, it 'black boxes' the decisions taken during the innovation process.

The other approach would be to open the black box, and to try to make the innovation *process* more responsible. Hence, process criteria become more important. A researcher of responsible innovation could try to broaden the issues taken into account *within* the innovation process, by informing stakeholders on different possible perspectives, facilitate the sharing of perspectives, values and interests between stakeholders, and stimulate social learning. Scenario- or multi-stakeholder workshops or organizing public dialogues could be examples of this. In the case of early diagnostics for AD, this might involve additional activities from the side of researchers on responsible innovation, to broaden the current Health Technology Assessment (HTA) undertaken in the LeARN research program. The HTA currently involves scientists, clinicians and health economists only and focuses solely on financial costs and quality of life. This HTA could include contextual factors, pre-conditions and broader considerations. De-contextualized early diagnostics euphoria can create constraints with regard to aligning disease management, integrated care, or life-course perspectives on AD.

So, the basic ambiguity in the term 'innovation', which may refer to either outcome or process, resonates in the ambition of responsible innovation. The two are not automatically aligned: a responsible outcome of an innovation process does not need to be the result of a responsible innovation process. And vice versa, holding to process criteria in an innovation process does not need to result in a responsible outcome.

### 3.5 Quandary five: speculation or plausibility

Innovation (in particular in emerging technology) is a rather elusive subject: it is, by definition, about entities that do not exist. Technological developments, which aim at innovations in the future, largely consist of promises and expectations that cannot directly be assessed in terms of veracity. They may even be highly speculative. At the same time, such claims are grounded in currently (perceived) problems and in current ideas on what the world is like.

Futures, moreover, are not innocent. From the sociology of expectations we learn that promises and expectations are 'performative', meaning that expectations 'do' something. Innovations, as they tend to go with many expectations, already have consequences before they are embedded in society, or even developed, through these expectations. Through their content, expectations are able to coordinate action, by allocating roles, creating linkages and obligations between actors and by defining agendas. In this way they shape technological developments. Expectations can also be used by actors to legitimize actions, mobilize funding and attention of other actors. They are used in decision making processes to reduce the uncertainty inherent in technological development (Van Lente 1993, Van Lente & Bakker, 2010).

Research in responsible innovation (and its funding) is also often triggered by the same visions of the future, asking whether the envisioned future is desirable. As Nordmann and Rip have pointed out for the case of ethics of nanotechnology, this type of 'parallel research' runs the risk of uncritically assuming that these expectations are plausible (Nordmann, 2007; Nordmann & Rip, 2009). Similar warnings could be issued for social and legal (ELSA) research into emerging technologies more generally.

Nordmann and Rip warn that in the case of nanotechnology, and other emergent technologies, ethicists have the tendency to go along too easily with speculative visions and expectations concerning technological development (or even describe speculative future scenarios themselves). Ethicists then continue to ask attention for the ethical concerns these (expected) technologies raise, "*as if such technologies were upon us already*" (Nordman & Rip, p. 42). Moreover, when ethicists discuss the ethical aspects of an expected outcome of technological developments they contribute to the credibility and the power of these expectations, even if they stress the negative consequences these developments might have. It is thus problematic that the ethicist presents remote possibilities as plausible technological developments. When these expectations fail to come true, research in responsible innovation may be futile, irrelevant, and squander the scarce resources for this type of research. Another drawback of such speculative ethics is that one misses out on (often more mundane) ethical issues occurring *during* the technology development process. The development process itself is black boxed. Nordmann and Rip suggest two strategies to deal with these issues. The first is to increase discussion about the quality of promises and representations of emergent technologies: some sort of reality check. The second is to focus on more specific technologies (in our case, say, a specific biomarker test for AD), rather than on general ideas of technological developments (for example the tendency towards molecularization in medicine).

Grunwald, on the other hand, stresses the value of speculating about the future, especially when considering the societal issues of new technologies. The purpose of a more speculative form of ethical reflection is (1) to provide a preliminary conceptual and substantive structure for a future field of ethics; (2) to point out critical questions that require increased examination in the future; (3) to contribute to identifying gaps of knowledge; (4) to learn something about and for us today (e.g. what is their implicit criticism about the present, how do they suggest us to change?). Rather than a 'reality check' Grunwald emphasizes vision assessment, to uncover the cognitive and normative content of the visions, to evaluate their validity and plausibility, and to confront diverging images of the future with each other, analytically, or with different stakeholders (Grunwald, 2007; Grunwald, 2004; Grunwald, 2010).

The development of molecular diagnostic instruments for Alzheimer's disease is definitely liable to speculation, and the question is how to deal with that. The Nordmann & Rip strategy would be to focus on a specific technology, like the combination of biomarker tests developed in LeARN, together with a reality check of the claims being made. Lucivero (Lucivero et al., 2011) elaborates what such a reality check (or rather plausibility assessment) would entail. She proposes to distinguish claims about the technology in the lab, about the use of the technology, and about its desirability. A careful check is needed of, for example, claims about the 'early' in early diagnostics. Are we still talking about patients with subjective complaints, or about testing a-symptomatic individuals? This has immediate implications for the context of use. But even if molecular diagnostics only concerns patients with complaints, the role of the biomarker tests may be envisioned as a complete diagnostic tool in itself, or as an addition to a complex set of tests. Also the reason why different stakeholders are interested in these diagnostics may differ, from getting knowledge about one's health state, receiving clues how to arrange care and treatment, gaining knowledge about the pathological disease mechanisms underlying the disease, or searching for reassurance that everything is all right. Desirability claims cannot be assessed on the basis of invariable norms and values; morality itself may shift partly because of technical developments. So, careful reflection on interaction of technology and morality is necessary. For example: how will norms about cognitive functioning change as a result of developments in AD diagnostics? And how does this affect the experience of AD?

Grunwald's proposal, on the other hand, would entail that we explicate the visions implicit in the LeARN project and more generally in molecular diagnostics. The problem definitions and the presuppositions of these visions should be assessed, and alternative scenarios should be developed to create a broad public debate on what kind of future vision is desirable.

### **3.6 Quandary six: responsibility for the future or responsibility for the present**

A final quandary that we encountered in the aim to contribute to a responsible diagnostic practice of AD, is whether we should focus on a responsible *future* practice, or on a responsible *current* practice. This issue is related to some of the ambiguities discussed above,

in particular the issue of process or outcome and the issue of speculation versus plausibility. Again, we adopt promises and expectations of the Alzheimer researchers, and try to formulate conditions any practice of early AD diagnostics should satisfy to be responsible. Or we could take a more sceptical stance and question how current innovations should proceed to ensure a responsible research practice. What is at stake here is not just the object of the responsibility claim, but also its time-frame.

There may be a difference here between social and ethical approaches of responsible innovation. From a social perspective, responsible innovation is usually about acceptability: an innovation can be considered responsible if it is actually accepted by all actors involved. This means that the product of innovation can be judged on its own, regardless of the innovation process. From an ethical perspective, however, it is possible to say that an innovation that is accepted by all involved is nonetheless not responsible, because either some stakeholders or specific considerations were neglected- or both. From an ethical point of view, then, the process is more important, implying that responsible innovation encompasses both the present and the future.

For our case, this means that contributing to a responsible practice of (early) diagnostics of AD should start right *now*, by facilitating the translation of research into clinical practice in such a way that the views of all relevant stakeholders are taken into account. Considerations of patients, informal caregivers, elderly people in general, and medical professionals should receive attention already in the research phases. After all, their views on what constitutes the potential benefit (and drawbacks) of the aimed for innovations may differ from what researchers perceive as its benefit (or drawbacks).

In our first explorations of the field, such discrepancies became already visible. After introducing our research one doctor responded with the remark “It is only the persons holding test tubes who are interested in this.” And clinicians, for example, asked: What is the value of these biomarkers for the diagnosis in clinical practice? What is *really* in it for the patient? Patients who go to a hospital to get diagnosed are send there by the general practitioner, a nurse said. This means that they already have complaints. If you want to have an earlier diagnosis, you don’t need novel diagnostic tools, but need to go to the general practitioners. Now, they often do not recognize signs of early dementia and do not refer patients to the hospital. Furthermore, the clinical diagnosis AD is not equal to interpreting images from MRI scans, which are mainly used for additional information or research purposes. Basically, some clinicians do not have high expectations about this type of research on the short term in clinical practice, and they suggest other routes to diagnose persons at an earlier stage, for example the education of general practitioners in early signs of dementia. If such considerations are left aside, the result of the innovation process risks rejection and contestation.

The quandary is not solved, however, by rendering the *now* responsible, because even in facilitating a responsible process here and now, we anticipate the future. Such anticipation itself can be more or less responsible. We indicated already that it is fraught with the risk of speculation. Nordmann’s criticism of what he calls ‘if and then ethics’ (Nordmann, 2007)

implies that researchers on emerging technologies should take responsibility for the images of the future they use. After all, images of the future do have repercussion in the present. If we go along too easily with the expectations of the research on early diagnostics, for example, we may reproduce an irresponsible bias towards biomedical definitions of the problem as well as technical solutions for this problem (George & Whitehouse, 2009). Taking responsibility for the present then also means that we should take a critical stance towards the problem definitions and assumptions underlying current attempts at innovation. Finally, working on the present process of innovation is inevitably directed towards the future in another sense as well. Responsible innovation, whatever its form, aims at a better technology for a better world. So even if we decide to focus on the process of innovation only, we inevitably claim to contribute to a *future* world as well, in which the innovations will be embedded in practice.

Yet, we should avoid the pitfalls of simplistic thinking about shaping the future. After all, the interaction of technology and society is replete with complexity and contingencies. Does it make sense at all, then, to claim that attending to the present innovation process will guarantee a responsible outcome in the future? Of course not. What we can do, however, is try to define minimum conditions for a future practice of AD diagnostics to be responsible. In addition, and perhaps even more important, we had better think about ways to ensure that innovation processes can be redirected once it becomes clear that the most recent outcome does not satisfy such minimum criteria. Responsibility for the future then takes the form of permanent and flexible guiding.

### **3.7 Conclusion**

Responsible innovation is not an oxymoron but not a straightforward task either. Our basic finding concerns the tension between simplicity and complexity. Any practical translation of the notion of responsible innovation has to find a path through the intrinsic and intricate complexities of socio-technical change – a path that has to avoid overly simplistic assumptions regarding innovation and responsibility, as well as a surrender to the full complexity of social and technical life.

In this paper we delineated six basic tensions that we encountered in our research into the early diagnostics of AD. The six quandaries refer to basic questions about responsible innovation. See Table 3.1. The quandaries echo the ambiguity of the term responsible innovation itself: is it to safeguard innovation by making it acceptable, or is it to enhance responsibility through innovation or other means?

Does this set of quandaries imply that responsible innovation is an evasive concept? Yes and no. It is impossible to certify innovations as responsible, because innovations are never finished and they are part of bigger social, technical and moral changes. That is, innovations will continue to raise questions about responsibility. Yet, the concept seems to be helpful as it points to the capability to choose. The identification of the six quandaries could help both researchers and policy makers, not only to make their choices more explicit, but also to be aware of choices that could be made.

**Table 3.1. Six quandaries of responsible innovation**

<i>basic question about responsible innovation</i>	<i>quandary of responsible innovation</i>
where to start?	technocentric or multi-actor perspectives?
where to end?	singular or multiple futures?
with whom?	developers or stakeholders?
what's the goal?	process or outcome?
what to question?	speculation or plausibility?
responsible for whom?	responsibility for the future or the present?

# Chapter 4

## Research approach: studying the meaning of early diagnosis

The empirical question in this thesis is *What are the meanings of early diagnostics for Alzheimer's disease in different settings?*. To be able to study the meaning of early diagnostics it is essential to gain a better understanding of what meaning is, how meaning is constructed, and how meaning can be studied. In this chapter, section 4.1 reviews three different theoretical approaches to study meaning and its social construction: discourse analysis, modes of ordering, and framing analysis. While the construction of meaning is a central and perennial question in any social study, these three approaches appear to be a useful starting point. They overlap to a certain extent, yet emphasize different aspects of the construction of meaning that are paramount in the case of Alzheimer's disease and early diagnosis. Discourse analysis emphasizes how politics and power can be traced in the construction of meaning; 'modes of ordering' highlight the networks involved in construction of meaning; and the framing approach emphasizes the role of interpretations and perspectives. Next, section 4.2 builds on the lessons from these three approaches and delineates how for the purpose of this dissertation the construction of meaning can be studied. Section 4.3 presents the research design choices made in this thesis. Finally, section 4.4 describes the methods for data gathering and analysis.

### 4.1 Three theoretical approaches on the construction of meaning

This section describes three theoretical approaches on meaning and its construction. They share the basic understanding that meanings, that is, expressions of signification and significance, are always part of social interactions and should be understood in this way. Yet the three approaches have different views on the roles of meaning and how meaning is constructed in social interactions. Subsequently this section describes discourse analysis (4.1.1), modes of ordering (4.1.2) and framing analysis (4.1.3).

#### 4.1.1 Discourse analysis

Discourse analysis is a very broad field, consisting of a number of interdisciplinary approaches that differ on the definition of discourse, their scope and focus of analysis. Discourse can be preliminarily defined as "*a particular way of talking about and understanding the world (or an aspect of the world.*" (Jorgensen & Phillips, 2002, p. 1) Discourse analysis is a highly political field of study in which construction of meaning is rather directly related to politics and power (to define).

What is shared by the different discourse analytical approaches is the view of language as a social practice that shapes the world. Social practices can be thought of as having a dual nature, on the one hand they are "*concrete, individual and context bound*" (Jorgensen &

Phillips, 2002, p. 27) and at the same time they are “*socially anchored, institutionalized and tend towards patterns of regularity*” (Jorgensen & Phillips, 2002, p. 27). In discourse analysis, language is considered to actually (partly) constitute the social world. This means that in discourse analysis, language is considered to be more than a vehicle to refer to reality, more than merely a reflection of the world ‘out there’. Discourse is not just a way of talking, or discussing (Hajer, 2006; Hajer & Laws, 2009). Language is more than a channel to communicate information about underlying mental states, or about facts of the world. Language and the ways of talking play an active role in creating and changing the world, identities and social relations. Different understandings of the world lead to different actions and therefore have social consequences. This means that in communication, not only messages or information are exchanged, but social reality is being constructed. The general idea of discourse analysis is the analysis of the structures and the patterns the language of people’s utterances follow when they take part in different domains of social life (Jorgensen & Phillips, 2002).

The term discourse itself is used very often and many discourse analytical approaches have been developed. The interests, scope and focus of discourse analytical approaches differs. The central area of interest of for example *critical discourse analysis* (Fairclough, 2003) is the investigation of reproduction of discourses and discursive change through new combinations of discourses. The main interest within *discourse theory* (Laclau & Mouffe, 1985), for example, is on the discursive struggle between discourses, representing particular ways of understanding the world, and on how some ways of understanding achieve dominance over others. The area of interest of discursive psychology is exploring how people’s selves, thoughts and emotions are formed through social interaction, and how individuals use available discourses flexibly in talk-in-interaction. The scope of different discourse analytical approaches differs mainly with respect to the role of the discursive in constituting the world. In critical discourse analysis, discursive analysis should always be accompanied by an analysis of social practices. Further, discourse theory argues that discourses are not only discursive, but also material. For example the existence of children playgrounds is the materialization of our understanding of persons to be divided in children, adolescents and adults. This categorization is not merely a discursive act, but also materialized. The analytical focus also differs. Discursive psychology for example focuses on everyday discourse and analyses specific interactions in great detail, while discourse theory is more interested in abstract, depersonified discourses. So discourse analysis can range from very detailed analysis within a conversation to describing cultures during decades of time (Jorgensen & Phillips, 2002). Being interested in the meanings of early diagnostics for Alzheimer’s disease at a societal level, I will go into discourse theory and critical discourse analysis in a bit more detail.

Discourse theory aims at understanding the social as a discursive construction. Discourse in this approach is understood as a (temporarily and contingent) *fixation of signs in a relational network*. But discourse can never be total. There are always other meaning potentials which may challenge and transform the structure of discourse. Discourses in discourse theory are viewed as incomplete structures in the same undecidable terrain that never becomes completely structured. Hence there is always room for struggle over what discourse should

prevail and how meaning should be ascribed to individual signs. (Jorgensen & Phillips, 2002) Its aim is not to uncover objective reality, but to explore how we create this reality so that it appears natural and objective. Social practices can appear so natural that it is hard to see that things could be different. The things that are taken for granted and of which their contingency is forgotten are referred to as objective or 'sedimented discourse'. This leads to the situation that this discourse appears neutral, a matter of fact, or is even rendered invisible. Hegemony is an important notion in discourse theory. Hegemony is dominance of one discourse. Hegemony is a notion that comes somewhere between political and objective, because by calling it hegemonic, it is stressed that alternative understandings are being suppressed and one single understanding is becoming or was naturalized. The overall idea, however, is that meaning can never be fixed. This opens up the way for *constant social struggle* about definitions of social reality. Analysis of discourse using discourse theory shows the course of struggles to fix meanings (which can never be fully achieved).

Critical discourse analysis studies provides theory and methods to study struggles between discourses and the relationship between the discursive and other social practices. There are different approaches to critical discourse analysis (Jorgensen & Philips, 2002; Fairclough 2003). What they have in common are that they emphasize that social and cultural practices are only partly discursive. The discursive (linguistic) practices are an important form of social practice contributing to the constitution of the social world. Discursive practices are seen as written and spoken language as well as visual images. Discourse in this tradition is constitutive for the social world and constituted by other social practices. It contributes to the (re)shaping of social structures, but also reflects them. Language-as-discourse is a form of action and in a dialectic relationship with other aspects of the social. It engages in concrete textual analysis of language use in social interaction. Finally, discourse is considered to be functioning as an ideology and contributes to the creation of unequal power relations between social groups. This makes critical discourse analysis critical: it aims to reveal the role of discursive practices in the maintenance of the social world, including unequal power relations and it aims to contribute to more equal power relations. Critical discourse analysis is committed to social change and often takes the side of oppressed groups. It diverges from discourse theory in a number of ways. First and most prominent the term discourse is restricted to the social practice of language-use, which in its term is shaped by other social practices. The social structure, the social relations in society as a whole and in specific institutions consist of discursive elements, but also of non-discursive elements. The starting point of research is everyday social interaction.

#### **4.1.2 Modes of ordering**

Aiming to understand how meaning is created on an issue such as early diagnostics for Alzheimer's disease my first impression was that there were not two discourses struggling for hegemony, neither was it apparent that there were specific oppressed groups that needed support. Without a large struggle for dominance or an injustice to target discourse analysis, the strong political emphasis of discourse analysis seemed a bit out of place. I recognized the same unease in the work *Organizing Modernity* by John Law (1994). In this book he asks himself the question "*what on earth is social order?*" (Law, 1994, p. 1) and he

describes social order as an endless attempt at ordering, through a *“recursive but incomplete performance of an unknowable number of intertwined orderings”* (ibid., p. 101), which is also the starting point of this thesis. He introduces the concept ‘modes of ordering’, to emphasize meaning construction as repetitive patterns in plural, fragmented, messy, complex, sociomaterial networks.

The concept of ‘modes of ordering’ is related to discourse analysis, and John Law explicitly draws upon this approach. A difference between the modes of ordering concept and discourse analysis, is that discourse analysis has a stronger emphasis on the discursive (the use of language), but is not necessarily restricted to that, whereas John Laws modes of ordering are material-semiotic, or socio-material. Another difference lies in the size of the distinguished ordering patterns. Discourse analysis often appear comprehensive, where John Laws modes of ordering are more humble, which is why he also refers to them as mini-discourses. *“My proposal is that we take the notion of discourse and cut it down to size. This means: first, we should treat it as a set of patterns that might be imputed to the networks of the social; second, we should look for discourses in the plural, not discourse in the singular; third, we should treat discourses as ordering attempts, not orders; fourth, we should explore how they are performed, embodied and told in different materials; and fifth, we should consider the ways in which they interact, change, or indeed face extinction.”* (Law, 1994, p. 95).

The underlying basic assumption in Law’s approach is that the social world is messy and complex (Law, 1994, p. 15). He assumes no social order in the sense of a superstructure of social reality. Or as he states it: social order as a noun does not exist. Yet, while the social world is messy, complex and contingent, there do appear to be ‘pools of order’ (ibid., p. 15). We experience the social world as somehow ordered and structured and we can discern patterns and regularities. That social reality appears to be ordered to a certain extent, is the product or the effect of a lot of work. The social is both the medium and the outcome. It is the result of *ordering* being performed and the ordering itself at the same time. This makes ‘social order’ a verb. Furthermore, he assumes an unknown number of intertwined orderings. There is no single social order(ing). Social ordering consists of plural ordering processes. This ordering is always incomplete, in flux, emerging, disappearing and interacting in the network of the social, and should be considered ordering attempts, rather than order itself. Finally, in line with actor network theory, he views ‘the social’ as materially heterogeneous including talk, texts, bodies, machines, architecture and so on. Social order in this view are thus plural processes of *socio-technical* ordering (Law, 1994, p. 1).

Law introduces the concept ‘modes of ordering’ to describe regularities and patterns, that he as an analyst observes, are being performed and *“generate, define and interrelate elements in relatively coherent ways”* (Law, 1994, p. 107). Relating to discourse analysis and poststructuralist approaches, Law describes what he means by the term ‘modes of ordering’ as little narratives. Yet they are also more than mere narratives. They are also performed, acted out, embodied, or materialized in the network of relations. He also refers to them as ‘logics’, patterns and regularities. These modes of ordering, do not exist outside their performance. They *“may be imputed to the particulars that make up the recursive and*

*generative networks of the social. They are nowhere else. They do not drive these networks. They aren't outside them. Rather, they are a way of talking of the patterns into which the latter shape themselves.*" (Law, 1994, p. 83-84)

So ordering modes are recursive patterns that are being performed in the network of the social. They function as intellectual tools for sense-making, as ordering-tools (ibid., p. 83). As an analyst, you can go out to look for these ordering patterns. If there appears to be order, in the sense of repetitive patterns, then these are empirical findings (for no social order is presupposed). However, by tracing and analyzing ordering processes in a messy and complex world, the analyst aims to make sense of sense-making, and is *"caught up in ordering too"* (Law, 1994, p. 2). The analyst is aiming to order ordering processes. This means that the analyst should take a modest position, for his or her analysis will also be incomplete, plural fragmented, and a lot may have escaped the analyst.

#### **4.1.3 Framing analysis**

In the framing literature the emphasis is on meaning as an interpretation of an issue, through which it appears in a certain way. Furthermore, framing analysis is often used to study meaning making processes in strategic situations such as social movements, or policy making, when the interest lies in understanding how people strategically make sense of reality and how they add meaning to ambiguous and complex situations. This intentionality of meaning-making processes plays a larger part in framing analysis as it does in for example discourse analysis. Also, framing analysis, unlike discourse analysis or modes of ordering, focusses mainly on the discursive and the cognitive level.

Framing analysis has many traditions in which it is rooted and different strands of framing analysis have been developed, which has led to a scattered conceptualization. A number of authors have provided an overview of the different conceptualizations aiming to clarify the dispersed literature on framing analysis. For an overview on framing literature see for example Zwartkruis, 2013; Dewulf et al., 2009; Entman, 1993, Reese 2001. What all traditions have in common is that frames function as 'sensemaking devices' (Weick, 1995), *"a central organizing principle that holds together and gives coherence and meaning to a diverse array of symbols"* (Gamson, 1992, p. 384).

As in discourse analysis, frames are considered more than mere perspectives, but as contributing to the shaping of social reality. In framing analysis often two mechanisms are described through which framing shapes social reality. The first mechanism is through selection and salience, or in other words: making some parts of reality more visible than other parts. The second mechanism is that frames propose a particular view on social reality by defining what is problematic, what the causes of this problem are, how to evaluate a situation and what to do about it.

What distinguishes the different traditions is among others the localization and the topic of framing analysis. One of the roots of framing analysis is cognitive psychology, which defines frames as cognitive structures that can help us to organize and interpret new experiences (Bartlett, 1932). Frames are located at the cognitive level and are often called cognitive schemata, referring to *"mentally stored clusters of ideas that guide individuals' processing of*

*information.*" (Entman, 1993, p. 53) In this tradition frames are mental structures that support individuals to organize and interpret new experiences. A second tradition can be traced back to anthropology and is an interactional approach to framing, in which it is argued that communication in whatever form cannot be understood without a frame of interpretation. (Bateson, 1954). Framing analysis focusing on communication analyses the *"dynamic enactment and shaping of meaning in ongoing interaction"* (Dewulf et al., 2009, p. 162) and a focus on the exchange of cues (Bateson, 1954). A third tradition that can be distinguished is rooted in sociology and social constructionism (Goffman, 1974) and is interested in frames in a broader and more abstract way as located in culture. Individuals interpret events within 'frames of understanding', which are socially constructed rather than individually cognitively constructed. This tradition in framing analysis can be found in studies on framing in media (e.g. Gorp, 2007), policy (Schön & Rein, 1995) or social movements (Benford & Snow, 2000). Culture is viewed as an organized set of beliefs, codes, myths, stereotypes, values and norms that are shared in the collective memory of a society or group, and are institutionalized in various ways (Gorp, 2007). Cultures have persistent repertoires of frames that are situated largely external to the individual, but that individuals draw upon. Frames as part of collective memory or culture can be found for example in Kuhn's work on paradigms (Kuhn, 1970), or in the work on policy theories, where frames are 'frameworks for understanding' (Schön & Rein, 1995), or views of the world (Gamson & Modigliani, 1989). The social constructivist framing studies often analyze specific practices or fora, such as policy practices, media practices or social movement organizations (Tewksbury & Scheufele, 2007). This implies that specific practices or fora are also considered a setting in which framing occurs (Zwartkruis, 2013). Many things can be the topic of framing analysis. Dewulf for example shows that in conflict studies on framing, issues, identities, relations and processes can be subject of framing studies. So in framing terminology this thesis, aiming to understand the meanings of early diagnostics for Alzheimer's disease, is about issue framing: *"the meanings attached to agenda items, events of problems in the relevant domain or context"* (Dewulf et al., 2009, p. 165).

The three theoretical approaches (discourse analysis, modes of ordering and framing analysis) help to understand what meaning is, how it is constructed and how to study meaning. The origin, content and research methods of each approach differ. Also, each approach adds a different emphasis. Discourse analysis emphasises the politics and power (to define) in meaning-making processes, modes of ordering views meaning mainly as patterns in a network, whereas framing emphasizes that issues can appear different depending on the scheme of interpretation most readily available. Despite the existing differences, there are also shared lessons arising from all three approaches.

#### **4.2 Lessons drawn: studying the meaning of early diagnosis**

Bearing in mind the aim of this thesis, namely understanding the meanings of early diagnostics for Alzheimer's disease to contribute to responsible innovation, four lessons are drawn from the review of the theoretical approaches above.

1. The networked nature of the construction of meaning. The main image I use for construction of meaning is that of a network. An element (such as early diagnostics) gains meaning through the relations with other elements.
2. Patterns in the construction of meaning. Every particular articulation is an act of constructing meaning. When the same relations are articulated more often they become more engrained.
3. The politics of ordering in a messy, plural world. The social world is messy and plural. If it appears as order this is the result of a lot of ordering work. This ordering work is inherently political.
4. Making sense of sense-making. The outcomes of the empirical analyses in this thesis are exactly that: the outcome of an analysis, as a product of ordering work by the analyst.

These lessons are further explained in detail below.

#### **4.2.1 The networked nature of the construction of meaning**

The main feature of meaning construction that emerges from all three theoretical approaches is that an element gains meaning by and within a network of relations. Hence, 'early diagnostics for Alzheimer's disease' can only mean something by being connected to other kinds of elements. One may imagine this as a flexible and dynamic structure of lines and dots, constantly brought into being through each articulation. Typically, there are multiple networks brought into being simultaneously. The task ahead, thus, is to trace the multiple networks of meanings and their dynamics.

#### **4.2.2 Patterns in the construction of meaning**

The three theoretical approaches, as well as this thesis as a whole, follow a social constructivist paradigm, stressing that social phenomena and their meaning are continuously 'made real' by actors. Social reality is in a constant state of being formed through social interactions. Any meaning of early diagnostics is the product and result of the constant construction of this meaning by actors.

The construction of meaning is not a chaotic phenomenon, but often occurs through the same patterns. Discourse analysis, modes of ordering, and framing analysis refer particularly to repetitive patterns in the social construction of meaning. Hajer for example defines discourse as "*an ensemble of ideas, concepts, and categories through which meaning is given to social and physical phenomena, and which is produced and reproduced through an identifiable set of practices*" (Hajer, 2006, p. 67). Frames are described by Gamson as "*a central organizing principle that holds together and gives coherence and meaning to a diverse array of symbols*" (Gamson, 1992, p. 87). And Law (1994) describes his modes of ordering as "*I'm imputing ordering modes to the bits and pieces that make up the networks of the social*" (Law, 1994, p. 21); as "*fairly regular patterns that can be usefully imputed for certain purposes to the recursive networks of the social*" (Law, 1994, p. 83); "*an attempt to find a way of imputing quite general patterning strategies to the material heterogeneous networks of the social*" (Law, 1994, p. 95)

Thus, to study the meanings of early diagnostics for Alzheimer's disease, the patterns through which early diagnostics gains meaning are analyzed. Which clusters of relations give meaning to early diagnosis? The guiding image here is that of a riverbed or an elephant-path.<sup>18</sup> When water runs the same route it becomes a riverbed, when a route is often taken it becomes a well-trodden path, which will become a more obvious route to follow.

#### **4.2.3 The politics of ordering in a messy, plural world**

The term 'politics' indicates that the social world is constantly constituted in ways that excludes other possible ways. Some gain, some lose. Politics is inherent and inevitable in meaning making processes because it is impossible to make sense of anything without ordering what we perceive, which necessarily means exclusion and backgrounding of many elements. *"There is no way of perceiving and making sense of social reality except through a frame for the very task of making sense of complex, information-rich situations requires an operation of selectivity and organization, which is what 'framing' means."* (Schön & Rein, 1995, p. 30)

The lesson drawn from theory is that the meaning of an issue, element, like early diagnostics for Alzheimer's disease can change fundamentally depending on the networks of relations in which it is mobilized (Van Gorp & Vercruyssen, 2012) and there are always networks of relations in the plural in which an issue can be mobilized. It is essential to be aware of this (ever-present, but not always obvious) politics and to follow its traces.

#### **4.2.4 Making sense of making sense**

A fourth lesson that emerges from the three approaches of meaning making is that such a study is necessarily ambiguous and reflexive. Authors within discourses, framing and modes of ordering refer to their concepts as 'ordering devices', 'sense-making devices' or 'tools for sense-making'. Hajer for example describes discourse analysis as providing *"conceptual tools that analysts use to capture how [policy] actors deal with ambiguity and allocate particular significance to special social or physical events."* (Hajer, 2006, p. 252) Researchers involved in discourse analysis, in the analysis of modes of ordering, or framing analysis use their specific instrumentation to study recurring patterns in social or sociomaterial practices.

There is a tricky double interpretation in these analyses. The first interpretation is that the outcome of analysis shows how *other* people order the world and make sense of the world. Yet the analysis *itself* also requires ordering, selecting, simplifying, leaving out. To say it in Law's (Law, 1994) words: the analysis requires ordering work too. This means that the research outcomes depend on the researcher and the interpretations of the analyst. *"I'm imputing ordering modes to the bits and pieces that make up the networks of the social. In*

---

<sup>18</sup> With the understanding of meaning as patterns it gains a fluidity and flexibility that is less present in the terms 'meaning-making', and 'construction of meaning'. 'Meaning-making' and 'construction of meaning' are words using the metaphors of building something. Riverbeds and elephant paths are not build, they are the result of repetitive movement. While the words construction of meaning and meaning-making are used throughout the thesis, my notion of meaning is more fluid than the terms meaning-making and construction of meaning suggest.

*effect I am saying that I think I see certain patterns in the ordering work of managers and its effects. I think that if I conceive these patterns in this way, then I can say that these are being partially performed by, embodied in, and helping to constitute the networks of the social.”* (Law, 1994, p. 21) This may also lead to some bias or blind spots: *“Frames must be constructed by someone, and those who construct frames (the authors of this book for example) do not do so from the position of unassailable frame-neutrality. They bring their own frames to the enterprise and, what is more, they may be unaware of doing so.”* (Schön & Rein, 1995, p. 36)

The analysis of the construction of meaning is not the same as the construction of meaning itself. Any analysis creates and employs constructs. In this thesis I study construction of meaning and I reconstruct my findings in a particular way. This thesis is the product of ordering work conducted by the analyst. It is making sense of making sense.

To (literally) illustrate this point, I relate this type of analysis to the work of Ursus Wehrli, a Swiss comedian and experimental artist, called ‘tidying up art’. Ursus Wehrli sorts out (orders) the mess of modern art by reorganizing the paintings. He stacks the different element according to their size, shape or color. Below you see what he did to the work of Paul Klee. *“We can see now what was barely recognizable in the original. Seventeen reds and orange squares are juxtaposed with just 2 green squares.”* (TED Talk, Feb 2006, Tidying up art). Of course this is meant to be funny. This humorous ordering work of Wehrli visualizes the point made in this section: the tracing of patterns in the complexity and messiness of networks of the social is an act done by the analyst, which is empirically based, yet highlights certain patterns for the sake of the research question, and necessarily leaves out other patterning.

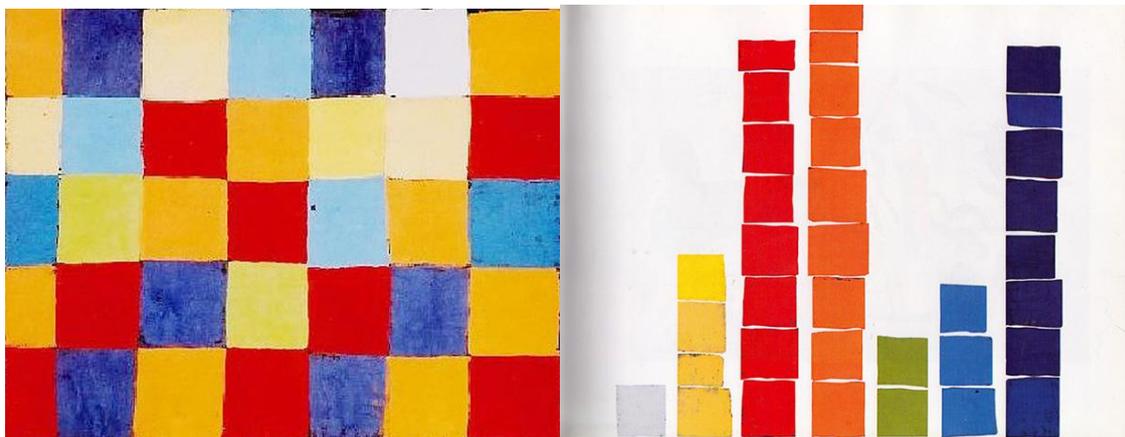


Figure 4.1: Left - Farbtafel by Paul Klee. Right - tidied up version by Ursus Wehrli

### 4.3 Research design choices

Section 4.2 outlined the lessons drawn from the theoretical approaches for studying the meaning of early diagnosis. Based on these shared lessons also some specific choices have been made in the design of this study. Subsequently I will discuss:

1. The tourist approach
2. A focus on language to analyze meaning
3. Medium sized constructions of meaning in practice
4. Meaning in action
5. A modest position

#### **4.3.1 The tourist approach**

One of the nice aspects of being a social scientist is the ability to travel into different worlds and try to understand these. There are so many places to visit and worlds to explore. Just go to any place, anywhere, and open a door: a whole world will unfold at the doorstep. Being a social scientist grants the opportunity to explore the worlds within the world. It is the entrance ticket to enter many places and curiously ask people what they are doing, how exactly they go about to do that, why they think that it is important, what the difficulties are they are facing, what their hopes and dreams are and whether I could accompany them on their job for a little while to understand more of their reality.

In this thesis I have used this “tourist approach”. Using the tourist approach in research is not only a very interesting alternative for backpacking the world, it is also a valuable position. One of the good things of travelling, in general, is the experience that things can be different. The things that are so normal at home and you never even stopped to think about, all of a sudden become visible when you are somewhere where they are different. It not only makes *you* wonder about what you first thought was normal, also the people you encounter and ask about their live, work or culture start to make explicit what is taken-for-granted in their daily lives (De Botton, 2007). So travelling is a way of becoming aware of all the things taken for granted when immersed in your own world and how things are different in worlds of others. The position as a visitor (‘tourist) and the activity of visiting many different places enables the tourist-researcher to see patterns across these settings as well as differences.

Van Lente used the tourist metaphor to explain the value of the work of researchers in the field of Science and Technology Studies in his inaugural lecture (Van Lente, 2015). A basic premise of Science and Technology Studies (STS) is that science and technology never ‘just exist’, or enter society from someplace else, but are socially constructed. Scientific findings and technology are viewed within STS as sociomaterial networks (Bijker et al., 1989; Latour, 1987). STS generally follows the work that is needed and the networks created for a technology to work. Here again we see the metaphor of the network – for a technology to work, the network needs to be build, alliances need to be created (Latour, 1987). To understand science and technology as social processes, the STS researcher should be a visitor of worlds and follow engineers, scientists and artefacts into many different places (Latour, 1996). For a technology to work all different kinds of threads need to be aligned and held together in complex and opaque ways. Because an STS researcher moves across different worlds to study these construction processes, he or she can compare and contrast, ask questions about taken for granted issues, and recognize patterns and dynamics across different settings.

I will use the tourist approach in this thesis to study the social and cultural implications of early diagnosis of Alzheimer's disease. The question, then, is what to visit and whom. While the traditional starting point in STS is to follow the builders of socio-technical networks, I decided to start at the places where the meaning of early diagnosis is discussed and how it relates to the reality of actors in these places. Rather than following the technology in and out of the lab, I use an inversed-Latourian-approach and start my investigations from different social settings where early diagnostics enters the conversations going on there. I use a travelling approach because Alzheimer's disease and early diagnostics for Alzheimer's disease is (unlike for example nanotechnology in its early stages) a topic that is actually being discussed in many places. By learning from these ongoing conversations I could learn in a more contextualized way how early diagnostics gains meaning. In line with Law and Moser (Law, 1994; Moser, 2011) I do not privilege one actor or one setting over another. I do not a priori assume that reality is constructed in one place. It can be that there are regularities, in the sense of patterns that seem to reproduce themselves. If this occurs, it is a result of the study that this emerges, not a necessity. I do not assume one setting which is privileged to define what matters of concern are.

Thus, for my empirical work I will travel to settings where Alzheimer's disease and early diagnostics are discussed. My aim is to understand what the meaning of this development is within very different contexts. My case studies are: public media – particularly Dutch newspapers, a health technology assessment, Alzheimer Cafés, and a national dementia strategy.

#### **4.3.2 A focus on language to analyse meaning**

In this study I mainly analyze discursive articulations, while taking into account the setting in which these articulations take place.<sup>19</sup> The construction of meaning is not confined to language alone. Meaning is also constituted by and constitutive for, for example, thoughts, actions, technologies, organizational structures, infrastructures, financial arrangements and even embodied. As described in section 4.1, the different theoretical approaches differ in terms of the elements that are part of the analysis. The framing approach mostly refers to discursive relations, discourse analysis (depending on the tradition) to discursive relations as well as social and material relations, and modes of ordering are socio-material. While the focus differs, all approaches acknowledge that language plays an important role in the creation of meaning and provides an adequate and easily accessible entrance to study the construction of meaning.

---

<sup>19</sup> The use of the term *articulation* in this thesis is based on its use in discourse theory. Discourse theory, drawing on a poststructuralist approach in linguistics, argues that signs consist of form and content. When we use a word – a sign - we attach meaning to a certain sound. This is a social convention. The meaning of a word is also determined by its relation to other signs. Poststructuralist linguistics argues that language is not fixed. Signs can change content depending on their context of use. Structures do exist, but only temporarily and not necessarily consistent. The structure is created in concrete language use, and can be reproduced or changed. In discourse theory *articulation* is defined as *the practice* that positions elements in relation to other signs in order to give meaning. Every practice establishes a relation between signs such that the identity of the element is modified. In discourse theory the term '*signs*' is used as signifier (a word is a sign) and the term '*element*' is used for signs which meanings have not yet been fixed and have multiple potential meanings. (Jorgensen & Phillips, 2002)

Another reason why a focus on language makes sense is that early diagnostics is an emergent technology, which partly exists in material form, but partly also only in hopes and dreams of their protagonists, worries of their antagonists, promises and expectations in research proposals or grand visions for strategic purposes. All of these mainly travel through spoken or written words.

### 4.3.3 Medium sized constructions of meaning in practice

Early diagnosis of Alzheimer’s disease gains meaning as an element in networks of relations. These relations are studied as they are being articulated discursively. Articulations occur anywhere and in principle meaning-making can be studied everywhere where people are. The level of analysis can range from aiming to pick the mind of a person up to describing general patterns within cultures during a specific era (see figure 4.2.).



Figure 4.2 locations of frames in framing literature

The level of analysis that is relevant for a study depends on the aim of the study. In my case, I am interested in the meanings of early diagnosis to understand social and cultural implications of early diagnostics for Alzheimer’s disease. Therefore I am interested in meanings that are to some extent institutionalized and socially anchored.

The interest of this thesis to study the construction of meanings of early diagnostics for Alzheimer’s disease as an operationalization of studying social and cultural implications of early diagnostics for Alzheimer’s disease, relates to the description of *culture* by Ann Swidler (1986). She describes culture as a ‘tool kit’ that is available to people and they can draw upon when acting. This ‘tool kit’ contains symbols, habits, stories, skills, rituals, world-views and routines that people have at hand to construct strategies of action. In discursive terms, the term ‘cultural repertoire’ (Swidler, 1986) describes what I am after. The term is used to emphasize that discourses or frames are flexible resources that can be drawn upon in social interaction. In framing analysis this is referred to as the ‘stock of commonly invoked frames’ (Entman, 1993). These concepts are situated at the cultural level and thus outside the individual person. Also issues, like early diagnostics for Alzheimer’s disease, have a culture. This issue culture is *“an ongoing discourse that evolves and changes over time, providing interpretations and meanings for relevant events”* (Gamson & Modigliani, 1989, p. 2).

By referring to a ‘cultural system’ there seems to be a cultural level that is accessible in its own right. Yet there is a trouble with this level of analysis. When speaking of a ‘stock of commonly invoked frames’ it does appear that there are a number of frames (or discourses for that matter) that appears rigid and as ‘things out there’. Jorgensen and Philips describe some discourse analytical studies as: *“something very like the geology of plate tectonics – a patchwork of plates/discourses are understood to be grinding violently together, causing earthquakes and volcanoes, or sometimes sliding silently one underneath the other. Discourse*

*becomes to be seen as potent causal agent in their own right, with the processes of interest begin the work of one (abstract) discourse on another (abstract) discourse*" (Wetherell and Potter 1992, p. 90 in Jorgensen & Philips, 2002, p. 104) Likewise in the same vein (but less poetic), Law states that *"the problem with discourse is that it always seems to be larger than life"* (Law, 1994, p. 95). Van Gorp addresses this point for framing analysis by addressing a comment from a reviewer on one of his articles who ridiculed his idea of a cultural stock of frames as *"a Wal-Mart in the sky"* from which individuals could pick any frame they like (Van Gorp 2010, p.104).

Then what or where is this cultural repertoire? Because there is no Wal-Mart in the sky, these cannot be studied as such. Van Gorp adjusts the notion a little: he states that the cultural repertoire is not *above* people but *among* people. The reason that researchers speak about the cultural repertoire as external to the individual is because a single individual is generally incapable to change this cultural repertoire, including metaphors, myths, stereotypes and so on. Yet individuals are central to the cultural repertoire. Any frame or the cultural repertoire is only there because it is used over and over again and thus can be mitigated through its (non-)use (Van Gorp, 2010).

While the notions of 'discourses', 'modes of ordering' and 'frames' are about tracing patterns in social reality and thus describing these patterns, that does not mean that these patterns are solid or fixed. Firstly, because language in everyday use is not static, it is dynamic. *"There is an available choreography of interpretative moves – like the moves of an ice dancer, say – from which particular ones can be selected in a way that fits most effectively in the context. (...) It shows in the way the tectonic image breaks down in studies that focus on discourse use in practice."* (Wetherell and Potter 1992, p. 92 in Jorgensen & Philips, 2002, p. 107).

A second way to understand discourses as dynamic comes from post-structuralism in linguistics where all three theoretical approaches draw upon. Structural linguistics argues that signs consist of form and content. When we use a word – a sign - we attach meaning to a certain sound. This is a social convention. The meaning of a word is also determined by its relation to other signs. A distinction is made between *langue* (the structure, which is fixed and unchangeable) and *parole* (situated language use). Poststructuralist linguistics, however, argues that '*langue*' is not fixed. Signs can change content depending on their context of use. Structures do exist, but only temporarily and not necessarily consistent. The structure is created in concrete language use, and can be reproduced or changed. A useful metaphor to understand the structural approach to language is the *fishing net* in which signs are the knots in the fishing net. These knots derive their meaning from their difference from one another and their position in the net. The post-structural approach in linguistics objects this metaphor and argues that meaning cannot be fixed unambiguously. They do acknowledge that signs acquire meaning from being different from one another. But in ongoing language, signs are constantly positioned in different relations to each other, so that they acquire new meanings. The creation of meaning is about the fixation of meaning *as if* a structure existed. It is through conventions and conflicts that structures of meaning are either fixed or challenged. Returning to the fishing net metaphor, a strive to fix meaning is trying to stretch the fishing

net so each sign is locked into a specific relation to other signs. Yet this is ultimately impossible, for fixation of meaning is always contingent: possible but not necessary.

The aim of discourse analysis like Discourse Theory exactly addressed this point (Jorgensen & Philips 2002, Laclau & Mouffe, 1985). One of the pertinent questions is how some fixations of meaning become so conventionalized that we come to think of them as natural. The aim of Discourse Theory is to analyze the processes of attempts to fix meaning and the struggles occurring in these processes. Discourse in this approach is understood as a (temporarily and contingent) fixation of signs in a relational net(work). But discourse can never be total. There are always other meaning potentials which may challenge and transform the structure of discourse. Discourses in Discourse Theory are viewed as incomplete structures in the same undecidable terrain that never becomes completely structured. Hence there is always room for struggle over what discourse should prevail and how meaning should be ascribed to individual signs.

#### **4.3.4 Meaning in action**

Since meaning-making only occurs when meanings are communicated, articulated, and circulated among actors I study meaning making in action. I start with the notion of meaning as constructed by placing one element, in this case early diagnostics for Alzheimer's disease, in relation to other elements. This will be studied in different settings. I will study how this is done in each of the four settings studied and the articulations taking place within these settings. The networks through which meaning of early diagnostics for Alzheimer's disease are constructed may be all-encompassing, or very small. This will be an empirical finding.

Often in framing studies deductive framing analysis is conducted where a number of frames are defined and the empirical analysis focuses on to what extent these frames are used in a certain domain (e.g. media or policy). But since the framing of early diagnosis of Alzheimer's disease is exactly the question of this thesis, and there are no well-defined frames established yet, I opted for an inductive analysis in which the *"spectrum of conceivable frames that are relevant for the topic under scrutiny are identified"* (Van Gorp 2010, p. 91).

Another option for analysis of meaning would be to study data which are rather 'clean' representations of a particular framing. This would have set the 'frames' for further analysis of more messy occasions where multiple stakeholders meet. However, I depart from the wall-mart in the sky idea. My interest is in meaning of early diagnostics that circulates and is actually used and alive. So when referred to specific documents in these settings, I will include them in the analysis. I have used, what I refer to as a 'quasi-naive approach' in this thesis. I entered the settings I studied without a pre-set list in order to understand what is at stake in that particular setting and how meaning is attributed to early diagnostics there. I follow Law (2006) in the reasoning that if there happens to be broader patterns of meaning-making it will be an empirical finding, rather than an a priori assumption.

I selected settings in which actors from different backgrounds meet. I have done this because I assumed that when persons with different backgrounds meet, they will be more explicit and articulated. It also increases the chance to study the dynamics played out when different meanings of early diagnosis of Alzheimer's disease confront each other.

### **4.3.5 A modest position**

This thesis is a modest attempt to make sense of the messiness of the social world with respect to early diagnosis. Such an attempt is modest because there is no way that I can describe the whole social world, not even only that part that is somehow related to early diagnosis of dementia. Telling a story that is understandable is in need of simplification and it will be incomplete. To write a thesis with a structured argument, describing messiness, without confusing everybody who reads it, requires that I need to do ordering myself.

## **4.4 Data gathering and analysis**

This section deals with the settings selected to study meaning of early diagnosis of Alzheimer's disease (section 4.4.1). Next, it presents the data gathering (4.4.2) and data analysis part (4.4.3).

### **4.4.1 Selecting settings to study meanings of early diagnostics for Alzheimer's disease**

To study meanings of early diagnostics for Alzheimer's disease I need to find occasions in which meaning is made explicit through articulation, interaction or contestation. After all, meaning is not something that can be observed as such. Meaning can be studied at many levels of analysis. As I explained in paragraph 4.3.3. I am interested in the issue culture on early diagnostics for Alzheimer's disease. There is no single setting where an issue culture can be studied. Issues are discussed in many different settings and the conversations in one setting is not isolated from other settings. Any setting can be seen as (1) part of a process of production of an issue culture and (2) an indicator of the issue culture itself.

This is why I study the meaning of early diagnostics in settings in which stakeholders with different background are present and interact. With so-called 'settings' I refer to a confined space in place and time, in which the meanings of early diagnostics for Alzheimer's disease can be studied. Using a theatre metaphor, I would consider a setting to be a stage on which the meanings of early diagnostics are being performed, so that I, as an analyst, can observe them. I consider these settings to be crystallization points, in which what is fluid is made temporarily joined together, hardens out to a certain extent and takes a specific shape. Or to say it in discourse theoretical terms: I study settings in which early diagnostics is mobilized as an element in webs of relations in which its meaning is temporarily (more or less) fixed.

To explore the topic of this thesis I travelled through the worlds of dementia, particularly Alzheimer's disease, and its diagnosis and visited many places. Throughout this exploration I considered what would be interesting settings to study in-depth. Settings were selected based on a number of criteria:

- Settings were chosen in which early diagnostics of Alzheimer's disease is a topic of conversation, because meanings of early diagnostics for Alzheimer's disease become explicit through articulation.
- Settings were selected that are open to stakeholders with different backgrounds and in which the stakeholders interact. When stakeholders with different backgrounds

interact there are less a priori assumptions about shared understandings, which means that more of the underlying assumptions will be explicitly articulated.

- Settings were selected to be sufficiently different from each other. I aimed to find a cultural setting, a policy setting, a medical setting and a setting in which persons deal with (the prospect of) dementia. This should prevent this research to be co-opted with one approach to dementia, preventing for example that this research is restricted to only medically, psychosocially, or only gerontologically oriented settings.
- Settings were chosen that were accessible to the researcher.

I studied the meanings of early diagnostics for Alzheimer's disease in four different settings. The settings selected are: (1) public media (Dutch newspapers), (2) a health technology assessment, (3) Alzheimer Cafés, and a (4) national dementia strategy. These different settings provide very different occasions in which early diagnostics is being discussed for different purposes, and by different stakeholders. I expect that the study of this range of settings provides interesting insights into the meanings of early diagnostics for Alzheimer's disease.

#### **4.4.2 Gathering data**

In the explorative phase I travelled through the landscape of early diagnostics for Alzheimer's disease. The exploration has been most intense at the start of the project and has continued in a more extensive activity throughout the whole duration of the study. This activity helped to gain familiarity with the phenomenon of early diagnostics of Alzheimer's disease: to understand what is going on around the issue of early diagnostics for Alzheimer's disease; which persons and organisations are involved and what is at stake. Furthermore it helped to select settings to study in depth. The main guiding question throughout these exploratory activities was: 'What is going on?' Next to this very general explorative question, I used sensitizing questions on the topic of interest for this study. From reading the literature on dementia from different disciplines (chapter 2) I realized that meanings of early diagnostics are highly connected to how dementia or Alzheimer's disease is approached. From the exploration of the concept 'responsible innovation' (chapter 3) I realized the steering power of notions of 'the future' for innovation. So in addition to the main guiding questions I used the following sensitizing questions:

- What is Alzheimer's disease?
- What is the problem with Alzheimer's disease?
- What futures are addressed?
- What is the meaning of early diagnostics for Alzheimer's disease?

I travelled through the Alzheimer landscape with these questions guiding the way: What are interesting settings when it comes to these questions? Where should I go? What should I see? Who should I speak to? What should I ask? What should I read?

All the places I visited were explored in a quasi-naïve way, guided by the general question of 'what is going on here' and the sensitizing questions described above. See appendix 1 for an excerpt of exploratory activities. When I visited places I took my voice recorder or took extensive notes (depending on the appropriateness of a voice recorder) of the conversations

going on there. I would start conversations with persons who I met. I made notes during a conversation, right after the conversation, or when coming home after a field trip. In a number of instances I wanted to explore particular practices or persons more in depth and I would ask if I could visit their practice, shadow them throughout their daily work, or conduct an interview with them. I prepared these visits and interviews by exploring the activities these persons were involved in on the internet and through literature. I conducted formal semi-structured interviews, guided by the sensitizing questions and additional questions that I had concerning their particular activities and approaches to dementia and early diagnostics of Alzheimer's disease. These explorations served to shape the research questions, the design of the research, the selection of research settings and also served as a basis for chapter 3 on quandaries of responsible innovation.

Based on these explorations I decided on the settings that were interesting for further study, also taking the settings selection criteria into account, as mentioned in section 4.4.1. Accordingly, the settings I chose to study meanings of early diagnostics for Alzheimer's disease in depth are (1) public media, (2) a health technology assessment, (3) Alzheimer Cafés, and a (4) national dementia strategy. For each setting there was an encounter, an exploration, a choice to further gathering data and finally the analysis of the data.

I studied the meanings of early diagnostics in public media and particularly in newspaper articles. Since newspapers do not have a particular stake in dementia or early diagnostics I expected newspapers to show a broad pallet on possible public interests in early diagnostics for Alzheimer's disease. I consider newspapers as a setting that both mirrors and constitutes the cultural repertoire on early diagnostics for Alzheimer's disease. For the newspaper analysis I gathered articles from the large Dutch newspapers from 1995 to 2010 from the LexisNexis database. The newspaper settings shows the meanings of early diagnostics for Alzheimer's disease as an issue of public interest.

The second setting that has been selected for this study is a Health Technology Assessment (HTA) that was part of the LeARN consortium with which we collaborated. HTAs are meant to serve as a bridge between the world of research and the world of decision-making. (Battista & Hodge, 1999) HTA is a type of policy research that assesses the consequences (societal, economical, ethical and juridical) of a medical technology to provide information to decision makers in their choices whether or not to adopt a specific health technology (in standard health care practice, in health care reimbursement systems, in a hospital, or in another situation). While the original aims of HTA are defined broadly to include assessment of all kinds of intended and unintended consequences, in practice the assessment is usually limited to the effectivity and costs of a novel technology. (Reuzel & Van der Wilt, 2000) The main aim of the HTA in the LeARN consortium is to provide evidence to decision makers on whether to adopt new biomarker tests for Alzheimer's disease in standard clinical practice (Handels et al., 2012). The HTA consists of different parts, such as the assessment of the accuracy of current diagnostic practice and the biomarker tests, and analyses of costs of new tests in relation to the health-effects. These evaluations will lead to assessments of the diagnostic tests in terms of costs per accuracy of the tests, and costs per quality adjusted life year. My colleague PhD Anna Laura van der Laan and I conducted semi-structured interviews

with the Work Package leaders of the LeARN consortium and we were invited to the annual meetings of the consortium. Based on these encounters the Health Technology Assessment, aiming to assess the social and economic value of the instruments developed by LeARN, emerged as an interesting setting to study. We conducted interviews with the researchers working on this project and were kindly invited to their discussion meetings that provided input for the design and data collection of the HTA study. Together we transcribed these interviews and meetings. We also requested for background reading on HTA and gathered documents produced by the HTA research team (articles and project descriptions). The HTA setting shows the meanings of early diagnostics for Alzheimer's disease when the societal consequences of the technologies developed in medical research centres are being assessed.

Because I was working on early diagnostics of Alzheimer's disease I felt the need to meet with people who actually have Alzheimer's disease. For that reasons I visited (amongst other places) Dutch Alzheimer Cafés. Alzheimer Cafes are monthly informal meetings for people with dementia, their partners, family, care givers and other interested persons. Alzheimer Cafés are organized by the Alzheimer Association as part of the support to patients and informal care givers. After an introduction of experts concerning a specific topic related to AD, the guests can share ideas, information and experiences. The Alzheimer Cafés turned out to be a fascinating setting and a melting pot of persons with totally different backgrounds but all highly involved with persons with dementia, or personally dealing with this condition. I visited the Cafés for one and a half year and was allowed to make notes during these evenings. I spoke with persons visiting the Cafés (persons with dementia, their partners, children, friends and neighbours, relatives worried that a loved one was developing dementia and occasionally persons anxious about developing dementia themselves). To become more scholared in the ideas behind this particular setting I took part in a course for volunteers of the Alzheimer Café, I read the books written by the founding father of the Alzheimer Café and I interviewed the local professionals involved in the Cafés. The Alzheimer Café setting shows the meanings of early diagnostics for Alzheimer's disease in conversations starting from the experience of people living (or working) with dementia.

There were also settings that I did linger around and studied for a longer time, but that are not present in this thesis. Amongst these are the nursing homes, the welfare organisations and (home) care organisations, and films on dementia and Alzheimer's disease. For all these settings the topic of early diagnostics - was not very present or not present at all. Whereas dementia was at the centre of attention, early diagnostics for Alzheimer's disease did not appear as an issue of conversation at all. I found it curious that the issue of early diagnostics, so much foregrounded in medical research on Alzheimer's disease, was a non-issue or a distant issue in many other settings that have been explored.

These observations accumulated to the selection of the policy setting. While looking for a policy setting where dementia and early diagnostics for Alzheimer's disease were a topic of conversation, the Deltaplan Dementia was initiated in the Netherlands. After the announcement of the plan in the media a lot of discussion aroused. In these discussions different ways of dealing with dementia and the important or marginal role of early diagnostics was explicitly addressed. I followed the development of the Deltaplan Dementia

during two years and followed discussions in the media. I analysed policy documents and conducted interviews with the initiators of the plan, policy makers, and other persons involved in the debate around this action plan (interviewees included professionals in psychiatry, geriatric, neurology, the Alzheimer Association, journalists, anthropologists). This setting particularly shows the politics involved with the co-existence of different framings of dementia and different meanings of early diagnostics.

**Table 4.1. Data gathering**

Setting	Data gathering
Public media	Newspaper articles on early diagnosis between 1995 and 2010
Health Technology Assessment (HTA)	Interviews with WP leaders of the LeARN consortium (4) Interviews with PhDs working on HTA (3) Participant observation discussion meetings (2) Document analysis of project description and (draft) articles on this HTA
Alzheimer Café	Participant observation of Alzheimer Café meetings from April 2010 until November 2012 (15) Interviews with organisers and volunteers (5) Participating in a course for volunteers at the Alzheimer Café (2 full days) Books and leaflets on the Alzheimer Cafés
Deltaplan Dementia	Newspaper articles (57) Interviews with persons involved in Deltaplan Dementia (10) Policy and research documents

#### **4.4.3 Analysing data**

In all cases I conducted a qualitative analysis through coding and writing memos (Birks and Mills, 2011). This was an iterative process. I went through the data repetitively with the sensitizing questions in mind: ‘what is this going on here in general?’, ‘what is Alzheimer’s disease’ ‘what is the problem with Alzheimer’s disease’ ‘what futures are addressed’; ‘what is the meaning of early diagnostics for Alzheimer’s disease’. I coded fragments of text with words close to the text, so the texts are categorized on their content through a large number of codes with Atlas Ti software. This is also referred to as ‘open coding’ (Baarda et. al., 2005).

The meaning of early diagnostics is understood as the result of a cluster of elements in relation to each other. While the identification of elements through open coding involved a fragmentation of the data, I simultaneously made memos of the patterns of recurring connections among elements in the data.

Based on these activities I constructed a preliminary outline of the main clusters of elements present in the data and the core around which this revolves. I would then again go through the data to see if this fitted the data or should be further adjusted.

For the construction of the clusters of elements, the methods of framing analysis proved to be very useful. I used the method to construct so-called ‘interpretative packages’ from media

studies for the newspaper analysis, the Alzheimer Cafés and the Health Technology Assessment. For the analysis of the Deltaplan Dementia the concepts used in collective action framing were more suitable. The specificities of these methods will be further explained in the chapters addressing these settings, being Chapters 5, 6, and 7 respectively.

**Table 4.2. Data analysis**

Setting	Methods used for analysis	Chapter
Public media	Interpretative packages	5
Health Technology Assessment (HTA)	Interpretative packages	6
Alzheimer Café	Interpretative packages	6
Deltaplan Dementia	Collective action framing	7

# **STAGING THE SETTING**



# Chapter 5

## The meanings of early diagnostics for Alzheimer's disease in Dutch newspapers - A framing analysis

*This chapter has been published as Cuijpers, Y., and H. van Lente, The meanings of early diagnostics for Alzheimer's disease in Dutch newspapers. A framing analysis. p. 295-214. In Popularizing Dementia, Public Expressions and Representations of Forgetfulness, edited by Aagje Swinnen and Mark Schweda. 2015. Bielefeld, Germany: Transcript.*

One of the key interests in current biomedical research and clinical practice is detecting Alzheimer's disease at milder stages. The goal of early diagnosis is to unravel the underlying pathological processes that precede the symptoms of dementia by identifying and validating biomarkers. The idea is that this will enable a more reliable and earlier diagnosis, maybe even at a pre-symptomatic stage, and speed up the development of disease-modifying treatments (cf. EU Joint Programme NDR, 2012; Mueller et al., 2005).

The quest for biomarkers is a medical endeavour and is also gradually being taken up in clinical practice and included in new diagnostic guidelines. Yet early diagnostic tests not only contribute to biomedical research, they also affect those who suffer from Alzheimer's. The mere prospect of an early diagnosis changes personal outlooks and societal responses to the disease. Thus, early diagnosis transcends the confines of medical and clinical practice and acquires different meanings in society. Many scholars have argued that Alzheimer's disease is much more than a medical phenomenon, that it is a psychological, social, and cultural phenomenon which is enacted in many practices with different meanings and values (cf. Lyman, 1989; Kitwood, 1990, 1997; Downs, 2006; Moser, 2008, 2011; Innes, 2009; Innes and Manthorpe, 2013).

Building on this line of research, this chapter investigates the meanings of early diagnostics in society and their relationship to broader conceptualizations of Alzheimer's disease by analysing how early diagnosis is framed in Dutch newspaper articles. We show that different meanings of early diagnostics are intertwined with specific understandings of Alzheimer's disease and its future. The focus on early diagnosis is new in studies of the meaning of dementia. We expect that it will contribute to a better understanding of Alzheimer's disease as a societal phenomenon rather than just a medical or personal problem.

### 5.1 Construction of meanings in newspapers

It is a basic tenet of social theory that meanings are not givens but result from interactions and interpretative struggles. Meaning is constructed by positioning an act or a thing cognitively, morally, or practically within a network of relations. Such a construction can take

place in any context: in face-to-face interaction, in practices, within groups, or in society at large (Weick, 1995). The construction of meaning has been addressed in particular in discourse analysis and framing analysis. These traditions examine meaning-making mainly by analysing particular ways of talking about and understanding the world (or an aspect of the world) in texts.

A general starting point of all approaches to discourse analysis is that ways of talking do not neutrally reflect the world but actively create and change it. For instance, newspaper articles are not mere representations of pre-existing realities, but rather a way in which the social world can be (re)produced and changed (Jorgensen and Philips, 2002). Framing approaches emphasize that meaning-making is enabled by highlighting particular aspects of a perceived reality while simultaneously occluding or downplaying other aspects. When changes are made in what is prominently displayed, the character, causes, and consequences of any phenomenon become radically different (Van Gorp, 2007). Discourse and framing analysis stress that ways of talking about and understanding the world in texts are both an indicator of social realities and an active way to constitute them.

In most cases, an existing discourse develops over time and consists of competing interpretations. Which interpretations are more readily available than others matters. As Gamson and Modigliani explain, “[m]aking sense of the world requires an effort, and those tools that are developed, spotlighted, and made readily accessible have a higher probability of being used” (Gamson & Modigliani, 1989, p. 10). In modern society, newspapers and other media are important sites where “various social groups, institutions and ideologies struggle over the definition and construction of social reality” (Gurevitch & Levy, 1985, p. 19). Newspapers thus provide an arena in which meanings are contested, making them a particularly good place to trace (struggles over) the construction of meanings of early diagnosis. News comes to the public in ‘sketchy dramatic capsules,’ leading to the fragmentation of meaning (Gamson et al., 1992). Although a collection of newspaper articles creates a kaleidoscopic picture of potential realities, symbols, and worldviews, this picture is limited to specific repertoires. It is not surprising that newspaper articles about early diagnostics for Alzheimer’s disease typically mobilize a vast array of arguments, moral appeals, topics, facts, and metaphors. In this sense, newspapers articles are part of a culture, and “each culture possesses a repertoire of symbols and world-views that its members can use as a toolkit to attribute meaning to the various events and issues with which they are confronted” (Van Gorp, 2012, p. 1275). Usually these constitutive elements are not encountered individually but are mobilized together. Such bundles of elements are what Gamson (1989) calls ‘interpretative packages.’ The interpretative packages on an issue, which Entman refers to as the “stock of commonly invokes frames” (Entman, 1993, p. 53), are an indicator of the cultural repertoire we draw on to construct meanings, in this case of early diagnosis of Alzheimer’s disease (Gamson & Modigliani, 1989).

Interpretative packages in this article are analytical (re)constructions of the networks of relations in which early diagnosis is positioned and acquires its meaning. These packages are organized in a specific way. “At [their] core is a central organizing idea [...] for making sense of relevant events, suggesting what is at issue” (Gamson, 1989, p. 3). Two types of meaning-

making devices are distinguished within interpretative packages: framing devices and reasoning devices. Framing devices are metaphors, exemplars, catchphrases, or visual images that are easily associated with a specific interpretative package (ibid. – referring to Gamson & Lash, 1983). Reasoning devices guide how to think about an issue. They consist of a set of typical arguments, logical constructs, causal relations, and moral attributions. An interpretative package typically implies a range of positions rather than a single one, allowing for a degree of controversy (Gamson, 1989). For example, when early diagnosis gains meaning as an intervention in health care practices, positions can differ on whether this is an improvement or not. Interpretative packages are not mere representations, but are also part and parcel of (re)producing and changing practices in our society. They constitute what is defined as problematic and thus make some responses or actions more appropriate or more logical than others in specific situations. As such, they function as guides for doing and acting (Van den Brink, 2010).

No earlier studies exist on the construction of the meanings of early diagnosis in popular media, although some have investigated images of dementia in news media. With the exception of Van Gorp (2012), these used pre-set frames to analyse the quality and type of reporting on dementia in newspaper articles. Clarke (2006) examines ‘the case of the missing person,’ where persons with Alzheimer’s disease are spoken for by others, such as caregivers, family members, medical experts, or scientists, wholly neglecting their own agency. She also shows that a medical model prevails in which cure is emphasized at the expense of prevention, long-term care accessibility, care programs, self-management strategies, and social support, which has the effect of reinforcing the power of medical experts, scientists, and pharmaceutical companies. Adelman and Karlawish (2003) conclude that media inadequately report on the uncertainties in the interpretation of research results and do not focus on the controversies over the allocation of resources. Other studies show that negative stereotypes of dementia persist and are spoken about in a language that exacerbates fear. These studies argue for the use of more positive language when reporting on Alzheimer’s disease as a way of reducing stigma (cf. Kirkman, 2006; Doyle, 2012; Van Gorp, 2012; Clarke, 2009). All of these studies aim to improve media coverage of Alzheimer’s disease, either through more adequate reporting on the outcomes of scientific research, using more positive language, and being more patient-centred, or by moving beyond the medical frame to include epidemiological, psychosocial, socio-structural, and ethical frames.

## **5.2 Method**

Using the LexisNexis database, we searched for articles that address both Alzheimer’s disease or dementia and early diagnosis or early diagnostic instruments in Dutch national newspapers (see appendix 2B for the search string used). The search was limited to articles published between January 1995 and January 2010. This yielded a total of 516 articles, 306 of which were about early diagnostics or signalling and dementia. Signalling refers to the recognition of the early symptoms of dementia. Early diagnostics figured as the central topic in exactly 100 articles, but was more often mobilized in relation to other topics.

The first step was to go through the articles and explore the content. The content appeared to be rich and varied, yet it also contained recurring patterns. A first ordering was made according to similarities in topic and by making notes on possible cores of interpretive packages and repetitive patterns. In the second step, we made a preliminary list of the different cores and possible meaning-making devices present in the articles. We then used this list as we went back through the articles with the question which arguments, logical constructs, moral appeals, metaphors, and examples had been mobilized. During this process, the articles that had been labelled according to the initial list of interpretive cores were adjusted and extended where needed. One newspaper contains several statements and can draw on a number of different interpretative packages. So rather than labelling full articles as related to one package, we labelled statements that referred to early diagnostics of Alzheimer's disease and decided whether these statements related to one of the core organizing ideas. If they did, we added the element to that cluster. If they did not, we added another core organizing idea. In the third step, the statements that were labelled with respect to a specific core were summarized. This allowed us to trace the clusters of elements related to each core and derive the reasoning and framing devices present throughout the newspaper articles. From this process, we generated a list of interpretative packages on early diagnostics for Alzheimer's disease. From these packages, we could answer the research question on the meanings of early diagnostics and how these relate to conceptualizations of Alzheimer's disease and the future.

### **5.3 Interpretative packages**

In total, we encountered nine different interpretative packages in which the meanings of early diagnostics and Alzheimer's disease and its future are constructed (see appendix 2A). In the following, we will describe the reasoning and framing devices of the interpretative packages. This overview is summarized in table 5.1 (Quotes are translated by the first author. The numbers refer to appendix 2C).

#### **5.3.1 Apocalyptic demography**

*Reasoning devices:* Within this interpretative package, early diagnostics appear as a step towards a solution to a huge socioeconomic problem. It is argued that early diagnostics for Alzheimer's disease are needed for early treatment, efficient care provision, improved health care, and reasonable health care costs. Dementia is presented as an enormous challenge for society that comes with an aging population. The very success of our health care system to extend life expectancy (324) has now presumably turned into a huge and urgent problem, which is emphasized by qualifications such as "epidemic proportions" (557), "a national disaster" (554), a "silent tsunami" (380), "common disease number one" (471). This development is usually illustrated with numbers of increasing prevalence of dementia and an alarming increase in health care costs.

From this problem definition, it is argued that the number of persons with Alzheimer's disease should decrease in the future, either through medications that slow down or arrest disease progression at an early stage or identifying risk factors for dementia and preventative

measures. This would not only save many persons from developing Alzheimer's disease, but also reduce the associated health care costs. The same problem definition points to the moral obligation of caring for persons with dementia in a well-organized and efficient health care system. And given the foreseen gap between increasing demand for care and the decreasing availability of care personnel, an early diagnosis is needed for a policy of self-reliance and informal caregiving.

*Framing devices:* Aging society, socio-economical problem, prevalence numbers, epidemic, disaster, costs of health care.

### **5.3.2 Scientific progress**

*Reasoning devices:* Early diagnostic tests in this interpretive package are presented as part of scientific progress towards a better understanding of the causes of Alzheimer's disease, which will help to develop disease modifying treatments and to improve clinical diagnostic practice.

Articles in this interpretive package report on (possible) new tests, such as genetic tests, blood tests, bio barcode assays, urine tests, MRI scans, PET scans, CSF analysis, SPECT, word tests, pupil dilation, and SPECT. Headlines consist of variations of 'new test enables early diagnosis of Alzheimer's disease.' Articles make claims like "this is the first non-invasive test to diagnose AD" (560) or "this can lead to clues for the development of disease modifying treatment" (366). Alzheimer's disease is understood as an accumulation of pathological mechanisms, and, within this context, a reliable biomarker test at an early stage of disease progression will provide "hope for breakthroughs to help millions of patients" (376). Such hope, in turn, is expressed in phrases such as "[t]here must be a breakthrough. We must understand how it works" (244).

Early diagnosis of Alzheimer's disease also figures as an example of the broader trend in scientific research towards predictive medicine (in contrast to curative medicine when the disease is already manifest). The argument is that the 'genetic revolution' has changed the logic of medicine. While medicine used to look at a disease with the aim of unravelling which molecules influence it, now it is possible to trace pathological mechanisms and find a suitable disease. "We have as it were medications, but are still looking for a disease that goes with that" (733). The aim of medicine is now to detect diseases on the molecular level as early as possible, a development which is "crucial for research on Alzheimer's disease, Parkinson's, and other brain diseases" (584).

*Framing devices:* New test to early diagnose Alzheimer's disease, break-through, revolution.

### **5.3.3 Complex scientific puzzle**

*Reasoning devices:* In this interpretative package, Alzheimer's disease appears as a complex condition with many unknowns. A variety of research methods are used to discover the inner workings of the mind, to understand the complex network of hundreds of billions of neurons and the multitude of connections between them. This complexity is what makes the disease fascinating. Early diagnostics such as biomarker tests and brain imaging appear as pieces of the big puzzle of unravelling Alzheimer's disease, a puzzle which includes many different

pieces including the condition of blood vessels, silent cerebral infarctions, micro bleeds, changed brain activity, blood pressure, insulin growth factor, statins, diabetes, depression, migraine, hereditary factors, lifestyle, smoking, education, and social life. While such factors can be informative for risks at a population level, they are understood to be limited in their predictive value for individuals.

*Framing devices:* Puzzle, complexity of the brain, mystery, unravelling.

### **5.3.4 Technological progress**

*Reasoning devices:* In this interpretative package, early diagnostics are presented as an iconic example of technological progress. The development of molecular imaging techniques such as (f)MRI, MEG, SPECT, and PET is said to trace possible deviations in the brain that are related to Alzheimer's disease. This diagnostic route is described as providing hope: "A better resolution is worth gold in this world" (404).

Big market players in imaging technologies such as Siemens, General Electric, and Philips Medical Systems present themselves as frontrunners in medical imaging technologies, and newspapers report on their enormous investments. Medical centers also proudly present their share in technological progress, such as purchasing the newest 7 Tesla MRI scanners. "Rotterdam is the first in the world to have a new MRI scanner for early detection of brain conditions" (457), and "[t]he MRI scanner, a wonder machine that secures brain activity in great detail, and has caused a revolution in brain sciences in the last decennia" (352).

*Framing devices:* Superscanner, unique in the world, the next step.

### **5.3.5 Economic competitiveness**

*Reasoning devices:* Many articles present Alzheimer's disease and early diagnostics as a market opportunity for companies and a driver of national economies in the same way the unravelling of the human genome boosted the pharmaceutical industry and the biotech sector. The EU and the Dutch government are both investing in molecular imaging research and refer to 'the knowledge economy' and 'innovation capacity.' Large innovation programs, such as the Center for Translational and Molecular Medicine and TI Pharma (biomarker research) are accompanied by great promises for the Dutch economy. The following quote illustrates this reasoning device:

The Netherlands has chosen [to invest in] the life sciences. This will give a boost to the wellbeing and welfare of the Dutch people. [...] TI Pharma not only contributes to increasing the quality of life, but also to strengthening the knowledge economy. [...] With these kinds of projects, the Netherlands takes the lead in becoming the world's most competitive knowledge economy. (376)

Medical imaging technologies are thus a 'growth market,' but so are therapies, herbs, supplements, brain training courses, exercise programs, and "whatever is for sale in the 'market of forgetfulness'" (340)

*Framing devices:* Innovation, knowledge economy, market, economic growth.

### **5.3.6 Health care provision**

*Reasoning devices:* Central in this interpretative package is the question of how to provide health care to elderly persons with Alzheimer's disease in a decent and affordable way. Early diagnosis appears as a (future) ingredient of good health care that will be provided by memory clinics, geriatric clinics, or general practitioners. An early diagnosis will allow patients and families to prepare more effectively: "The longer patients can manage at home with the help of family and friends, the better it is" (387). In addition, budget cuts in health care and the increased burden on informal care are both a cause of concern. As one angry reader wrote in a letter to the editor, "[i]t is shameful that in a rich country like the Netherlands, care for dementia proves insufficient. Shameful and unloving!" (398)

*Framing devices:* Integral care, stay at home longer, the earlier the diagnosis the better, informal care, nursing homes, timely organization of care and support.

### **5.3.7 Successful aging**

*Reasoning devices:* The big concern in this interpretative package is how to avoid or delay memory problems and dementia. Here early diagnostics become part of the project of 'successful aging,' which is tied to changing expectations about life, changing social norms, and government policies towards self-reliance. Additionally, successful aging is treated as the responsibility of the aging person: "You can do something yourself to gain 10 more healthy years" (344). Newspaper articles report on the risk factors for dementia and the possibilities of preventing them. Generally, "all risk factors for a heart attack (high blood pressure, high cholesterol, obesity, and smoking) are also risk factors for dementia in old age" (549). The advice to age healthfully, including preserving one's cognitive functions and memory, is to keep an active and healthy lifestyle. "Remaining active is good for everything: memory functions, balance, self-confidence, and your mind" (344). Individual responsibility is reinforced by an emphasis on self-reliance. As one article expresses it, "[t]he message is clear: The elderly will have to fend for themselves" (386). This mentality of successful aging and the fear of being 'unsuccessful' feeds an entire market of brain training programs, physical exercise, hormonal treatments for women in menopause, and food supplements.

*Framing devices:* Successful aging, healthy aging, active aging, vitality.

### **5.3.8 Fear, worry, and approaching mischief**

*Reasoning devices:* This interpretative package is about the fear of growing old, becoming less vital, and eventually getting Alzheimer's: "The whole public perception of dementia is negative" (484), "a shrivelled brain and dying neurons; that is what awaits us with increasing age. Is there any way to prevent this chimera?" (651). In addition, the prospect of becoming an informal caregiver and experiencing the decline of a loved one is a cause of fear and worry. An illustrative quote of this notion is: "Dementia is a horrible disease and a cruel way to die" (549). Persons who are developing dementia as well as general practitioners are said to often ignore the signs of dementia as long as possible because "[f]ear, shame, and a negative perception play a big role. Dementia still remains a taboo" (387).

Memory decline is considered as one of the most feared ailments of old age. Some visitors of memory clinics who complain about their memory do not have symptoms of dementia but

are fearful and depressed (723, 708, 651). Persons in this group, known as the 'worried well,' have no rest until it is established that they do not have dementia (595). The Dutch Alzheimer's Association started a campaign called 'worries about Alzheimer's' to explain the difference between normal forgetfulness and dementia, how a diagnosis is conducted, and the benefits of an early diagnosis.

*Framing devices:* Worry, fear, chimera, horrible disease, worried well.

### **5.3.9 Good life and death**

*Reasoning devices:* This interpretative package revolves around what people value in life. A diagnosis of dementia changes the life prospects for the person diagnosed as well as for their close relatives. The idea of a 'good life' and one's choices in life and on death are related to the rise of predictive and early diagnostic tests for Alzheimer's disease. The central question is: (When) would you like to know? The unnecessary fear for 'first signals' needs to be balanced with the relief of having certainty about 'what is going on.'

The notion of a 'good life' also relates to the idea of a 'good death' and end-of-life decisions. This discussion has evolved over the years. Since 1999, euthanasia has been legally permissible in the case of dementia in the Netherlands. Many persons with dementia welcome this possibility and defend their autonomy. Others, however, point to the moral obligations of the state to organize the health care system in a reassuring way and to promote a societal climate that does not exclude persons with dementia. In this view, the current increase in possibilities of and requests for euthanasia in the case of dementia is considered as the moral bankruptcy of society. While it is legally possible to request to be euthanized in early-stage dementia, many general practitioners do not cooperate, leading to situations in which persons try to organize their own deaths, which is often accompanied by all the unwanted consequences. This discussion has changed with medical-technological advances in diagnosing Alzheimer's disease earlier and with higher certainty. Because dementia seemingly has become less of a taboo and expectations have been raised about being able to give a diagnosis at an earlier stage, it is predicted that more people will request euthanasia. As one article puts it: "If you start developing dementia, you should sound the alarm in time because that is the moment you can still make a request for death. If you do not do it then, you are sentenced for life" (395).

*Framing devices:* Personal choice, autonomy, end of life, right to know, right not to know, civilization

After the delineation of these nine interpretative packages in newspaper articles, we now return to the question of the meanings of early diagnostics and how they are intertwined with specific understandings of Alzheimer's disease and its future. This is summarized in table 5.1.

Table 5.1: Meanings of early diagnostics for Alzheimer’s disease, related to meanings of Alzheimer’s disease and a likely or needed future

<b>Interpretative package</b>	<b>Meaning of early diagnostics</b>	<b>Meaning of Alzheimer’s disease</b>	<b>Likely or needed future</b>
<b>Aging society</b>	Step towards a solution in terms of cure and care; Improving health care and decreasing health care costs	Huge socioeconomic issue	A national disaster to be averted; Decreasing the number of persons with dementia; Reducing health care costs by staying at home longer
<b>Scientific progress</b>	Increase knowledge on Alzheimer’s disease A step towards a medical solution or prevention; Imaging techniques and biomarker tests push the boundaries of brain and neuroscience	A biomedical condition; A condition of the brain	Increasing knowledge, earlier and better diagnosis and medical intervention
<b>Scientific complex puzzle</b>	A step in trying to unravel the complex puzzle of Alzheimer’s disease; Increased understanding of mechanisms involved	A complex condition which is the outcome of many accumulating mechanisms, biological, personal, and social	Unravelling the mysteries of the brain and finding pieces of the puzzle for increased understanding and improved diagnosis and intervention
<b>Technological progress</b>	New technologies leading to fundamental changes in health care towards predictive medicine; Tracing underlying mechanisms and predicting the development of AD in an individual or the risk profile of a person	Neurodegenerative disease, the underlying mechanisms of which accumulate into dementia; A huge application area for new technologies	More and more detailed imaging technologies; Molecular and personalized predictive medicine at an early stage of the disease
<b>Economic competitiveness</b>	Product in the health care market	Huge market or application area	High tech, knowledge-intensive industry; Preventative medicine Development of innovative regions with a strong knowledge economy
<b>Health care provision</b>	Improvements in accuracy of the diagnostic process at an earlier stage as the start	Bio-psychosocial phenomenon; A condition that can be detected in the brain, a	Improved patient care and guidance;

	of a well-organized, suitable care trajectory	condition of a person, a changed prospect on life, a changing relationship between close relatives, a condition requiring the organization of integrated care	Impoverishment of public health care provision
<b>Successful aging</b>	Gaining knowledge about risk factors of dementia and enabling preventative measures The end of successful aging	A feared condition due to a life-long process, to be avoided through personal lifestyle and health choices	Personal future: stay vital and healthy in old age; Becoming responsible for your own aging process; Medical future: Prevent and delay dementia
<b>Fear and worry about approaching mischief</b>	A doomsday scenario becoming reality; Patient information providing relief and clarity	A horrible and cruel disease	Personal: Deterioration of the body and brain; Health care: Impoverished care; Medicine: Provide comfort or clarity at the stage of subjective complaints
<b>Good life and death</b>	Verdict enabling a self-chosen death when faced with dementia	Life changing condition	Improving possibilities and guidance for euthanasia for early stage dementia

#### **5.4 Conclusions: multiplicity in ‘popularizing’ early diagnosis of Alzheimer’s disease**

While the quest to identify Alzheimer’s disease at increasingly early stages is mainly a medical endeavour, the prospect of early diagnostics of Alzheimer’s disease extends beyond the laboratory and gains meaning in a variety of social settings. Newspaper articles allowed us to trace the different meanings of early diagnostics and dementia and how they are constituted through a number of frames. We have delineated nine interpretative packages that, taken together, constitute the cultural repertoire of early diagnostics for Alzheimer’s disease as expressed in newspaper articles. We studied the reasoning and framing devices of ‘interpretative packages’ that allow the construction of a multitude of meanings. This analysis shows through which relations the early diagnosis of Alzheimer’s disease is made ‘meaningful,’ and, at the same time, how early diagnosis (re)produces, reinforces, or changes ways of dealing with Alzheimer’s disease.

Our analysis indeed shows that the popularized meaning of early diagnosis in newspaper articles goes beyond a biomedical framing. Early diagnosis of Alzheimer’s disease gains meaning in an array of interpretative packages that we identified as ‘aging society,’ ‘scientific progress,’ ‘scientific puzzle solving,’ ‘technological progress,’ ‘economic competitiveness,’

'health care provision,' 'successful aging,' 'fear and worry about dementia,' and 'good life and death.' Earlier framing studies on dementia have shown the dominance of a biomedical approach. This study, on the other hand, shows how an innovation of a biomedical nature gains meaning through a multitude of framings of dementia.

Alongside the framing of dementia as a biomedical problem and a (bio-psycho-social) condition, dementia is framed as an important event in a person's life course, a generally feared condition that should be averted, a market opportunity for new technological innovations, and a socioeconomic problem and a challenge for the health care system due to the growing number of persons with the disease.

The interpretative packages highlight different societal aspects of early diagnostics of Alzheimer's disease and the ways they create and change the social world as well as different valuations of these changes. Early diagnosis from a medical, economic, and technological framing appears as a positive development that will increase knowledge about dementia and improve diagnosis, medical interventions, and preventative strategies. Within a health care framing, early diagnosis is ambivalent because it promises to improve patient care through timely care and support while, at the same time, health care policies emphasize self-reliance, informal caregiving, and staying at home for as long as possible. This may impoverish the care system. Thus, it is questioned whether formal care and support will be available and accessible after a person has received an early diagnosis. The packages on successful aging and fear and worry highlight both an increased awareness of possible early signs of dementia and a desire to delay or prevent their onset. These packages tie in with the experience of aging and the desire to delay senescence (the process of decline with age). On the one hand, this shows the hope of preventing dementia through personal lifestyle adjustments and, on the other, an increasing anxiety about the first signs of dementia. The package on good life and death stages questions about how to draw a balance between reducing unnecessary fear of 'first signals' and a desire to know 'what is going on' when dementia begins to manifest itself, what constitutes a good life at old age with dementia, and how and when to opt for a self-chosen death. The euthanasia issue is precarious because it is intertwined with changing expectations of (successful) aging and fear about an impoverished health care system.

Four things stand out when we relate our findings to earlier articles on representations of dementia in news media. The first is that while earlier articles stress the dominance of medical conceptualizations in newspaper articles (Van Gorp, 2012), this analysis shows that medical conceptualizations are discussed through a multitude of framing packages. Secondly, earlier articles have shown that news media emphasize the negative images of dementia (cf. Kirkman, 2006; Doyle, 2012; Van Gorp, 2012; Clarke 2006). This view is confirmed in this analysis. This critique, however, was also raised in some newspaper articles, which is indicative of a societal awareness and reflexivity on representations of dementia. Thirdly, our analysis confirms 'the case of the missing person.' Persons with Alzheimer's disease figure as objects of concern – spoken for by scientists, policymakers, informal caregivers, and so on – and not as subjects (Clarke, 2006). Contrary to what Clarke claimed, we found that issues on long-term care accessibility, care programs, prevention and the good life are being addressed in news media. Our framing analysis shows that the repertoire in which early diagnostics for

Alzheimer's disease is positioned and acquires its meaning is diverse and guides thinking about early diagnosis of Alzheimer's disease in a range of directions. It makes clear that the social construction of early diagnosis of Alzheimer's disease is guided by both reasoning devices that drive this development forward as well as reasoning devices that pinpoint possible problematic situations.

# Chapter 6

## Early diagnostics and Alzheimer's disease: Beyond 'cure' and 'care'

*This chapter has been published as Cuijpers, Y., H. van Lente, Early diagnostics and Alzheimer's disease: beyond 'cure' and 'care'. In Technological Forecasting and Social Change, Volume 93, April 2015, p. 54-67.*

### 6.1 Introduction: 'cure' or 'care'

A central assumption in policy circles and research funding is that scientific research and technological innovations provide answers to societal challenges of aging. This is also the case with innovation in the field of Alzheimer's disease. The argument is that due to an aging population the number of persons with Alzheimer's disease will increase drastically in the coming years and that this will lead to huge problems in the health care system and the economy. This crisis account of aging (Mort & Roberts, 2010; Ney, 2009), is then turned into a major societal 'challenge' to be addressed by innovation. This way of reasoning has been found in general in relation to issues of aging and has been typified as the 'aging-and-innovation discourse' (Neven, 2011). Early molecular diagnostics is one of the key innovations positioned as a step towards the (partial) solution, for example in the Dutch 'Deltaplan dementia' (Ministerie van VWS, 2013), the EU 'Joint Planning Neurodegenerative Disease Research Strategy' (European Union Joint Programme Neurodegenerative Disease Research, 2012) and the US 'Alzheimer's Disease Neuroimaging Initiative' (Mueller *et al.* 2005).

Early diagnostics here refers to both the possibility of an earlier diagnosis and the specific technologies to achieve this. The possibility of an earlier diagnosis can refer to different situations: an early diagnosis of dementia (as a cluster of symptoms and signs), a diagnosis of the pathology of Alzheimer's disease in a pre-dementia stage, as well as the diagnosis of Alzheimer's disease before any signs are present at all (called the asymptomatic stage) (De Vugt & Verhey, 2007). The specific technologies of early diagnosis are MRI scans, PET scans, and biomarker analysis.

The discourse and the underlying biomedical model have been criticized by many scholars in the past decades. According to the biomedical model, Alzheimer's disease is a condition of a person, caused by deterioration of the brain. Consequently, the way to deal with dementia is by medical control; although there is currently no cure, dementia should be diagnosed, managed and treated by medical authorities. The biomedical model has been critiqued for neglecting the social components, thereby affecting choices in policy and research, and having negative effects on the experience of living with dementia. Claudia Chauhan (Chauhan *et al.*, 2012), for instance, showed how Alzheimer's disease as we currently know it has actively been constructed as a medicalized condition with a biomedical model of dealing with

it. This “excludes alternative problem definitions” and has led to a “triumph of cure over care” in policy domains. In the same vein, Ingunn Moser studied how Alzheimer's disease has been made to matter in different locations, among which parliamentary politics. She argued that “pharmaceutical and biomedical versions of the disease [are made] present, visible, strong and dominant”, and alternatives are “made absent, invisible and less real” (Moser, 2008, p. 107). Care is not positioned as an alternative way of dealing with the matter, rather it is turned into ‘doing nothing’, an (expensive) option of last resort (Moser, 2008). The prevalence of a biomedical model of Alzheimer's disease does not only affect policy, politics and division of resources, but is also critiqued for having negative consequences on the experience of living with dementia and on dementia care (Lyman, 1989). In reaction to the biomedical ‘cure model’, ‘care models’ emerged from the 1990s onward, with a main interest in the experience of persons with dementia, social settings and relationships. Thomas Kitwood is, for example, one of the pioneers of alternative models with his approach of person centred care (Kitwood, 1997; Kitwood, 1990; Kitwood & Bredin, 1992). He developed a broader framework for the understanding of dementia, not only including neuropathology but also social psychology, with the aim to provide good care and a better life for persons with dementia.

So, ‘cure’ and ‘care’ have appeared as two strategies to deal with Alzheimer's disease, with different overarching discourses and logics. In these critiques cure is defined as (aiming for) medical treatment, and care as ‘alternative strategies’, including provision of physical, practical, emotional and spiritual support. ‘Cure’ is often positioned as an ‘oppositional construct’ to argue the benefit of alternative approaches”, ((Zuccherro et al., 2010) in (Innes and Manthorpe, 2013, p. 3)). This positioning of cure versus care suggests that a choice needs to be made between a cure or a care approach: should one try to banish Alzheimer's disease from existence by investing in research to understand the causes of dementia and find a medical treatment, or should one search for the best ways to live *with* Alzheimer's disease and find ways to support patients and informal caregivers? In the cure versus care opposition, the prospect of early diagnostics becomes problematic. And when the underlying logics of cure and care are presented as opposites, a stalemate looms.

In this paper we investigate the various meanings of early diagnostics in society, and analyse how this is intertwined with different ways to define Alzheimer's disease and strategies to deal with it. The ongoing discourse on early diagnostics for Alzheimer's disease evolves and changes over time, and provides diverging meanings and interpretations for relevant events. A researcher may encounter all kinds of devices, like metaphors, images, arguments, and moral appeals. These different elements are not encountered as individual items, but they come in clusters, and are organized around a central organizing idea, and thus provide different, what Gamson and Modigliani refer to as, ‘interpretative packages’ (Gamson & Modigliani, 1989). We conceive discourse on early diagnostics for Alzheimer's disease as a set of interpretative packages, which make sense of early diagnostics. Distinguishing a set of interpretative packages creates room for a range of positions, rather than one overarching discourse, or two competing discourses. We scrutinize the meanings and assumptions by investigating interpretative packages related to early diagnostics and Alzheimer's disease.

We define interpretive packages as clusters of topics, arguments, and concerns that are articulated recurrently in relation to the innovation and thus create a web of understanding, through which is made sense of this innovation.

We analyse these interpretative packages in two distinctly different settings where problems, solutions and futures are defined. The first setting, a health technology assessment project, is closely related to the research on early diagnostics, which can be typified as mainly a 'cure' context. The second setting, Alzheimer's Cafés, where patients and their family meet, provides contrasting 'care' perspectives and assessments of the disease and the ways to cope with it. We draw on literature from STS as well as from dementia care to unravel the different ways to deal with Alzheimer's disease and aging.

## **6.2 Theory: Alzheimer's and storytelling**

The concepts 'dementia' and 'Alzheimer's disease' have a turbulent history of contestation. During the last century, the concepts have been the "*product of complex negotiation between a wide number of interested parties – including patients, caregivers, physicians, researcher, corporations, and policy makers – who all have a stake in how we perceive, name, and respond to illness.*" (George & Whitehouse, 2009, p. 1). Contestations continue about how to define Alzheimer's disease and how to deal with it (see e.g. Lyman, 1989; Kitwood, 1997; Whitehouse & George, 2008). Is Alzheimer's disease a disease, or part of normal aging (e.g. Whitehouse & George, 2008; Jonker et al., 2009)? What are the causes of the symptoms of Alzheimer's disease? It appears that persons with severe brain damage can experience little symptoms and the other way around. How can this be explained? And can changed behaviour be considered to be the result of neurological deterioration, or to be the interplay between neurological impairment, physical health, and psychological and social factors (Kitwood, 1997)?

There are different ways to distinguish conceptualizations of dementia and ways to deal with it. The main theoretical models that are currently distinguished are a biomedical model, a psychosocial model, a disability model and a social gerontological model (Innes and Manthorpe, 2013; Downs et al., 2006; Dröes, 2010). The biomedical model perceives dementia as a pathological condition that should be diagnosed and treated. It is characterized as an illness with progressive decline, of which you should recognize the symptoms and gain insight into the underlying causes. Since effective treatment is not available yet, it is of utmost importance to develop effective disease modifying treatment or preventative measures. A psychosocial model and a disability model put the person central and aim to increase the well-being of patients. The psychosocial model focuses on the consequences of dementia for individual persons with dementia and their caregivers. This leads to attention to the experience of the person with dementia and the strategy to adjust care and support, to better cope with this condition (Innes & Manthorpe, 2013; Dröes, 2007). The disability model of dementia focuses on the irreversible limitations to the functioning of a person. These limitations or disabilities in daily functioning, ask for structural adjustments to rehabilitate and stimulate the person and for aids to keep persons functioning

independently at a certain level for as long as possible (Dröes, 2010). The social gerontological approach critiques the notion that elderly are a burden to society and deplors their social exclusion. It pushes the idea that life with dementia can remain fulfilling and points to the wider social and structural factors that shape the experience of dementia (Innes & Manthorpe, 2013).

In current practices these different models do not exclude each other; they co-exist and relate to each other. Downs (Downs et al., 2006) speaks about an eclectic use of different models. As we recalled above, Moser stresses the politics at work in: how in certain contexts some modes-of-ordering are made visible, more real, and others are neglected, made invisible. And in her book *The Body Multiple* Annemarie Mol (Mol, 2002) describes how in different practices, illnesses are 'done' differently, or, in her terms, 'enacted'. For example, arteriosclerosis in the consulting room with a patient is something else than the entity derived from X-ray pictures of a radiologist. Also Innes and Manthorpe stress that "*How we approach dementia (...) will impact on how we 'see' the problem; how we might try to approach it; and how we might try and respond to or look for a solution.*" (Innes & Manthorpe, 2013, p. 88). It influences how not only professionals in health care, but also policy makers, persons with dementia, their caregivers and others respond to the challenges dementia poses on them. Innes and Manthorpe also note, however, that underlying assumptions and motivations are often implicit, blurred and multiple. The intricate relationship between the different versions and representations of Alzheimer's disease and the way to deal with it, is a central lesson of studies of medical practices in science and technology studies (STS).

Practices of dealing with a condition such as Alzheimer's disease are thus somehow structured. Annemarie Mol, for example, argues that medical practices are structured through ideals, such as the ideal of patient autonomy (the 'logic of choice') or through ideals of 'good care' (the 'logic of care'). These different ideals bring along "*a specific mode of organizing action and interaction, of understanding bodies, people and daily lives, of dealing with knowledge and technologies, of distinguishing between good and bad, and so on.*" (Mol, 2008, p. 8). In her study of nursing homes, Moser emphasizes the performativity of 'modes-of-ordering': they make some responses or actions in a specific situation more appropriate, more logical, than others (Moser, 2011). Different modes-of-ordering (she distinguishes a somatising and a relational mode-of-ordering) shape how dementia is enacted upon, and along with this, shape the care for dementia, and the way of living and dying with dementia. Hence, there are more 'worlds-in-progress', while in different locations some might prevail different modes-of-ordering co-exist.

The meaning of early diagnostics for Alzheimer's disease as a way to deal with Alzheimer's disease in aging societies, is interwoven with the different understandings of Alzheimer's disease and ways to deal with this condition.

As an entrance to study the meaning of early diagnostics, and the connections being made between early diagnostics and ways of approaching and dealing with Alzheimer's disease we investigate the arguments, anecdotes and other stories that are shared and circulate in

settings where Alzheimer's disease and early diagnostics are a topic of conversation. Storytelling is the way in which humans construct and make sense of the world around them and their own action (Bruner, 1986; Hajer, 2006; Polkinghorne, 1995). Through stories meaning is created and shared. Stories create ordering by connecting different elements to a central purpose.

### **6.3 Methods**

The central question of this paper is how the development of early diagnostics for Alzheimer's disease is entangled with specific definitions of Alzheimer's disease and articulations of problems and solutions in dealing with Alzheimer's disease in the (near) future. We do this by analysing the various meanings of early diagnostics in two very different settings.

We investigate the meanings by distinguishing the 'interpretative packages' in the stories that are being told in different settings. We define interpretative package as a cluster of recurring topics, arguments, and concerns (thus different elements). These interpretative packages capture some aspects of early diagnostics in an ordered mode of understanding. They provide "webs of understanding" (Innes, 2009) to make sense of early diagnostics in a setting. Depending on the stakeholder, the topic and the kind of conversation, different interpretative packages can come up. These interpretative packages are constitutive for stories as they form a repertoire, which is available about early diagnostics. In different settings the repertoires may differ and some interpretative packages are more exotic to one setting than to the other. So interpretative packages are recognizable and recurring patterns of themes and elements that expose a web of understanding behind the development of early diagnostics.

We have selected two settings for this analysis, where sense is being made of early diagnostics and Alzheimer's disease through a vivid exchange of stories between different stakeholders. One setting can be considered to be more cure-oriented (a health technology assessment (HTA) working group within a biomedical research program); the other as more care-oriented (a series of Alzheimer Cafés in a Dutch city).

The HTA setting is part of research on early molecular diagnostics of Alzheimer's disease in the Netherlands that is taking place within the LeARN program (Leiden Alzheimer Research Nederland), and is partially financed by the ministry of Public Health. One of the conditions for this funding was clinical and societal relevance of the research. Therefore, the consortium devoted one work package to a health technology assessment (HTA) to evaluate the clinical and economic value of early molecular diagnostics. It inquires how different instruments perform, how much it costs and how the quality of life and health care costs change through the introduction of early diagnostic tests. This assessment includes monitoring a cohort of patients to measure the accuracy of different diagnostic instruments and the quality of life, a panel to determine the added value of these instruments in clinical decision making and a model to assess the costs of health care consumed by patients and their informal caregivers (with and without these novel instruments). Medical professionals (neurologists,

psychiatrists, geriatrics, radiologists), chemical analysts, and health economists work together and exchange knowledge and ideas. Here we expected to find cure-related accounts with a medical, or evidence based approach to dementia.

The second setting is the Alzheimer Café. Alzheimer Cafés are monthly informal events for persons with dementia, their partners, family members, caregivers and other interested persons. They provide a space and time for the visitors to informally exchange ideas, information and experiences, and to provide support to individual persons with dementia or their relatives to help them deal with the situation. The Alzheimer Café was initiated in The Netherlands to tackle the taboo on dementia within society, between partners, and within families (Miesen, 2002). The concept of the Alzheimer Café quickly diffused across the Netherlands. Currently there are over 180 Alzheimer Cafés and their number is still growing. Also in other countries, such as the UK, the Alzheimer Café example is being followed (Halley et al., 2005). The formal goals of Alzheimer Cafés are to educate, to speak openly about the problem, and to recognize and emancipate patients and family members. Every meeting lasts about 2 h and is organized around a theme (such as causes of dementia, dealing with dementia, communication) and led by a moderator (Blom & Miesen, 2000). Attendants of Alzheimer cafés consist of patients, their husbands, wives, friends, relatives, informal caregivers, volunteers, persons who are worried that they or somebody close to them is developing dementia, nurses, pastors, caretakers, municipality officials, general practitioners, and other local professionals. Everybody brings along their own experience, questions and knowledge on dementia and the way to deal with this condition. In this setting we expected to find care-related, person-centred and experience based accounts of Alzheimer's disease.

In both settings we collected different types of documents: reports, interview transcripts, articles, books, educational material, and notes and transcripts gathered through participant observation (See Tables 6.1 and 6.2). This diversity of data sources provides a rich pool of arguments, anecdotes and stories. We analysed our documents with the following research steps. We first separated phrases (text blocks) that express (a) the role of early diagnostics (b) what Alzheimer's disease is and (c) what the future will bring and how to address it. Within this collection of phrases we labelled themes, such as 'stigma' or 'plaques in brains' or 'demographic trend'. We investigated how these themes are connected in the documents. In this way, we could identify clusters of connections, which we analysed as different 'interpretative packages'. Next we summarized these different interpretative packages. The last step was to check whether all themes and connections were captured by the set of interpretative packages. For this process of labelling we used ATLAS.ti software.

Table 6.1. Data sources for HTA

---

Interview with Work Package leaders (1, 2, 3, 4)*
PhD students working on the HTA (5,6,7)*
Discussion meetings (8,9)*
(Draft) articles (10, 11)
Extended Work Package description (12)

---

\*In collaboration with Anna Laura van der Laan.

Table 6.2. Overview of studied Alzheimer's Cafés

---

<b>Date</b>	<b>Theme of Café</b>
April 2010	Dementia in different phases (13)
May 2010	Forgetfulness or dementia? (14)
June 2010	Early diagnosis (15)
November 2010	Film screening (16)
January 2011	Dementia and existential questions (17)
February 2011	Behavioral problems and dementia (18)
March 2011	The role of the general practitioner (19)
April 2011	Daycare and daytime activities (20)
June 2011	Case management for dementia (21)
October 2011	Applying for care and help (22)
November 2011	Auxiliary service (23)
February 2012	Occupational therapy (24)
May 2012	Behavioral symptoms of dementia (25)
June 2012	Healthy living (26)
November 2012	Dementia for the immediate environment (27)

---

The analysis of the Alzheimer Cafés is based on observations during Alzheimer Cafés in one region in the Netherlands from April 2010 until November 2012. During these cafés, the first author was allowed to make notes. Next to observing she also engaged in conversations with the visitors, and took on a similar role as volunteers of the Alzheimer Café. For background information about the philosophy, and organization of the Alzheimer Café she interviewed the organizers and participated in a course for volunteers of the Alzheimer Cafés. During all these occasions she made notes and transcripts.

While the analytical concern and the methodological steps in both settings are similar, the emphasis differs due to the nature of the settings. In the HTA setting early diagnostics and the solutions it could provide are more central, while in the Alzheimer Café setting, the emphasis is on dementia and how to deal with it.

**6.4 Results**

**6.4.1 Setting one: health technology assessment**

Health technology assessment is a standardized practice in health care to examine clinical, economic, societal and ethical implications of technologies in health care. It is intended as a bridge between medical research and policy making. While others have analyzed and criticized the limitations of the HTA approach (e.g. Blom & Miesen, 2000; Brouselle & Lessard, 2011), we consider this setting as an excellent entrance to gain understanding about what kind of solution early diagnostics provides, and how it is shaping and being shaped by enactments of disease and the way to deal with it. We could identify six interpretative packages of how early diagnostics is entangled with representations of Alzheimer's disease and how to deal with it. Our findings are summarized in Table 6.3.

**Table 6.3. Summary of interpretative packages in the HTA.**

Setting 1: Health technology assessment				
Meaning of early diagnostics	Understanding of Alzheimer’s disease	What the future will bring	How to address the future — what should be averted?	How to address the future — what to aim for?
Value for money	Biomedical condition Highly affecting well-being of patient and informal caregivers. Societal burden	Increasing number of persons with dementia. Advances in imaging techniques and biomarker analysis.	More expensive health care. Decreased quality of life of patients and informal caregivers.	New cost-effective medical technologies. Decreasing societal costs. Increasing quality of life.
Changing health care	Biomedical condition Measurable or visualizable pathological changes in the brain highly affecting quality of life of patients and informal caregivers. Societal burden of increasing health care costs.	Increasing number of persons with dementia. Advances in imaging techniques and biomarker analysis. Maybe disease modifying treatment.	Increasing health care costs. Decreased quality of life of patients and informal caregivers. Uncertain consequences of early diagnostics in clinical practice.	Improve diagnostic accuracy. Increase health and well-being of patients and informal caregivers. Decrease societal costs. Assessments of consequences of early diagnostics in clinical practice.
Innovation trajectory	Biomedical Pathological changes in the brain that can be measured or visualized. Application area for	Progress through innovation.		Instruments to measure or visualize changes in the brain that signify Alzheimer's disease. Implementation of best

---

**Setting 1: Health technology assessment**

Meaning of early diagnostics	Understanding of Alzheimer's disease	What the future will bring	How to address the future — what should be averted?	How to address the future — what to aim for?
Changing definition of Alzheimer's disease	imaging techniques and biomarker tests.			technologies in clinical practice.
	Biomedical condition Measurable or visualizable pathological condition in the brain. Dementia syndrome recognized by expression of a cluster of symptoms.	Ongoing development of imaging technologies and biomarker tests. Increased knowledge on pathological processes in the brain. Updated diagnostic guidelines.	Diagnosis based on symptoms.	Better predict disease progression. Provide diagnosis at an early stage, or predict disease, based on neuropathology rather than symptoms. Change diagnostic guidelines.
Step on the road to medication	Biomedical A presently irreversible, untreatable medical condition.	Development of disease modifying treatment.	Lack of disease modifying treatment. A distressing disease course. Far reaching consequences for the quality of life of patient and caregiver.	Progress in health care. Speed up development of disease modifying treatment. Diagnose the disease in early phase when medication is expected to be most effective.
Early management	Psychosocial Untreatable condition. Worry for persons with memory complaints.	More and more technological diagnosis.	Conducting a diagnosis as a goal in itself.	Diagnosis (better information) at a pre-dementia stage. Provide certainty to worried patients. Better management of the condition and patient in early stages.

---

***Early diagnostics as value for money***

The first interpretative package in the HTA practice views early diagnostics of Alzheimer's disease as a proposition about costs and benefits. This interpretative package concerns the efficient allocation of scarce resources in health care and is embedded in health economics. It can be summarized as follows.

“Health care is expensive and is getting more costly. New technologies could potentially improve health care and increase the quality of life for patients and informal caregivers, but may also lead to an increase in costs. Therefore, it has to be examined whether they are value for money. For early molecular diagnostics it is not clear yet.”

This interpretative package centers on the advances made in imaging techniques and the analysis of cerebrospinal fluid in the past decade, leading to new and emerging diagnostic tests based on biomarkers, which could improve the diagnosis of Alzheimer's disease.

While novel medical technologies could potentially provide benefit to patients and informal caregivers, they also contribute to the rising costs of health care. The task, thus, is to consider whether molecular diagnostic instruments have substantial added value for the patient and their caregivers, and whether they are cost-effective.

*“Look, the whole reason why we are doing this research is because it is not clear if you should use these markers in the standard diagnostic procedure in the clinic or not.” (5) “The HTA is about how much money you can put in to get how much quality back. And about how much money you can save by making an early diagnosis.” (1)*

In this interpretative package, Alzheimer's disease is considered as a disease that highly affects the well-being of patients and informal caregivers, and places a substantial burden on communities, given the rising number of persons with Alzheimer's disease in the near future, and the related rising pressure on health care resources. According to this interpretative package, it is of utmost importance to validate these new tests, in terms of patient well-being, costs, and on their additional value to current clinical practice.

(Sources: 1, 2, 5, 10, 11, 12.)

### ***Early diagnostics as having uncertain consequences for (future) health care practices***

A second interpretative package highlights the struggle with the uncertainties of the (future) consequences for health care practices, when newly developed early diagnostic instruments are adopted: How would these tests improve the accuracy of a diagnosis? What consequences does this have on the quality of life of a patient and the informal caregiver? What would be the consequences for health care costs?

It can be summarized as: “Consequences of new health technologies are complex to assess. You first need to know how they will change the possibilities for diagnostic and clinical practice, and what it means for patients, informal caregivers and the total costs of health care. It is a tremendous task, but we need to do it.”

In this interpretative package the focus is on the chain of consequences to be measured and modeled in order to determine the influence a test will have on health, well-being and societal costs. This is a complex task involving many uncertainties. *“This is what we are after: what is happening exactly? What is being done with information from these tests? What does the whole process look like from adding a new test to, ultimately, the health effects?” (8)* To bridge the gap between research and clinical practice a lot of information and assumptions are needed: the technical quality of the tests, the performance in terms of sensitivity and

specificity and predictive value, the value of a test if added to other tests, how this will change diagnostic decision making, how this effects treatment and patient management, and how this will affect health and well-being of patients and informal caregivers, and eventually what the consequences are for societal costs. With every step in this model uncertainties grow and need to be dealt with. *“When you add a different test, or change the combination or sequence of tests, this will lead to a different accuracy. The added value in accuracy can lead to different decisions in care which will lead to a certain health effect and use of means in healthcare (for example a decision to do follow up tests).”* (8)

In this interpretative package different pressing questions are voiced. The central worry here is choices need to be made about what will be included and excluded in the model before it ‘explodes of complexity’, as a researcher phrased it. Furthermore, tests need to have consequences for patient management. Since currently there is no disease modifying treatment, or care program available yet for these patients, what will be the added value for patient management? *“What will be the consequences for treatment? Which clinical decisions are taken based on the scan results? You have to take into account the intervention options. A test by itself does nothing. The most important is having intervention options. And the cost-effectiveness depends on the possibilities you have for that.”* (9)

Another issue is that while these novel tests are being assessed it is not yet clear what the outcome of a test means. Whether these patients will really develop Alzheimer's disease, and within what period, is part of this research and is not known yet. *“A: You might think it is malign to have a positive scan result, but the question is what relevance this has. If you say to a person: I am afraid you will function less well in ... the term becomes important. Is three years important? Is two years important? (...) B: What is a useful outcome of test? Everybody knows they will function less well in 20 years.”* (8)

What to do with patients on whom you already conduct these tests, and that have positive biomarker or imaging test results, but show no deviation on neuropsychological examination? Should you tell them the results of the specific tests, while it is not clear what these results mean? And what do you have to offer them, besides a follow-up appointment? *“A: How do you currently deal with subjective complaints? Persons who do not have... (...) B: Sometimes it is being said that (...) the scan suits their age. They are often elderly patients and they can have deviations in the (...) scan without cognitive complaints. So we communicate it like that. (...) A: (...) So whether it is positive or negative, it is ‘suitable to the age’. So really it doesn't make a difference? B: No, but it is the correct answer at this moment in time. On which you could ask the question ‘than you shouldn't apply for a scan’. And of course that is a little bit the field of tension we are in now. Especially with subjective complaints. This is not really a clinical... it is a research question.” (...) B: “So there has to be a clinical indication for a clinical scan. That does not mean that I think it is important for a patient to hear the full 100% information from a scan, but I do think (...) it has to have consequences, even if it is just to see a patient a bit earlier on follow-up, or not at all.”* (8)

In this interpretative package, the task of HTA is to assess the value of these novel tests in clinical practice, which comes with the challenges of dealing with many uncertainties that need to be faced.

(Sources: 5, 8, 9, 10.)

### ***Early diagnostics as innovation trajectories***

A third way to view the efforts to develop early diagnosis of Alzheimer's disease is to position them as different competing innovations. Summarized: "Progress in health care is possible with innovation. Early diagnostics is an umbrella term for various technological developments. They are rooted in different sets of expertise. So, technologies have their own trajectories and they compete."

'Early molecular diagnostics' is an umbrella term for different innovative techniques such as MRI and PET scans as well as the chemical analysis of cerebrospinal fluid (CSF analysis). For these techniques some tests are established and used in clinical practice and a lot of them are still being developed. And for all these techniques many different kinds of tests are developed, focusing on different mechanisms related to Alzheimer's disease, different biomarkers, different structural deviations in the brain, or different ligands and radioactive labels (PET).

Within this interpretative package it is emphasized that these specific tests are developed based on long-time experience and expertise in either PET, MRI or CSF analysis, of the different medical centers that are involved. Not only are they experienced in the application of existing tests, but also in developing new diagnostic tests for neurological conditions. Also past experience of industrial partners has informed the choice for pursuing research on some specific biomarkers. Past performance has been an important driver for the creation of a new research program on early diagnostics for Alzheimer's disease. These tests for Alzheimer's disease are part of built up expertise in specific areas, and thus embedded in innovation trajectories and research lines.

In this interpretative package, the development of early diagnostics is considered as research and innovation, and comes with many obstacles, drawbacks, unexpected results and problems during the development. For each test that is being developed there are long chains of steps that are needed to actually have a test ready that could be evaluated on its diagnostic value. Some tests turn out to be not good enough; each test has its own strong points and weak points.

A central argument in this interpretative package is that a successful test, or combination of tests, could change the diagnostic practice a lot. This could have far reaching consequences. CSF analysis for example is relatively cheap and samples of liquor (cerebrospinal fluid) could be easily send to a laboratory to be analyzed, which means it can be easily implemented in current diagnostic practice. If PET turns out to be the best, implementation is more complex and expensive, since broad application would create the need for PET scans in more hospitals, as well as facilities that can produce the radioactive labels that are needed for the PET scans.

(Sources: 1, 2, 3, 8, 9.)

### ***Early diagnostics as changing the definition of Alzheimer's disease***

A next interpretative package centers on the way Alzheimer's disease is defined and diagnosed and how novel technologies will change this. "We are now capable of diagnosing Alzheimer dementia at an earlier stage, which changes the notion of what it means to be diagnosed with Alzheimer's disease. But also the basis on which a diagnosis is made is shifting. The diagnosis of Alzheimer's disease used to be on the basis of exclusion of other conditions. The importance of early diagnostics is that it can show actual traces of Alzheimer's disease in the brain. In this way, the whole notion of Alzheimer's disease changes from symptoms to pathology. With early diagnostics we can work on better definitions for research, drug development and monitoring of patients."

This interpretative package resonates with a long standing concern in research on Alzheimer's disease. Alzheimer's disease is the most common form of dementia. Currently a person is diagnosed with Alzheimer's disease when he or she expresses the symptoms of dementia of the Alzheimer's type. This is a so called 'syndrome diagnosis'. MRI scans were mainly meant to exclude other conditions. Within these criteria the definite diagnosis Alzheimer's disease based on pathology (based on depositions and accumulation of the proteins amyloid and tau in the brain) could only be made post mortem, based on biopsy and autopsy.

The emergence and ongoing development of brain imaging technologies however, made it possible to study the changes occurring in the brain due to Alzheimer's disease not only after death, but during life. Early diagnostic instruments aim to signal changes in the brain that can accurately predict if a person will develop the symptoms of Alzheimer's disease or not. This could shift the clinical diagnosis from a diagnosis based on symptoms, to a diagnosis based on pathology during life. "We can follow these parameters over time in a person. This is revolutionary within the thinking about Alzheimer's!" says one of the leading scientists (3). "I think in the future the bulk of the diagnosis will be molecular diagnostics. Molecular imaging and CSF analysis will eventually be a better predictor of the disease than symptoms.", says another leading scientist of the LeARN program (1).

A good diagnostic test will have to be sensitive and specific. However, most tests (also not the ones currently used) cannot provide 100% certainty. A problem that occurs is that there is no complete correlation between the development of specific neuropathology and symptoms of Alzheimer's disease. There are for example persons with cognitive complaints who do not have amyloid plaques in the brain, and persons without complaints who do. What should be decisive in a diagnosis in those cases: the symptoms or the pathology?

*"C: And the question is how you look at Alzheimer's disease. Do you call it Alzheimer's disease if somebody has clinical symptoms, or if someone has Alzheimer pathology? A: That is exactly the key question. (...) We cannot solve that now, you could discuss about this endlessly."(8)*

*"I think the whole idea; the whole thinking of Alzheimer's disease will change. And the lay person should also realize this. That is what we are already doing at the memory clinics, we*

*say to people: you have Alzheimer's disease. And then they expect that they will be in a nursing home with a diaper between their legs. And then we have to say: no, it will not go that fast. Because in the old days we diagnosed the condition in a much later stage. Nowadays we can do it much earlier, in a milder stage, and for that reason it is so important to support you so you can live a good life for another ten years. So what you have been through with your mother, exactly that we will try to... But of course it remains a nasty condition, so you cannot go around that. But the idea that there is nothing you can do is... Successful dementia for example, well, ten years ago, you should not have come with such an idea, and I think that now, it is well possible to handle this handicap in successful ways. (...) I think the general image of dementia, of Alzheimer, will have to be adjusted. Because you are earlier with the diagnosis. So it is not that when you hear the A-word, it means the end.” (1)*

(Sources: 1, 2, 3, 5, 11.)

### ***Early diagnostics as a step on the road to medication***

Another interpretative package brings together diseases, diagnosis and medication. “Early diagnostics should lead to better medication. Progress in health care is about finding better medication. When patients are diagnosed more accurately, the matching of patients and drugs is better. Furthermore, an early diagnosis enables treatment at an early stage when medication is expected to be most effective. Even when treatment is lacking currently, it is important to anticipate its future availability.”

In this interpretative package it is stressed that Alzheimer's disease is an irreversible disease with a distressing disease course and far-reaching consequences on the lives of persons affected by it, and that there is currently nothing that can be done about it. Medically speaking, in the present and near future, receiving an early diagnosis is of no use for it does not lead to specific treatment options. The ambition, therefore, is to make sure persons have a better life and end of life, by developing disease modifying treatment. *“To optimize the benefits patients can gain from treatment, instalment early during the course of the disease is desirable. However, AD is characterized by a long preclinical course (accumulation of the histological changes is estimated to precede clinical symptoms for as long as 15 years). Due to the lack of symptoms during the early phases of the disease, early treatment will depend completely on diagnostic tests that permit early diagnosis. Such tests are currently lacking.”* (12)

If there would be disease modifying treatment, this should be provided to patients as early in the disease process as possible, for instance in the stage of mild cognitive impairment (MCI), when they do have memory complaints, but not yet dementia. It should be possible to predict who will develop dementia in 2, 3 or 10 years. So, prevention is even better than cure. You cannot be too early to keep people healthy. *“A: If you talk about asymptomatic Alzheimer's disease, that is the wrong way to go. You should not call that a disease. Maybe an Alzheimer profile... but there is no benefit in labelling that a disease. That is essential now. B: Yes because there is no treatment. But that could be very different when there is a treatment available.”* (8)

In this interpretative package, early diagnostics and the development of treatment go hand in hand. The question is at what time from now a medical intervention will be developed. *“As soon as there are biological interventions possible, pills for example, then things will change drastically. Everybody would like to have a scan; there will be a massive run on that. The question is at what time from now that will happen. We have to be realistic, because we have been saying that it will happen in 5 years for 25 years now.”* (1)

Moreover, one cannot develop a good therapy without a good diagnosis. *“If you treat a population of patients with anti-Alzheimer drugs, but 20% of these patients actually do not have Alzheimer's disease, you will never find a medication that can treat Alzheimer's disease.”*, says one of the senior researchers (3). A good diagnosis is needed to test new medical treatments. And when a new treatment would become available, diagnosis is of utmost importance to provide it to the right patients.

So the importance of the development of early diagnostics is to speed up the development of treatment and to provide treatment to patients in an early stage. *“This is what justifies the whole research so far.”* (3)

(Sources: 1, 2, 3, 12.)

### ***Early diagnostics as part of early management***

This interpretative package addresses how early molecular diagnostics can benefit patients in the present, with no disease modifying treatment available. *“The quality of new technologies for health care is determined by its benefit for patients. Since there is no medication for Alzheimer's disease, early diagnostic technologies have nothing to offer in terms of cure. Instead, early diagnostics should be part of management of the disease in early phases.”*

This interpretative package contains the criticism that the diagnosis seems to be becoming a goal in itself and does not answer the question what is the use of it for a patient. Scientific research to make amyloid visible in a 7 Tesla MRI scan for example, can be meaningful in itself. *“But if you translate this to the interest of the patient, you have to be honest. Scientific insights can be of interest for the patients, eventually. That is, for the patient ‘in general’, not for the individual patient in the present.”* *“You should not sell science as good patient care.”* (1) For the present patients, *“It is not about the diagnosis, it is about what you do with it. Early management, not early diagnosis. I think there is too much focus on diagnostics as a goal in itself, which is typical.”* (1)

Currently a lot of tests are conducted to support a diagnosis. These tests are synthesized by a physician who will diagnose the patient, that is, when somebody already has symptoms of dementia. But with early diagnostics, when the symptoms are still subjective, persons are most worried, about whether this is just a temporary problem, or that it will develop into a dementia.

In this interpretative package, the aim of early molecular diagnostics is to provide better information at an earlier stage of the condition, when patients can still understand and

comprehend the diagnosis and what it entails. It provides possibilities for patients, informal caregivers, and professional caregivers to better manage the condition: to timely make plans, and arrange care and support. *“There is a danger that the care will be backgrounded. That a diagnosis becomes a goal in itself, and that persons will not be supported enough afterwards. So our plea is that a diagnosis should always be coupled to care. You cannot put somebody in a scanner (...) and then say — yes we found it. It has to have consequences. You can already see this happening as well. It will become more technological, but there is also much more care available than 10 years ago: memory training, education, informal caregiver support, Alzheimer cafés. So these developments go hand in hand. This research program is about the technical side.”* (1)

(Sources: 1, 2, 3, 8, 9.)

**6.4.2 Setting two: Alzheimer Café**

The second setting we used is the Alzheimer Café. Alzheimer Cafés are installed to help persons who are faced with dementia to better cope with this condition. Many local professionals attend these meetings, as well as patients, their caregivers, family and friends, and persons who are worried about dementia themselves, or that a loved one might be developing dementia. This setting might not be the most obvious place to learn about early molecular diagnostics. It is a non-medical setting, and seems distant from technological developments. Yet, here new technologies are on the horizon as well, so it is an interesting setting to study to understand how the development of early diagnostics is interwoven with specific definitions of Alzheimer's disease and articulations of ways to deal with Alzheimer's disease. In the discussions, lectures and conversations in the Alzheimer Cafés we could identify five recurring patterns of which we constructed the following interpretative packages. Our findings are summarized in Table 6.4.

**Table 6.4. Summary of interpretative packages in the Alzheimer Cafés.**

Setting 2: Alzheimer Café				
Meaning of early diagnostics	Understanding of Alzheimer’s disease	What the future will bring	How to address the future — what should be averted?	How to address the future — what to aim for?
Identifying a biomedical condition	Biomedical Progressive disease of plaques and tangles in the brain, that leads to dementia. Of which forgetfulness is a foretoken.	Predict which patients with subjective complaints or mild cognitive impairment will (not) develop dementia.	Late diagnosis. Misunderstandings. Unnecessary worries.	Early signalling and diagnosis. Provide a prognosis, comfort, prevent misunderstandings, regulate risk factors, receive available treatment, organize care and support, plan life.
Part of good patient management	Psychosocial/disability A disease with many faces.	Providing care and support means searching and trying what suits	Exhaustion of informal caregivers. Crisis situations.	Timely provision of care and support that suits these persons in this situation.

---

**Setting 2: Alzheimer Café**

Meaning of early diagnostics	Understanding of Alzheimer's disease	What the future will bring	How to address the future — what should be averted?	How to address the future — what to aim for?
		these persons in this situation. There are hardly ever real solutions.	Unnecessary suffering.	Adapt life to the new prospects. Improve coping with the condition. Improve daily life. Enable staying at home as long as possible.
Attributing a (socially significant) label to a person	Social gerontological A culturally laden label. A taboo.	Diagnosis at an increasingly early stage.	Mismatch between social perception and actual functioning of a person. Taboo. Stigma. Disqualification or social exclusion of persons with Alzheimer's disease.	A confirmation and reassurance. Foster understanding about dementia. Psycho-education. Reduction of taboo. Social inclusion.
A life event putting things in the 'Alzheimer perspective'	Psychosocial/Life event Certainty of a tragic fate. A means to reinterpret past events and to adjust life plans.	Changed prospects on life. A certain and continuous process of far reaching loss Increasing care responsibility for close relations.	A paternalistic notion of knowing what is good for a person.	A changed prospect on life. Respecting coping mechanisms of a person. Know what you are up against. Recognition.
Reducing the societal burden	Societal burden Burden on health care costs and health care system. Biomedical/psychosocial A need to provide timely care and support to patients and informal caregivers.	Increased number of patients with dementia. Increased health care costs. Budget cuts in health care. Worries about availability of care and support in the near future.	Misunderstandings. Crisis situations. Patients and informal caregivers falling between two stools. Gap between an early diagnosis and the access to professional care and support.	Timely signalling of signs of dementia. Timely organizing care and support. Availability of payable care and support. Delayed uptake in nursing home/stay at home longer. Increased use of social network of patients to provide care and support.

---

***Early diagnostics as identifying a biomedical condition***

The first interpretative package relates to the understanding of memory complaints as a foretoken of Alzheimer's disease, which should be diagnosed by a doctor. "In case of worries

about forgetfulness, go and see your doctor. With new diagnostic test a diagnosis can be conducted in an increasingly early stage. Alzheimer's disease is a disease of which forgetfulness is an important symptom. However, it is not the only cause of forgetfulness, so it is important to find out what is going on.”

In this interpretative package it is stressed that the most well-known first indicator of Alzheimer's disease is forgetfulness. Forgetfulness can have many underlying causes, like depression, stress, normal aging, and use of alcohol, but it could also be the first signs of dementia. The question is when forgetfulness is the first sign of Alzheimer's disease. To find out what the causes are of the complaints, a person can go to a doctor or a memory clinic. *“Alzheimer is a medical diagnosis. In the pre-stages of Alzheimer you cannot speak of dementia, but you can speak of mild memory problems, which in some cases will lead to dementia. It is difficult to interpret. Also other complaints can be a foretoken of dementia, such as changes in character or behaviour. This depends on the type of dementia.”* (14)

In a memory clinic a set of tests will be conducted to distinguish if complaints of the patient or his/her relatives might be related to normal aging, mild cognitive impairment (a gray area of more complaints than can be related to aging, but less than dementia), or dementia. And what the underlying disease process is (Alzheimer's disease, vascular dementia, or something else). *“The more research with scans progresses, the better they can distinguish one dementia from another.”* (20) The patients receive a diagnosis: ‘you are overly worried, you function very well’, ‘you have normal forgetfulness related to aging’, ‘we understand you are worried, it is not completely normal, but the complaints are not severe enough to speak about dementia’ or ‘you have dementia of a certain type’.

*“Often persons visit the memory clinic who are needlessly worried. There is so much information about dementia that this leads to fear (...). Forgetting something is normal when you age. Forgetting the name of your grandchild once is normal, as forgetting a card in a game of bridge once in a while.”* (19)

In this interpretative package the importance of an early diagnosis is to provide a prognosis, to comfort persons that are overly worried, to prevent misunderstandings, to regulate risk factors such as high blood pressure, and to provide treatment with the medication that is available. For good management of this condition, it is important that after a patient has received a diagnosis, (s)he moves into a care trajectory.

In this interpretative package it is stressed that there is still uncertainty and lack of knowledge concerning the causes and mechanisms involved in Alzheimer's disease. Researchers all over the world are working hard to better understand this condition and to find ways to stop or slow down the progression. Current research is aimed at early diagnosis: predicting which persons with subjective complaints or with mild cognitive impairment will develop dementia, and which won't. Scientific research now conducted aims to improve these predictions. Next to this a lot of research is directed at the development of drugs to stop or slow down disease progression, but so far nothing really works.

(Sources: 13, 14, 15, 19, 22, 23, 24, 25, 26.)

### ***Early diagnostics as early patient management***

This interpretative package is about how patients and informal caregivers can best cope with the changing situation which comes with the gradual changes related to Alzheimer's disease. "It is key that patients and informal caregivers make sense of early signals of dementia and can adapt their life to this new situation and related prospects. An official diagnosis should support their understanding and provide entrance to health care arrangements. The core issue of Alzheimer's disease is how patients and caregivers can cope with it."

*"A lot has changed in the past decennia in the attitude towards dementia. In the past people pretended as long as possible that there was nothing to worry about. Dementia was seen as a verdict, where there is nothing to be done about. Now we want to know what is going on as early as possible, to try to slow down symptoms and prepare for what is ahead: disease wise, but also for the person and the family, and make a support plan around that person and family." (19)*

*"Guest: What if mom does not want to see a general practitioner? Speaker: That is a matter of collaborating. You could for example try to go to a general practitioner with other complaints and slip it in. You can also visit the general practitioner yourself. A plan needs to be made. The worst thing you can do is pretend that there is nothing going on." (19)*

There are different organizations that offer their help to find out what is going on and to make a plan of what is needed to keep on functioning in your daily life and live independently (e.g. the elderly welfare organization, or a case manager). The argument is that a lot of support, care and help are possible when faced with the prospect of dementia. However, when coping with dementia and problems related to dementia, there are hardly ever real solutions. Providing good care involves searching and trying what suits the persons involved and their situation.

Yet, there are so many rules, laws and administrative procedures, that obtaining help is quite complex. For reimbursement and access to the professional care and support available, often a diagnosis dementia is needed. This means that there is a need for a timely diagnosis — not too late and not too early. A timely diagnosis means entrance to a care trajectory, precepts and guidelines and avoids that the informal caregiver becomes exhausted.

*"I talk to a couple before the café starts. The woman tells me that she received a diagnosis Alzheimer two months ago. She already knew she had Alzheimer's and had been to the general practitioner, who would not refer her to a memory clinic. Even her bridge partners knew it. She was not able to play bridge anymore. She forgot all the cards. (...) Eventually she went to another general practitioner who send her to the memory clinic. There, the scan showed that it really was Alzheimer's. The doctor (...) had fully understood her. He had asked if she wanted to hear the diagnosis, and she had said yes. It will make you calmer, the doctor had said, and that was exactly the case. Now she has the confirmation that she is not crazy, and that she really has Alzheimer, which she had expected all the time. Now, she says she gets Exelon plasters and goes to a day-care four times a week. She looks optimistic and relieved. Her husband looked like he was not as relieved as his wife. I asked him if the diagnosis*

*had also made him calmer. No, not really, he said. I asked if things changed for him afterwards. Also not, he replied. It is very difficult at home. She is so aggressive. It is very heavy.”* (20)

In this interpretative package Alzheimer's disease is portrayed as a disease with many faces. The disease progresses differently in individuals. The specific symptoms and the speed in which the disease progresses differ from person to person. And different persons cope in different ways with this condition. Some individuals may panic, some accept it easily, and others are calm and even happy. To organize good support and care for everybody involved, timely signaling of problems and receiving a diagnosis is deemed very important.

(Sources: 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 27.)

### ***Early diagnostics as labelling persons***

In this interpretative package, the diagnosis Alzheimer's disease is not as much seen within the medical or health care domain, but in the social domain. “Now that Alzheimer's disease is diagnosed at an increasingly earlier stage, the mismatch between the public perceptions related to the label dementia and the actual functioning of a person will increase. A diagnosis Alzheimer's disease attaches a label to a person. When this happens, it has various profound social consequences.”

A diagnosis means that a person is labeled with a certain condition. Alzheimer's disease is an attribute of a person which not only identifies the disease a person has, but also labels the whole person with this condition.

In the cafés it was articulated that this label can result in different responses. Depending on the persons involved, a diagnosis may come as a confirmation and reassurance and reduces uncertainty and bring understanding. On the other hand, a diagnosis can function as a stigmatizing label, disqualifying a person, by for example when relatives start talking in their place, or taking tasks of their hands. A woman came to the café to share the positive experience she has with the day care facilities for her mother, although *“her mother prefers not to speak about the dementia. She wants to function within normal life and she does not want to draw too much attention to the symptoms of dementia.”* (20) In a café about early diagnostics, I ask the question whether the visitors would like to have a diagnosis at an early stage. A response is that you should consider what this is like for the patients. *“I am afraid to be set aside with a ‘label’”,* says one of the visitors of the café. (15) The facilitator responds that this is often the case, but that this label can bring peace as well. *“Without it irritation may occur: “She forgot it again.”* (15) Symptoms of dementia can be interpreted as slackness, inattentiveness or unwillingness. To avoid the negative effects of a label in the home situation, psycho-education is very important for the patient and their close relations. They have to find the right path together.

This interpretative package emphasizes that *“because there is a lot of attention for dementia and because of new technological possibilities, people visit a doctor earlier and a diagnosis Alzheimer's disease can be given at an increasingly earlier stage of the disease progression. Because of that persons who are diagnosed with dementia now are still capable of much more*

*than in the past.*" (15) This means that the public understanding of Alzheimer's disease might not coincide with the functioning of a person who is diagnosed with this condition. One of the aims of organizing Alzheimer Cafés is to reduce this taboo, to talk about dementia, and to foster understanding that persons with dementia are not crazy.

(Sources: 14, 15, 23, 25.)

### ***Early diagnostics as a life event putting things in an 'Alzheimer perspective'***

In the next interpretative package, the knowledge of having Alzheimer's disease that comes with a diagnosis, becomes an important element in the story of the life of persons with dementia and their close relations. "Being diagnosed as having Alzheimer's disease is a life changing event. It requires a deep existential response and changes a person's past and future. Do you really want to know this in an early stage?"

Expectations about life change drastically and certainly when diagnosed with Alzheimer's disease. Facing Alzheimer's disease signifies facing a certain and continuous process of far reaching loss for the patient and their close relations. Dementia is a terrible disease and a tragic fate.

*"I enter the café, it is still early and I join a lady who sits alone at a table. She tells me her husband has been diagnosed with early stage dementia recently. How was it for you, to hear the diagnosis, I asked. Well that was a huge shock. (...) We now know what is going on, but it also gives other prospects. Not quite rosy. I just retired. I am 67. My husband is older. But still..."*(26)

In this interpretative package it is highlighted that persons who are faced with this condition need to reconsider the prospects on their lives, in the light of this dismal future they are facing. *"My husband has early stage dementia, which was diagnosed 1,5 year ago at the memory clinic. When we heard it, it felt like a verdict. And that is what it is. It feels like we are having Alzheimer together. My husband is very open about it; sometimes he says 'I happen to have Alzheimer'. He also told it to our children, his brothers, sisters and friends. It makes it easier to talk about and also to make jokes about it."* (27)

Close relations, who are faced with the great responsibility to provide informal care to the person with dementia, are up against a huge and burdensome task, accompanied by grief, anger, sadness, and feelings of guilt of falling short. Not only the prospects on life are reconsidered, there is also a move to look back to reconstruct 'when it started', and to put past events in the light of this newly gained knowledge.

In this interpretative package, questions arise concerning the desirability of these prospects on life at an early stage. Would you like to know if you or your relatives are developing dementia? And when? Are the little things mum forgets and her restlessness when your father is not at home, a first symptom of dementia? When your father has had Alzheimer, will you also get Alzheimer?

For some patients the diagnosis comes as a recognition of what they expected (or dreaded) and a relief that at least now they know what they are up against. But there is also a tendency

to avoid such knowledge: *"I would like to be ahead of problems, but on the other hand, I would not want to know either"*. (14) Often persons deny changes and refuse to see a doctor. Should the family respect this, or should they seduce the person to see a doctor for his/her own good?

In our current health care system, the idea is that persons should know what is wrong with them and that a person should receive a diagnosis, honest and clear. This has not always been the case. *"Should everybody be told this 'truth'? Do we always have to tell? It is very understandable to deny as long as possible that something is wrong."* says one of the care professionals in a café. (16) Is it always good to tell the truth, seen that reactions to a diagnosis differ greatly? Do you want to face this truth early on, or live in ignorance (or denial) as long as possible?

(Sources: 13, 14, 15, 16, 19, 20, 21, 22, 23, 25, 26.)

### ***Early diagnostics as reducing health care costs***

This final interpretative package relates to the reduction of health care costs, which is necessary with the prospect of the increasing number of persons with dementia and the subsequent pressure this puts on health care and the economic system. *"A timely diagnosis can reduce health care costs by preparing care givers and thus allowing patients to stay home longer. In an aging society, patients with Alzheimer's disease are a burden. Demographic trends will run to financial and nursing limits."*

This interpretative package starts in a similar way as the aging-and-innovation discourse: In the coming years the number of persons with dementia will increase, while the number of persons to be able to provide care will decrease. This is because persons get older on average, and the baby boomers are aging. A timely signaling of problems that may be first signals of dementia is important, because this can avoid misunderstandings and crisis situations, by timely organizing support and care. A lot of care and support is available at the moment. This enables persons to stay at home longer, and reduces the need of expensive nursing homes.

Some visitors of the cafés expressed the worry that they do not want to be a burden for their children or society. This is accompanied by worries about how long care and support will stay available and payable, given the budget cuts in support and care at home. *"You have told us all about these possible forms of support and care that can be provided, but will this stay available, and for how long? Financially? With the budget cuts? We read all about it in the newspapers. We cannot afford it ourselves."* *"I am really worried about the future."* A care professional says *"We are all searching to find the best way within the budget cuts."* *"But despite this, it is very important that you keep asking for help when you need it. Do not let rumours about budget cuts, or a decline of a help question scare you off."* (22)

(Sources: 15, 16, 18, 20, 21, 23, 26.)

The tables (6.3 and 6.4) summarize the different interpretative packages and how they are related to understandings of Alzheimer's disease, what the future will bring and how to

address it. When in the understanding of Alzheimer's disease one of the models of dementia is prevalent this is added in the column on this topic. Next to these models (biomedical, psychosocial, disability, social gerontological) we also found the understanding of Alzheimer's disease as a societal burden, as an application area of new technologies and as a life event, which could not easily be related to the models that were described in the introduction. Probably this is because the original four models mainly evolved in relation to patients, where in this article the innovation is central, and thus other considerations come to play.

## **6.5 Discussion and conclusions**

Research on early diagnostics of Alzheimer's disease does not only bring new findings and promising technologies, but also introduces and reinforces particular definitions of the problem and forecasts of the future. In this paper we studied the various meanings of early diagnostics, how they are related to understandings of Alzheimer's disease and to strategies to deal with Alzheimer's disease in the future. We did so by studying in two different settings: a health technology assessment group and a series of Alzheimer Cafés.

First of all we can conclude that a broad variety of articulations is present, in both settings. This finding is in line with the literature on medical practice, which has stressed the different ways in which diseases are represented, understood and enacted.

Secondly, we found that, notwithstanding this variety, the huge diversity of ideas appears to be clustered. We have captured these as generic interpretative packages, which provide webs of understanding of the meaning of early diagnostics, related to what Alzheimer's disease is, and how we may envision efforts to deal with it in the future. A particular understanding of the disease tends to be related to a particular approach to cope with the situation, and with a particular idea on what the contribution of early diagnosis could be. In total we have described eleven interpretative packages, six in the setting of HTA and five in the setting of Alzheimer's Cafés.

Thirdly, in the different stories (the research data) that this analysis is based on, we found that in one conversation, during one meeting, or in one interview, more interpretative packages come up. So each individual interview or meeting can be viewed as a string of interpretative packages that are articulated. People move between different interpretative packages. The interpretative packages can be considered the 'beads' and every story a unique necklace.

While this clustering in eleven interpretative packages is a huge reduction in itself, and they are simplified and purified to some extent, our findings differ from earlier accounts which stress two opposing views, or logics, of health care. The first is a view which portrays a disease and its problems as a biomedical puzzle, to be solved by medical interventions and further medical research. The other, opposing view, portrays a disease and its problems as a condition of a person, to be dealt with through careful attention to the personal situation of the patient and his or her family. The first pole has been labeled as stressing 'cure', the

second as stressing 'care'. This bi-polar condition is unfortunate and distorts a rich and sensible reflection on how to deal with diseases such as Alzheimer's in an aging society.

Our findings, however, go beyond this dichotomy of 'cure' versus 'care'. We did not find two logics at work, but eleven. A division in 'cure' and 'care' and models of Alzheimer's disease such as the biomedical, psychosocial, disability or social gerontological model, are based on how to best support and help patients and informal caregivers. However, we also found interpretative packages about the competitiveness in technology development and about innovations looking for application areas in clinical practice, about shifting notions of what is considered as normal aging and what is considered pathological, an interpretative package about the aging populations and the increasing number of persons with dementia that put a stress on the current economic and health care system, as well as a interpretative package on expectations about life and existential questions arising with a diagnosis Alzheimer's disease. Within developments of early diagnostics more comes to play, besides supporting or helping patients and informal caregivers. Of course, when we would have chosen other settings we may have found less or more, or slightly different interpretative packages. The basic lesson, however, is that when stakeholders reflect on early diagnostics there will be more than just two sets of positions, concerns and understandings.

We found that the envisioned implications of early diagnostics are entangled with cure and care strategies in various ways. First of all, early diagnostics is said to contribute to both the cure and care strategy, and thus making a cure versus care discussion less relevant. The co-existence of both approaches has been elaborated on before e.g. as co-existing in memory clinics when dealing with early stages of dementia (Moreira 2010) and in nursing homes (Moser 2011). Secondly, with a focus on early diagnostics more comes to the fore than consequences for patients, such as the organization of the health care system, and medical research agendas. Furthermore people with a diagnosis Alzheimer's disease are not mere *patients*, but also *persons* with a life and a view on life. We claim that a cure/care dichotomy brings along a narrow focus on how to deal with dementia, which obscures other interests, such as leading a fulfilling life, keeping a viable health care system, scientific advancement, or innovative competitiveness. Such considerations are equally important and should not be backgrounded.

In terms of the aging-and-innovation discourse, our analysis of interpretative package confirms that early diagnostics for Alzheimer's disease is not a self-evident part of a solution to the increasing number of persons with Alzheimer's disease in aging societies, such as the Netherlands.

The aging and innovation discourse mobilizes interpretative packages on reducing the societal burden, it emphasizes the importance of early diagnostics as a step on the road to medication, of identification of a biomedical condition, of changing of health care and of early management, and of progress through innovation. It leaves out how exactly early diagnostics will become part of good patient management, uncertainties about the value for money, worries about budget cuts in care provision and reimbursement, the uncertainties about the value of early diagnostics while disease modifying is not yet available, the (social)

effects of the label Alzheimer's disease for a person, the life event this signifies, and how this changes the definition of Alzheimer's disease.

The two settings we studied provide richer accounts than the aging and innovation discourse. Both settings stress the importance of an early diagnosis as the identification of the condition underlying symptoms such as forgetfulness, as well as the need to timely provide care and support. But the social gerontological approach and the life event that a diagnosis of Alzheimer's disease entails are absent from the health technology setting, just like the discussion about the performance of specific diagnostic instruments, and shifts in the definition of Alzheimer's disease towards a more neuropathological definition are absent in the Alzheimer Café. The two settings thus seem to be complementary — a finding with practical and optimistic consequences. Instead of a paralyzing stalemate between 'cure' and 'care', the understanding of the problems and the ways to address it will have various overlaps. The theoretical and practical task ahead, thus, is not to articulate the two positions of 'cure' and 'care' further, but to map the overlaps of interpretative packages and thus to reconcile concerns and strategies. Another, less optimistic, conclusion would be that some interpretative packages are less visible, appropriate, or maybe even silenced in the modes-of-ordering present in these settings.

The richness we encountered, however, does not imply that the tension between 'cure' and 'care' as two fundamentally different modes of representing health care has vanished completely. However, we did not encounter 'cure' and 'care' as two sets of parties that confront each other, or two bodies of argumentation. The tension between care and cure does not appear as two poles, but as a theme that submerges in many different interpretative packages. The polarization only occurred occasionally, when the allocation of research budgets or the attraction of patients was discussed, the cure–care opposition was used to mold the discussion and to mobilize allies.

To conclude, we can expect that every narrative about early diagnostics will mobilize some of these interpretative packages in particular ways and will leave out others, as part of politics, agenda-setting or the acquisition of resources by stakeholders. Our study emphasizes that different ways of approaching Alzheimer's disease are closely connected to the way we 'see' the problem and respond to it, or look for a solution. The explication of eleven interpretative packages creates the possibility to identify which ones are mobilized and which ones stay outside of discussions, arguments and conversations, and thus can serve as a way to understand the politics at work and identify and detect overlooked issues that should be included.



# Chapter 7

## Deltaplan Dementia

With the rise of dementia as a public health concern national dementia strategies are being developed (G8, 2013; Rosow et al., 2011; World Health Organization, 2012) across the globe and also in the Netherlands. In the Netherlands the Deltaplan Dementia (or in Dutch Deltaplan Dementie) was initiated as part of the Dutch national dementia strategy in 2013.

The Deltaplan Dementie was chosen as an interesting setting to study the meanings of early diagnostics for Alzheimer's disease. In this setting early diagnostics gains meaning as part of the strategies and discussions on how to deal with dementia as society. For this chapter, the development of the Deltaplan Dementie has been followed for two years, which allows the study the dynamics of co-existing meanings over a longer period of time. To develop the Deltaplan, public, political and business interest and resources needed to be mobilized, and a plan had to be formulated in which different stakeholders would collaborate. The development of this plan also triggered a public debate on how to deal with dementia. All these occasions led to explicit articulation of different framings of dementia, as well as a dynamic between different framings, in which early diagnosis was mobilized as one element (among many) in a broad narrative on how the Dutch can deal with dementia.

This Chapter consists of two parts. Part A analyses how multiple framings of *dementia* co-exist during the development of the Deltaplan Dementie. This part has been published as a book chapter (Cuijpers, 2016). Part B focuses on the meanings of *early diagnostics* as articulated in the process of the development of the Deltaplan Dementie. Within the plan and the disputes surrounding it, early diagnosis gains particular meanings.



# **Part A. Dikes and dementia: How multiple framings of dementia co-exist during the development of a national dementia strategy**

*This part has been published as a book chapter: Cuijpers, Y., Dikes and Dementia: How multiple framings of dementia co-exist during the development of a national dementia strategy. p. 185-203. In Emerging Technologies for Diagnosing Alzheimer's Disease, Innovating with Care, edited by Marianne Boenink, Harro van Lente and Ellen Moors. 2016. London, United Kingdom: Palgrave Macmillan.*

## **7.1 Introduction**

With the rise of dementia as a public health challenge, national dementia strategies are being developed worldwide (World Health Organization, 2012; G8, 2013; <http://www.alzheimer-europe.org>). Since multiple approaches to dementia co-exist (Downs et al., 2006; Innes & Manthorpe, 2012; Moser, 2008), it is safe to assume that the development of national dementia strategies is not a straightforward activity. There is a politics involved because every approach will reflect a particular view on what the problem is and every solution will favor a particular view at the expense of others (Innes & Manthorpe, 2012). Every national dementia strategy somehow has to deal with this multitude of approaches. However while the aim of national strategies to collectively address dementia is clear, it is less clear how and why certain directions for action become part of national dementia strategies. In this chapter I address the prevalence of particular views on dementia as a matter of 'framing' and I investigate how the multiplicity of framings co-exist in one, Dutch, case of a national strategy.

The Netherlands has had several national dementia programs running since 2005. Building upon these earlier activities, in 2013 a new national action plan (the Deltaplan Dementie) was launched (VWS, 2013). The development of this plan and its launch were accompanied by struggles on how the problem should be defined and which strategies would be most appropriate to collectively deal with dementia. These struggles will likely have their counterparts in other countries in which national dementia strategies are being developed.

This study provides a reconstruction and analysis of *which* framings of dementia are articulated in the course of the development of a Dutch dementia strategy, and *how* stakeholders deal with the co-existence of multiple framings of dementia. First I will elaborate on theory on collective action framing which I have used to analyze the data and to structure this chapter. Secondly I will show the framings used to draw public and political attention, followed by the framings in the research program that are part of the Deltaplan Dementie, and finish with an analysis of framings in the media and interviews with the

participants of the public debate. I show not only how dementia is framed in a national dementia strategy, but also how different frames are assumed to co-exist. Finally, I present three models of how frames are assumed to co-exist. In the conclusion, I will reflect on the consequences of these three models and point out the importance of acknowledging the power differences between frames and how to deal with them.

## **7.2 Theory and methods**

The launch in 2013 and the implementation of the Dutch Deltaplan Dementie is an occasion in which articulations of, interactions between and contestations about multiple framings of dementia as a public health concern are made explicit. In this way, the Deltaplan can be seen as a crystallization point in which what is fluid is temporarily joined together and solidified. This process shows the dynamics of the construction of dementia by actors responding to each other.

I can fruitfully draw on framing analysis (for example Entman, 1993; Schon, 1995; Gamson, 1992; Van Gorp & Vercruyse, 2012) and, in particular, on theories of collective action framing (Benford & Snow, 2000) to analyze the way in which dementia gains meaning in the development of and the discussions surrounding the Deltaplan Dementie.

Frames can be defined as sense-making devices that operate through two processes: firstly, by making some parts of reality more visible than other parts (referred to as 'selection' and 'salience' in framing literature) and secondly, by proposing a particular view on social reality by defining what is problematic, what the causes of these problems are, how to evaluate a situation and what to do about it (Gamson, 1992). Framing generally involves the telling of stories to make sense of a situation. These stories are called frames when they are strong, generic narratives. In the case of collective action framing these narratives typically also include a story that urges for action. The characteristic *content* of collective action frames consists of three parts: (1) diagnostic framing of defining the problem (2) prognostic framing of what should be done to deal with the problem and (3) motivational framing to mobilize action (Snow and Benford, 2000).

The content of frames is shaped by a number of *processes*. First of all through the telling of stories to make sense of a situation (discursive processes). But next to this, frames are often strategically aligned with the interests of possible constituents and resource providers to increase the chances to mobilize support and resources. Furthermore, since the aim of collective action frames is to change something, they are often confronted with disputes within the movement (framing disputes) and contestations from opponents, bystanders and media (framing contests), which in their turn shape the collective action frame.

The data used for this chapter are (i) newspaper articles that appeared on the Deltaplan Dementie in the large national newspapers from 2010 to 2015 (n=57) collected through the newspaper database LexisNexis, including calls for the need of a Deltaplan Dementia, news

articles announcing the launch of the plan, opinion articles and letters to the editor, as well as editorial articles reflecting on the public debate (ii) the official documents on the Deltaplan Dementie, (iii) interviews with ten stakeholders who were involved with either in the development of the plan, or public debate on the plan (the initiator, a director of the Alzheimer Association, the director of the Deltaplan Dementie, a policy maker from the ministry of health, an employee from the governmental funding agency, two scientists that provided input during the development of the plan and three dementia professionals who contested parts of the plan in the media). The interviews were semi-structured and the topics included a reconstruction of the development of the Deltaplan, the involvement of the actor in the plan or in contesting (parts of) it, the motivational, diagnostic and prognostic framing of dementia by the actor.

## **7.3 Results**

### **7.3.1 Together we build the dike**

So how is dementia framed in the drawing of the Deltaplan Dementie and subsequent discussions? I will first analyze the development of the plan from the perspective of the initiators. What was the motivational framing of the plan and the general direction of its diagnostic and prognostic framing?

*"If no measures are taken now, this disease will become the epidemic of the future."* (Deltaplan tegen dementie: VUmc waarschuwt voor epidemie, De Telegraaf, 11 april 2012). The neurologist pleading for the Deltaplan, starts 'beating the drum more loudly' to warn that in our aging society more and more people will develop dementia and society is utterly unprepared for the upcoming 'dementia wave'. In line with the metaphor of a wave, the term Deltaplan Dementie is launched. The term 'Deltaplan' itself is a powerful metaphor within Dutch society. It refers to the gigantic project to protect the Netherlands against floods (initiated after a disastrous flood in 1953) and makes the Netherlands to what it is today. *"In 1953 in the Netherlands we were flooded totally unexpected: the deltaworks were the answer. Now we build a dam in advance, because we can see the flood, the increasing number of persons with dementia, coming. It is five to twelve."* (ibid.) The original Deltaplan is seen as a victory of mankind over the forces of nature. The Deltaplan Dementie should battle dementia, in the same successful way as the Dutch deltaworks have beaten the water. The main message thus is that as a nation we need to join forces in the battle against dementia. *"We are working on a battle plan in which government, business, banks, health insurers and scientists all at the table."* The Deltaplan aims unite the forces of government, health care organizations and companies. *"Together we build the dike!"* (VWS, 2013) Although the metaphor used has a clear national ring, the underlying type of argumentation is hardly unique. The motivational framing of a disaster to be averted has been a generic and successful strategy to draw public and political attention and mobilize resources to address the problems of Alzheimer's disease since the 1980s (e.g. Chaufan et al., 2012; Diesfeldt,

2014; Johnstone, 2013). It has been referred to as ‘apocalyptic demography’ (Robertson, 1990, Robertson, 1997), or ‘health politics of anguish’ (Fox, 2000).<sup>20</sup>

In the case of the Deltaplan Dementie, however, a second generic strategy was applied to urge government and business to join. One driver to beat the drum for a Deltaplan Dementie was that investments in dementia research were needed to secure the position of the Netherlands in European research programs. To urge for public investments in Alzheimer research the Deltaplan Dementia is strategically aligned to the Dutch innovation policy. This is done by emphasizing the societal challenges posed by dementia and stressing the need for investments in science and innovation to face these challenges. Investing in science and innovation, it is argued, will lead to a triple-win situation because innovation will solve the societal problems posed by dementia, help the elderly and boost the economy at same time. This is a strong, widespread and appealing discourse to argue for the need of innovations to face societal challenges related to aging, formerly defined as an ‘aging and innovation discourse’ (Neven, 2011). This strategic frame alignment (and its success) are particularly visible in a Letter to the Parliament, written by the Minister of Health when he announced to invest 32.5 million euros in the Deltaplan. *“Following the effort to improve dementia care in the Netherlands and to anchor international programs in our country, Dutch scientists and Alzheimer Nederland have taken the initiative to develop the Deltaplan Dementie. (...) We expect the Deltaplan to contribute to increasing awareness on dementia, controlling of costs, maintaining of labor productivity of informal caregivers and provide economic chances for different industries. With the collaboration between government, science and business the Deltaplan fits perfectly with innovations aimed for by the cabinet through the top sector policy. (...) We trust the plan will be a success (...) firstly for persons with dementia and their relatives, secondly for care professionals who can improve the quality of care provision, and finally that the Deltaplan will be an impulse for scientific research in this field and for related business sectors.”* (Ministry of Health, 2013)

Thus the motivational framing is shaped for a large part by strategic processes common in the field of dementia and aging to mobilize resources. Furthermore, the initiators and developers of the Deltaplan Dementie stress unity: ultimately, there is one goal and one plan, and everybody benefits. A multitude of stakeholders should unite forces to jointly battle dementia.

To be sure, in the starting phase of drawing attention and resources for a Deltaplan Dementie there are already some distinct directions as to what the Deltaplan should target, and which remained to structure the plan throughout its development. The terms ‘the patient of today’ and ‘the patient of tomorrow’ are structuring the Deltaplan and are often repeated in the report of the plan, in the media and interviews conducted for this study. Research for ‘the patient of today’ aims to improve the quality of life and care for current patients. Research

---

<sup>20</sup> In the theory on dementia chapter (chapter 2), the history section (2.1.4.) shows that the exact same rhetoric was used in the 1980s. The drawbacks of this approach were discussed in section 2.1.5.

for 'the patient of tomorrow' aims for long term outcomes helpful for future patients. This mainly includes biomedical research to understand the underlying disease mechanisms that are expected to improve prevention, diagnosis and enable the development of disease modifying treatment. Again, this distinction is not typically Dutch. The phrase "*care today, cure tomorrow*" was for example also used during the recent WHO summit on dementia (World Health Organization, 2015).

### **7.3.2 Keeping all frogs in the wheelbarrow**

The decision of the government to invest 32.5 million euros in the Deltaplan Dementie to be exclusively spend on scientific research (the whole plan also covered other areas), led to the creation of a research program called Memorabel.

The process of creating a research program involved a further elaboration of the content. This process included alignment with EU programs (JPND - Joint Programming Neurodegenerative Diseases and CoEN – Cooperation between Centers of Excellence in Neurodegenerative disease research) attuned to building upon the strength of the Netherland. It included the research agenda of Alzheimer Nederland based upon the input of a panel of informal caregivers and persons with dementia. And because the Deltaplan promised to unite forces, it also involved enrolling the relevant scientists. An invitational conference was organized with researchers from the dementia field. Additional extensive conversations were conducted with stakeholders in the field who were hesitant to enroll in the program.

What problems should the research program address and which directions should be pursued? While the Deltaplan suggested a general consensus that action was needed to battle dementia, as soon as problems and directions for research had to be specified, a fragmentation occurred. This is clearly visible in the research program Memorabel. It starts by acknowledging that multiple approaches to dementia co-exist: "*The Deltaplan aims to cope with the societal challenges of dementia, a heterogeneous condition that affects people worldwide.*" (emphasis by author) In its aims it states that: "*Views on the approach of dementia differ, though they are essentially complementary. Dementia touches upon many sectors and policy terrains (care, cure, prevention, living, welfare) and the number of organizations and professionals involved in care and support for people with dementia is extensive and their involvement and expertise divergent. This demands careful programming.*" (Memorabel, 2013) This formulation followed a long and laborious process to draw out the research program. The employee of the funding agency explained the assigned: "*We need to service all aspects (...) of the disease, everything that is involved. (...) So we need to service researchers who say (...) we need to know more about the genetic aspects because that is where advances can be made (...) But also people who say that we need to work on medical treatments now, because there is a short term benefit to gain. But also people who say that all that is not going to work with dementia, because it is too complex, we have been trying to find medication for twenty years and it is not working, so please lets*

*invest the little money there is in good care, and a movement that says (...) we should work on prevention. (...) All these elements are in the program. All approaches can apply for research funding.*" (interview funding agency) In other words, while preparing the research program, definitions of 'the' societal problem of dementia, multiplied. This multiplication enters the research program through the input of different professional sectors and policy terrains in the research program that have diverging approaches to dementia, yet should collaboratively contribute to facing up to the challenges dementia raises for society. In principle all Dutch dementia research in the Netherlands is united in the research program *"but you cannot keep all the frogs in the wheelbarrow"* (Interview policy maker ministry of health).

The final research program consists of a list of topics for research, organized around four themes: (1) causes and mechanisms of disease, (2) diagnosis, (3) treatment and prevention, and (4) effective care and support. It started with the dissemination of a 'building blocks' document in the form of a bullet list of research topics for each theme. This list was based on the European research programs JPND (Joint Programming Neurodegenerative Diseases) and CoEN (Cooperation between Centers of Excellence in Neurodegenerative disease research), adjusted to the research strengths of the Netherlands and supplemented with the research agenda of Alzheimer Nederland (the Dutch Alzheimer Association). An invitational conference was organized in The Hague on September 2012. Attendants of the invitational conference could provide input and comments on the 'building blocks' document during working groups sessions. Among the many comments made in the reports made by these working groups, I would like to highlight one repetitive comment: *"the connection between different themes is missing", "a synthesis is missing", "it is not clear how the cohesion between different outcomes of different parts of the program will be established"* (quotes taken from the reports of the working groups of the invitational conference). While surely this was improved in later versions, the fragmented character is still present in the eventual research program.

During the development of the research program we see the assumption that different framings of dementia are essentially complementary. The effort to join forces to defeat dementia, led to a fragmentation of diagnostic and prognostic frames. The problem of dementia is redefined into a large number of particular problems that specific scientific disciplines address. They are considered to be fragments of a whole that can be synthesized into or added up to a complete whole. The main idea seems to be that if all professionals get funding it will add up to be an encompassing program in which everybody works on a part of the puzzle.

These multiplications make it difficult to understand how the separate research activities add up to a full-fledged research plan on how to deal with dementia in Dutch society. With the assumption that different approaches to dementia are essentially complementary, the

question rises if the different parts really add up to a whole and how a synthesis can be achieved.

### **7.3.3 Framing contests becoming public**

Now we move to the public arena, where a different dynamic played out. During the development of the plan and after its launch, a stream of letters to the editors and critical opinion articles emerged in the national newspapers, written mainly by scientists and medical professionals. In these opinion pieces, framing contests became publicly visible. Journalists writing about the plan also started to position different stakeholders in terms of proponents and opponents of the plan. In the media, framing contests thus played out in an antagonistic fashion. Different framings of dementia and the problems it poses for society did not seem complementary, but in tension with each other. They might even exclude each other.

In these opinion articles, all parts of the collective action framing in the Deltaplan Dementie were contested: the motivational, the diagnostic and the prognostic framing. The quote *“Big numbers in combination with the fear for a tsunami of patients are maintained by scientists and pharmaceutical industry”* nicely captures the contests of the motivational framing (De ziekte van Alzheimer bestaat niet, NRC Handelsblad 11 april, 2012). The use of a disaster rhetoric was contested for exaggerating the problem and playing on the fear and instigating anxiety for a condition that is already one of the most feared conditions in Dutch society. The use of the aging-and-innovation discourse was contested by questioning the integrity of the Deltaplan and its initiator, wondering in whose interest the Deltaplan Dementie has been developed. The diagnostic framing of dementia as a disease of which research will in the future unravel the causes and develop a treatment is deemed misleading. Too much emphasis on medical interventions is considered to be out of place and misleading. The articles show a long list of issues that the Deltaplan seemingly overlooks or that deserve more attention.

In the arena of public media, different framings of dementia created tension. On the one hand the struggles appear in the media in terms of actors being ‘for’ or ‘against’ and questions on ‘who is right?’. On the other hand journalists speak of ideological struggles, illustrated by headlines such as: ‘reader does not know which expert to believe anymore’, ‘ideological struggles between researchers on Deltaplan Dementie’, and ‘is dementia really such a big problem?’. Several articles start distinguishing different ‘schools of thought’ to make some sense of the discussions going on.

Which diagnostic and prognostic framings are behind the critiques? To better understand where these critiques stem from, interviews were conducted with a number of persons who raised their voice in the media. From these interviews, not one unified picture arose. The main reason is that in every interview a quite particular diagnostic and prognostic frame was articulated, which partly overlapped with other interviews, but not completely. Some of the interviewed persons explicitly said they were still searching for the right way to frame what

they were after. One said s/he felt to be part of a paradigm shift that is setting in, but which has a hard time to gain foothold.

Interviewees used two diagnostic frames to explain the problem of dementia. The first framing focuses on dementia as a disease, and argues that dementia should be seen as a heterogeneous, complex condition, overlapping with normal aging processes, and finally leading to a dementia syndrome. Even though the research program Memorabel also refers to dementia as a heterogeneous condition, this framing was explicitly articulated as a 'counterframe', opposing the framing of dementia as a neurodegenerative disease. A second diagnostic framing centers not on the nature of the condition, but stresses that dementia is first of all a condition of a person and that the person should be central. *"I think medicine is a humane discipline and it should be about people. Many branches of medicine have become so super-specialist that it is only about cells and organs."* This is not so much a counterframing, opposing a framing of dementia as a disease as it is a shift in emphasis in what problems should be addressed. These discussions have been roaming the dementia field for decades (for example Lock, 2013; Kitwood, 1997; Dillmann, 2006; Downs et al., 2006).

These diagnostic framings also lead to particular strategies to deal with dementia (and thus to specific prognostic framings). Some interviewees consider a 'cure' impossible, while others keep open the possibility that perhaps, on the long run, a kind of disease modifying treatment will be possible. Putting the hope for a cure between brackets, learning to live with the condition, as a person, as informal caregivers and as society becomes most prominent. Rather than 'battling dementia', 'living with dementia' becomes the aim to strive for. From this line of reasoning two lines of action emerge. The first is that while dementia cannot be cured in the stages that it manifests itself, there may be possibilities to delay its onset through preventative measures and a healthy lifestyle. The second is that society needs to become prepared to live with dementia. This means that when adhering to this framing of dementia, the distinction made in the Deltaplan Dementia between research for 'the patient of today' and for 'the patient of tomorrow' collapses. Following this framing the structure of a national dementia strategy would not be 'care today, cure tomorrow', but would be more in line with Peter Whitehouse's rephrasing: 'care today, care tomorrow, cure good luck and prevention yes' ([www.themythofalzheimers.com](http://www.themythofalzheimers.com)). A national dementia strategy should be geared towards facing the reality of a society including persons with dementia. From this position medical research is still valuable, but is positioned next to other kinds of research on dementia. Similar pleas to re-invent the science of dementia in which medical research has a more humble position have been made by for example Portacolone et al. (Portacolone et al., 2014). Box 7.1 summarizes the issues mentioned in newspaper articles and interviews that deserve more attention in the alternative framings of dementia and in a research program on dementia.

**Patients**

- Understand the needs and wants of patients and informal caregivers

**Human life**

- Approach elderly with dementia as persons in their final stretch of life
- Focus on what makes life worthwhile and enjoyable

**Prevention**

- Preventative strategies
- Lifestyle approaches

**Cultural**

- Tackle societal discomfort with dementia
- Change cultural perception of dementia

**Societal**

- Enable a dementia friendly society
- Social inclusion of persons with dementia
- Raise awareness on dementia and how to deal with persons with dementia

**Health care system**

- Support for informal caregivers
- More attention for long term care
- Integration of professional approaches
- A demand driven health care system

**Box 7.1. Examples of issues foregrounded in alternative framings****7.4 How frames co-exist**

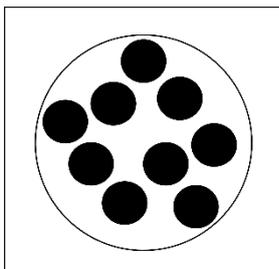
This chapter started from the assumption that since multiple framings of dementia co-exist, the development of a national dementia strategy is not a straightforward activity. This chapter has reconstructed which framings of dementia surfaced during the development of a Dutch dementia strategy and how these co-exist. This reconstruction confirmed the starting assumption: the efforts to collectively tackle the societal challenge dementia poses, unleashed a multitude of framings of dementia.

Surrounding the Deltaplan Dementie we see a struggle on who gets to define what a dementia strategy should constitute. As I hope to have made clear in part three, it does matter who gets to define. Framing struggles surrounding a national dementia strategy is 'politics of signification' in action. While Peter Whitehouse wrote his book 'the myth of Alzheimer's, what you aren't being told about today's most dreaded diagnosis' in 2008 (Whitehouse, 2008), we can say that in 2015 framing struggles have become public and we are being told a lot about today's most dreaded diagnosis. Furthermore all stakeholders are aware of the existence of multiple framings of dementia and the scientific controversies raging the field. The question now has become how to deal with this multiplicity. This reconstruction shows different models on how framings are considered to co-exist.

In the initial phase of the Deltaplan, the main aim was to draw public and political attention and resources. This was done drawing upon proven strategies such as a disaster rhetoric and

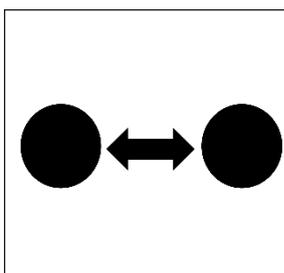
an aging-and-innovation discourse. Dementia is framed rather homogeneous as a societal challenge that should be addressed. During the further explication of the plan a multiplication of frames occurs. During the development of the research program different approaches to dementia are considered to be essentially complementary. The main difficulty is how these different parts can be synthesized again. Whereas in the public arena of newspapers a less peaceful picture arises. Contestations arise and discussions play out in an antagonistic fashion in terms of care versus cure, for or against. Journalists start wondering who is right and delineate different 'schools of thought' or even paradigms in the dementia field. Personal interviews with participants of the public debate show multitude of frames moving in different directions and revealing a rather different type of preferred research agenda.

This reconstruction shows not only different framings dementia but also three models of how these are assumed to co-exist.



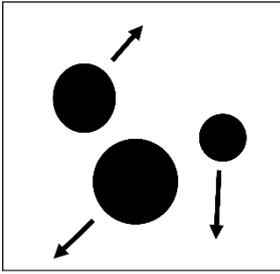
**Figure 7.1** Parts of a whole

Parts of a whole To raise public and political awareness and resources for dementia, professionals working on dementia were presented as willing to join forces to jointly face the societal challenge dementia poses to society. This endeavor needed to be specified in the research program Memorabel. Also in the research program different framings are considered to be essentially complementary. They are seen as parts of a whole. Dementia as a large societal issue is fragmented or specified into a multitude of approaches, which are supposed to add up. This model assumes an essential harmony and possible peaceful co-existence.



**Figure 7.2** Antagonistic positions

Antagonistic positions In the public debate following the launch of the Deltaplan Dementie different framings were positioned as being in active opposition. Criteria are sought to settle who is right and who is wrong. And discussions start to focus on who is most powerful and whose interests are served by a particular framing.



**Figure 7.3 Moving in different directions**

Moving in different directions During the public debate and the interviews with participants of the public debate, the different framings appear as different directions that can be pursued. Rather than wondering who is right the question becomes which directions to pursue with how much effort and resources. Emphasis on one direction or another is a political and normative choice of how we as society want to deal with dementia in society. These different directions do not co-exist in peaceful harmony, nor are they perpendicular to each other. There are coalitions, as well as disagreement, frictions and tensions on particular issues between different framings.

While all models may apply at times, I would like to argue here that it is important to reflect on which model is most appropriate when. To deal with dementia in society, the problems dementia poses are specified. This is very useful. The grand societal challenge dementia poses cannot be dealt with without specifying what it is we are talking about. At the same time, with for example the controversy between the two medical approaches of dementia, it may be argued that one is right and the other is wrong. Yet specific research may be interesting whatever theory is adhered to. Furthermore the model of multiple framings moving into different directions can reveal the tensions between different schools of thoughts and shows that even if you put all expert-scientists together in one room, the choice which directions to pursue will remain a political one.

I would like to end this chapter with a brief reflection on what should be a minimum requirement for responsibly dealing with a multiplicity of frames. I have shown how different framings of dementia are made to co-exist. Yet an issue that remains on the table and is highly relevant is how to deal with power differences. I will use the example of the drawing of the research program to illustrate my point. The funding agency used the first model (different framings as essentially complementary) to service all aspects and all approaches to dementia. Yet they did not clearly acknowledge that there may be a disbalance between different approaches to dementia. One of the main critiques on the Deltaplan Dementia was that it appeared to be a rather medically oriented plan. The medical approach to dementia has had a strong foothold for the last decennia and has a well-articulated, fine-grained and specific research agenda. My interviews with professionals who approach dementia as a condition of a person, or as a societal phenomenon (the 'living with' approaches) showed that they had a much more sketchy research agenda. Some of them stated they were still searching for the best way to frame what they were after. Moreover, these researchers are not as well organized (institutionally) as medical research(ers) on Alzheimer's disease. The framing contests in the media particularly addressed this disbalance, and thus showed an antagonistic model. This created a discussion in terms of cure versus care (Cuijpers & van Lente, 2015b). The democratic way of gathering input for the research program by the funding agency aimed at servicing all researchers and all approaches to dementia did not take into account the difference in power and voice between different approaches. If the

funding agency would have adhered to the second model of antagonistic positions, or to the third model of frames moving into different directions they might have realized that approaches favoring 'living with' dementia may need more time and space to further develop their position, strengthen their vision and articulate research directions.

# Part B. The dynamic meanings of early diagnostics in the Deltaplan Dementie

## 7.5 Introduction

The main question in this part B is when and how ‘early diagnostics for Alzheimer’s disease’ gains meaning in the debate on how the Dutch should deal with dementia. It complements the analysis of Part A: the framing of dementia during the development of and discussions around the Deltaplan Dementie. Part A showed the differences in defining the problems of dementia and in the proposals to deal with dementia as a society. It also showed how different framings co-exist and how this changed with the further development of the Deltaplan, by (1) the different activities undertaken, such as the mobilization of public and political attention, the creation of a research program, engaging in public debates, and (2) with the contexts in which the articulations took place.

This section, Part B, is an extension of the analysis in part A, with a focus on meanings of early diagnostics for Alzheimer’s disease, and follows the same structure. The meanings of early diagnostics are analysed, firstly in the call for action to join forces in a Deltaplan Dementie (section 7.6.), secondly in the research program Memorabel (section 7.7.), thirdly in the public debate on the Deltaplan (Section 7.8) and finally in in-depth interviews with actors participating in the public debate on the Deltaplan (section 7.9). Section 7.10 provides the discussion and conclusion on the dynamics of the multiplicity of meanings of early diagnostics for Alzheimer’s disease in the Deltaplan Dementie.

The analysis was based on the same data as used for Part A. Whenever early diagnostics appears in the data, it was coded. The construction of meaning of early diagnostics was analysed by tracing the relationships to other elements in specific articulations. By following the same structure as in part A it was possible to show how early diagnostics gains meaning within the different framings of dementia.

Rather than adhering to a single definition of early diagnostics for Alzheimer’s disease and thus limiting what to include in this study, I followed the definitions in the data (see also Chapter 2.2.1. for a disclaimer on the terms ‘early’ and ‘diagnostics’). And I traced how stakeholders define the term. In the coding different definitions and wordings are included, such as:

- early diagnosis, early diagnostics, timely diagnosis, effective diagnosis.
- mobilizations in terms of biomarker research, molecular diagnostics, biomarker tests, and imaging techniques when they are discussed without referring to them as ‘early diagnostic instruments’ as one of the possible applications.

- signalling of early signs and symptoms of the condition, also without directly mentioning a diagnosis (which may or may not be implied).

## **7.6 Together we build the dike – drawing attention and mobilizing resources**

Part A showed that to draw public and political attention to dementia, the initiators of the plan used different motivational framings. In the public announcements of the plan and in the drawing of the Deltaplan Dementie, dementia figures as ‘the socioeconomic challenge of the 21<sup>st</sup> century’. The Deltaplan should prepare the Netherlands for the upcoming ‘dementia wave’ to prevent a ‘national disaster’. This disaster rhetoric was used to stress the urgency of dementia as a public and political issue that deserves more attention. To urge government and business to collaborate a so called ‘aging and innovation discourse’ strategically aligns the Deltaplan with Dutch and EU policy. In this motivational framing the need for investments in science and innovation was stressed. Science and innovation could reduce societal costs, serve patients, and stimulate the economy at the same time. During this phase of the process, early diagnostics was mobilized in relation to both the disaster rhetoric, and the aging-and-innovation discourse.

### **7.6.1 Disaster rhetoric and early diagnostics**

Early diagnostics appears in the disaster rhetoric as a (partial) solution in the form of (1) a ‘timely’ diagnosis to improve the quality of care serving ‘the patient of today’ and (2) as early ‘molecular’ diagnostics to speed up research on disease modifying treatment and prevention serving ‘the patient of tomorrow’.

#### *Timely diagnosis to improve the quality of care for ‘the patient of today’*

*“In more than 50 % of the cases dementia is recognized too late.”* (Ministerie VWS, 2012, p. 6) It is seen as a task of general practitioners to diagnose dementia faster, for which they should receive extra schooling: *“Also we will provide extra schooling to general practitioners so they can recognise dementia faster, because there is still underdiagnosis.”* (“Deltaplan tegen dementia, VUmc Alzheimercentrum waarschuwt voor epidemie,” 2012)

The concept of ‘timely diagnosis’ emerges in relation to health care costs: *“Timely diagnostics, intervention and support of informal caregivers leads to lower admissions (YC: in nursing homes) and thence to a cost reduction of an estimated 30%.”* (Ministerie VWS, 2012, p. 7) The term ‘timely diagnosis’ is generally used to refer to the time that is right for an individual patient and family to receive a diagnosis. ‘Timely’ then means not too early and not too late, but the right time considering the family’s situation (Cuijpers & van Lente, 2015b; Dubois et. al., 2016). In the Deltaplan it is assumed that a timely diagnosis will also reduce societal health care costs. The need for a diagnosis to reduce societal health care costs resurfaces in the section of the Deltaplan Dementie that proposes a national registration of dementia patients. *“It may sound crazy for such a large group of persons with*

*a fatal condition, but important questions are not answered yet: How many persons actually have a diagnosis dementia? Which types of dementia? In which setting is this person diagnosed? Who takes care of them? Which interventions and services are used by these persons? How does this evolve over time?"* (Ministerie VWS, 2012, p. 18) In this proposed national registration system a diagnosis means that a person is labelled as having dementia. The idea is that the national registration for dementia patients will enable health care policy makers and researchers to track and trace patients with dementia throughout the health care system. This information can then serve as a basis for improving health care policy. *"To make adequate policy on quality of care and the capacity of services it is of crucial importance to gain insight in the content and size of the problem."* (ibid, p. 18) *"(the) unique value of the register lies in the established quality of the diagnosis. As such it can serve as a checkpoint for all other chain information systems."* (ibid, p. 18). In the description of the benefits of the national registration system it is described as *"Improving the quality of care through more, timely and differentiated diagnosis."* (ibid, p. 20).

Early diagnosis, thus, is mobilized in relation to the disaster rhetoric, as a timely diagnosis serving 'the patient of today'. A timely diagnosis is presented as an improvement in care and support for the patient of today. However, timely diagnosis is also related to a reduction in health care costs and thus to contributing to avert a socioeconomic disaster due to dementia. The argument is that a timely diagnosis enables policy makers to improve the provision of care to patients with dementia in terms of decisions to be made in public health care.

This ambiguity is interesting to note, because when it is stated that an earlier diagnosis leads to improved care and support, the suggestion is that the diagnosed person receives care and support of a higher quality. However, when it is claimed that the quality of care will be improved through timely diagnosis, it may also mean that a timely diagnosis enables health policy makers to maintain a viable health care system with enough capacity.

### ***Early 'molecular' diagnostics to speed up research on disease modifying treatment and prevention for 'the patient of tomorrow'***

In relation to 'the patient of tomorrow', early molecular diagnostics is considered to contribute to what is referred to as 'a true solution' of the socioeconomic challenges of dementia: *"The rise of costs that is accompanying dementia can be curbed if we succeed in delaying or preventing the development of dementia in persons. A true solution for dementia can only be brought closer through scientific research. If we understand the onset of the disease better we have a chance to develop disease modifying drugs and preventative strategies, and thereby to reduce the demands on costs and manpower."* (Ministerie VWS, 2013, p. 8) Early molecular diagnostics (signs such as biomarkers and instruments such as imaging techniques) are attributed a key position to speed up scientific research on prevention and disease modifying treatment: *"There are important new developments that make it possible to speed up research, such as the identification of new risk genes, the availability of new biomarkers, the development of new image processing techniques to study*

*the brain.*" (ibid, p. 8) All in all, early diagnostics is considered an important and promissory direction to be pursued: *"possibilities should be developed to recognize dementia in the first stages in the brains, at least 10 years before the first noticeable memory changes."* ("Kabinet investeert extra in bestrijding dementie; 'Deltaplan' moet kosten tot 2020 met 3 mld verlagen," 2013)

The outline of the Deltaplan Dementie contains a detailed description of the research to be conducted under the header of 'the patient of tomorrow'. In this section biomarker research gains a prominent position. *"Amongst the most important new drivers for clinical research belong the identification of no less than 10 new risk genes, the availability of new biomarkers (i.e. CSF and PET), the description of disrupted neuronal networks in dementia, and the publication of new diagnostic criteria under the auspices of the NIA-AA."* (Ministerie VWS, 2013, p. 22).

The new diagnostic criteria of the NIA-AA (National Institute on Aging–Alzheimer's Association guidelines for the neuropathological assessment of Alzheimer's disease (Hyman et al., 2012)) shed a new light on the use of biomarkers in clinical practice, which is discussed in the Deltaplan Dementie. *"The most important new aspects (of the NIA-AA criteria) are:*

- *Alzheimer has a long prodromal phase (up to 20 years). This creates a 'window of opportunity' for intervention.*
- *Different disease processes (e.g. amyloid-beta, tau, TDP43, progranuline, synaptic loss, vascular damage) play a role.*
- *Incorporation of biomarkers in clinical practice (better and earlier differential diagnostics) and in the design of clinical trials.*
- *Application of earlier and more precise diagnostics to faster determine the effect of new treatments."* (Ministerie VWS, 2013, p. 22).

It is quite particular that diagnostic criteria anticipate the use of biomarkers in clinical practice in the future, as usually diagnostic criteria describe, or prescribe, the best current practice (Boenink, 2017). In the Deltaplan report the prominent role of biomarkers in these criteria was described as a 'catalyst' for research, rather than as a guideline for current clinical practice. *"The new criteria mention the progress made in biomarker research, but above all show that a lot of work needs to be done to implement biomarkers at a large scale. While strictly meant to improve diagnostic practice for the patient of today, the criteria mainly function as a catalyst for research for the patient of tomorrow."* (Ministerie VWS, 2013, p. 22)

This section shows that the development of early diagnostics, in terms of biomarkers and medical imaging, is mobilized as *the* promising direction in medical research which will lead to a 'true solution' to dementia. Early diagnostics are expected to speed up research on prevention and disease modifying treatment, which, in the end, would reduce the numbers of persons with dementia in the future. The elaboration on the novel diagnostic guidelines

reveals that with biomarkers and medical imaging positioned as the drivers for medical research, these clinical guidelines also have to relate to early diagnostics somehow. The discussion on these guidelines in the Deltaplan also reveals that it is not (yet) clear how (or if) these tests should be implemented in clinical diagnostic practice.

### **7.6.2 Early diagnostics and the aging-and-innovation discourse**

In the announcements and the outline of what a Deltaplan Dementie should constitute, early diagnostics does not only gain meaning as averting a disastrous dementia wave by serving 'the patient of today' and 'the patient of tomorrow'. Early 'molecular' diagnostics, in terms of biomarker research and imaging techniques, also figures as an important area for research and innovation and as a 'strength of the Netherlands'.

One of the motivations for the development of the Deltaplan Dementie was to secure the position of the Netherlands in European research programmes by investing in research. *"The European Commission stimulates the member states to formulate national programs to contribute to the internationally agreed long term strategic research agenda."* (Ministerie VWS, 2013, p. 9) Explicitly mentioned subjects of this research agenda are *"speeding up dementia research starting from collaborations between centres of excellence on three subjects: animal models, biomarkers and imaging."* (ibid., p. 9, emphasis by the author). A position in these European research programs would contribute to the knowledge base and competitive position of the Netherlands in, amongst others, the areas of biomarker research and medical imaging.

To motivate the Dutch government to invest in a national dementia program, the Deltaplan is not only aligned with the European research agenda, but also with Dutch innovation policy, which focuses on so-called 'top sectors'. Top sectors are defined as areas in which Dutch business and research excel and in which the Netherlands should even strengthen its leading position through collaborations between business, universities, research centres and the government. The Deltaplan presents early molecular diagnostics as one of these areas of excellence and claims to build on the strength of the Netherlands, both in research and industry. *"The Netherlands has a strong knowledge base and competitive power in the area of dementia."* (Ministerie VWS, 2013, p. 8) And among these strengths are the development and use of biomarkers and imaging techniques. *"The research field in the Netherlands is characterized by outstanding performance on world level in the areas of psychosocial and clinical fundamental research. Some examples: (...) development of new markers for an early diagnosis (in CSF, blood, imaging); studying the development of the disease on the basis of repetitively measured markers (CSF, blood, imaging); (...); detailed (clinical and biomarker) phenotyping."* (ibid., p. 23) This is coupled to the Dutch industrial sector. *"The Netherlands has a strong industrial position in the area of medical imaging and image analysis."* (ibid., p. 23). *"The Deltaplan aims (...) to offer innovation and market opportunities for pharma- and nutrition industry, medical-diagnostic technology, domotica and e-health."* (ibid., p. 10, emphasis by the author). Investments by the Dutch government are needed to join European

research programs and to maintain the knowledge base and competitive position of the Netherlands: *“through the broadening and upscaling of scientific research, the Deltaplan contributes to the realisation of the European research agenda and is the leading position of the Netherlands maintained and confirmed.”* (ibid., p. 10). Further strategic alignment can be seen in the explicit coupling of the Deltaplan to specific ‘roadmaps’ within the top sector policy: *“For the topsector Life Sciences and Health, these are particularly the roadmaps Homecare and Self-Management, Imaging, Molecular Diagnostics, Specialized Nutrition, Pharmacotherapy and HTA/Quality of Life.”* (ibid., p. 9, emphasis by the author).

Thus early diagnostics gains meaning in an innovation discourse of excellence and competition in terms of a race between countries in which the Netherlands should maintain its leading position. The Dutch government is urged to invest in research on biomarkers and imaging techniques to secure the competitive power of science and industry.

The meaning of early diagnostics has been constructed with the aim to draw attention and mobilize resources, (1) as a timely diagnosis enabling health policy makers to maintain a viable health care system with enough capacity, (2) as early diagnostics instruments and biomarker research to enable a true solution for dementia in terms of disease modifying drugs and preventative strategies, (3) as an important research area to invest in to secure the position of the Netherlands in European research programmes, and (4) as an area in which the Netherlands has strong innovative capacity, and in which should be invested to maintain that innovative competitiveness and to offer market opportunities to businesses.

## **7.7 Keeping all the frogs in the wheelbarrow – research program *Memorabel***

The Deltaplan Dementie received an investment of 32,5 million euros in 2013 from the Dutch government to set up a research program. Part A discussed the different framings of dementia in the plan, how they co-exist and how they were presented as essentially complementary. Servicing all aspects of the disease would add up to a full-fledged research program. This section focuses on the meanings of early diagnostics for Alzheimer’s disease within the research program *Memorabel*. The outline of the research program and the reports made on the input given during an invitational conference in 2012 serve as the data to analyse through which relations early diagnostics gains meaning in the research program.

The motivational framing of the research program *Memorabel* is completely in line with the Deltaplan Dementie: to control the growing problems dementia poses to society, the innovative force of the Netherlands should be mobilized in the areas of science, innovation and health care (policy). The structuring of the research program was in line with the ‘Delta-speak’ (as involved researchers referred to the terminology used by those involved in the Deltaplan) and categorized according to whether it targets ‘the patient of today’ or ‘the patient of tomorrow’. In research serving ‘the patient of tomorrow’ early diagnosis is related

to research on the development of treatment and prevention. *“Research and innovation for the patient of tomorrow. This is about research and development activities (...) aiming to prevent, (early) diagnose, delay and treat dementia and will often lead to applicable results in the long term (ZonMw, 2013, p. 11). In research serving ‘the patient of tomorrow’ the term effective diagnostics instead of ‘timely diagnosis’ is used to improve the provision of health and social care. Improve the care for the patient of today. Here it is about activities (...) that result in the short term in a better quality of life and in effective diagnostics, treatment, prevention, care and support for dementia, across the whole chain of care, welfare and housing.” (ZonMw, 2013, p. 11).*

The Memorabel research program consists of four different research themes, in which early diagnostics gain particular meanings:

- (1) cause and disease mechanisms
- (2) diagnostics
- (3) treatment and prevention
- (4) effective care and support.

Theme one, on the *causes and disease mechanisms* of dementia, revolves around genetic and epigenetic (external, environmental) factors contributing to increased risk or to protection against the development of dementia. In this theme early diagnostics for Alzheimer’s disease, in the form of biomarker analysis and imaging techniques, are given a crucial role. They are positioned as a prerequisite for progression in research on the causes and disease mechanisms of dementia. *“To identify new risk or protective factors it is of crucial importance to further characterize the preclinical stages of dementia through i.e. imaging, imaging genetics, biomarkers, neuropsychological tests and other tests of the brain functions.” (ZonMw, 2013, p. 16). The importance of early ‘molecular’ diagnostic tests appear as self-evident: “In the coming years the focus of research will shift to the preclinical phases of the disease. To do so new imaging techniques (such as MRI, DTI fMRI, PET) biomarkers in blood and CSF, and brain tissue after autopsy will play an increasingly important role.” (ZonMw, 2013, p. 15). Or as something to be expected: “In the coming years different developments are expected that enable us to map the earliest signs of dementia even better: think about new imaging techniques (MRI, DTI, fMRI, PET), new methodologies, to combine complex technologies (e.g. imaging genetics) and the further development and refinement of tests to measure brain function.” (ZonMw, 2013, p. 16). Within this theme early diagnostics gains meaning as the unquestioned next step to further research on the causes and mechanisms of dementia.*

The second theme, *diagnostics*, revolves completely around research on diagnostics. This research is divided into two tracks. One track for diagnostics for ‘the patient of today’ and a second track for diagnostics for ‘the patient of tomorrow’. In both tracks the meaning of early diagnostics is constructed differently. The first track concerns improvements of current diagnostic practice so that the patient receives the best available care and support, including

a better and earlier diagnosis: *“A large part of the persons with dementia receives the diagnosis at a late stage. A better and earlier diagnosis can be beneficial for the patient and informal caregivers because knowing the diagnosis provides clarity about the changing and often incomprehensible behaviour, and enables more effective support when needed.”* (ZonMw, 2013, p. 17) ‘Early diagnosis’ thus refers to the timing of conducting a diagnosis for a patient, to benefit the patient and the informal caregivers with their situation in daily life. In this track a ‘better diagnosis’ refers to the diagnostic tests but also includes proper communication of the diagnosis to the patient (the patient should receive good diagnostic information and advice), attuning the type of tests used to the setting in which the diagnosis takes place (e.g. general practitioner, nursing home, memory clinic), as well as the patients’ situation and the stage of disease progression. This track was written from the context of the diagnostic practice, in which patients, informal caregivers and doctors play a central role.

The second track of the theme on diagnostics, includes research on *“biomarkers in the broadest sense of the word: MRI, PET, EEG/MEG, CSF, blood”* (ZonMw, 2013, p. 17). These biomarkers should identify or trace processes in the brain that may lead to dementia. It is stressed that a lot of progress has been made in diagnostic instruments based on these biomarkers and that this has worked as a catalyst for medical research on dementia. These insights have led to changes in the definition of the disease and changing insights in possible treatments. While it is clear that these instruments function as a catalyst in the context of medical research, questions arise on the value of these tests in the context of diagnostic practice: *“The improved diagnostic tests also raises questions: How to deal with amyloid positive test results on PET or liquor in asymptomatic individuals? Which diagnostic trajectory is appropriate in which setting (primary care, secondary care, etc.). How does the disease process unfold? (...)The new criteria do not assist mixed pathology, while it is known that this is the case in the large portion of elderly. (...) Another important question is how the availability of biomarkers can actually be implemented in daily routine. (...) The renewed diagnostic methods should be implemented with clear guidelines. Which markers are indicated in which stage, in which setting, for which patient?”* (ZonMw, 2013, p. 17). The value of early diagnostic instruments for diagnostic practice remains a balancing act and it is stated in the track that a lot of work needs to be done before they might be implemented in diagnostic practice. This track shows that because early diagnostic tests are mobilized as a prerequisite for furthering medical research, the question arises how or if these tests should be implemented in the context of clinical practice, and there is no straightforward answer.

In theme three on *treatment and prevention* early diagnostics for Alzheimer’s disease are not explicitly mentioned (ZonMw, 2013). Yet, they are implied in relation to research on medical treatment and prevention. And they could be implicitly included as part of psychosocial treatment. In the case of medical treatment, the results of research have been disappointing. Different causes for these disappointing results have been identified. One of the causes might be that *“treatment in the dementia stage is too late.”* (ZonMw, 2013, p. 18). Therefore *“New research should aim for treatment in the preclinical and prodromal phase and for*

*alternative therapeutic strategies*" (ibid., p. 18). Markers and imaging techniques should reliably predict which patients will progress to develop dementia and which will not, and markers should be developed to monitor disease progression. Within this theme, without being explicitly mentioned, early diagnostic instruments is considered to be a necessary next step in the progression of research on treatment. For prevention it is stated that early intervention is needed before any signs are present (primary prevention), or when persons show early signs (secondary prevention). While (again) not explicitly mentioned, the focus on preventative interventions to decrease the risk for persons that have cognitive problems or other risk factors, points to the need to be aware of and act upon the first signals of dementia. By doing so, this theme is carried by the assumption that it will become possible to identify risk factors, or preclinical and prodromal stages of dementia. Finally, psychosocial interventions are addressed in this theme, aiming for social inclusion, strengthening self-management and dealing with changes in behaviour and functioning for the patient of today. Taking into account the needs and wants of patients and informal caregivers is a central issue. (Early) diagnosis is not explicitly mentioned when psychosocial interventions are addressed.

Theme four addresses *effective care and support*. It mainly aims to determine the efficacy of methods of (early) diagnosis, treatment, care, living and welfare and it also addresses ethical aspects. On diagnosis in general it is stated that "*the (cost)efficacy of many of the complex diagnostic routes and interventions are still unclear, hampering a suitable financial reimbursement and implementation.*" And that "*Currently there are three diagnostic guidelines (...) that should be better integrated.*" (ZonMw, 2013, p. 21). Given that current diagnostic practice is diverse and not straightforward, it is difficult to assess the (cost)effectiveness of complex diagnostic routes. Early diagnostics is not a prominent issue in this theme, but is addressed in one sentence "*Concerning early diagnostics, it is helpful to ascertain the net benefit with attention to the psychic and social factors and the imperfection of the diagnostics methods (including false positives and false negatives).*" (ZonMw, 2013, p. 20). That is, the desirability of early diagnostics for effective care and support is not self-evident but a (research) question. To determine the value of adding early diagnostic instruments to current diagnostic practice is not an easy task, because current diagnostic practices are diverse and because the value depends on a balancing between (as least) psychological, social, ethical and medical consequences of early diagnostics.

Part A showed that with the development of the research program a fragmentation occurred as to what 'the' societal problem of dementia constitutes. Yet, the idea was that with a broad research program all dementia research in the Netherlands should be united, that the different themes should facilitate all aspects of the disease, and that all approaches are essentially complementary. Such a reconciliation is not repeated with when analysing the construction of meaning of 'early diagnostics': the different approaches are not essentially complementary, but reveal the ambiguity surrounding this issue. On the one hand, early diagnostics for Alzheimer's disease has a pertinent position in medical research on causes and mechanism of dementia, prevention and (medical) treatment within the research

program Memorabel. The move to diagnosis and possible interventions at earlier stages of the condition seems a dire need to progress in medical research. Driven by this reasoning the diagnosis is pushed towards earlier stages of the disease, also in diagnostic guidelines. On the other hand, it is not clear whether it is useful to shift the diagnosis to earlier stages of the disease and to use early diagnostic instruments for Alzheimer's disease in clinical practice and patient care. Thus, the development of early diagnostic instruments does not appear as a central issue in the theme on effective care and support. The value of early diagnostics for patient well-being and in clinical practice is a complex question and part of the research to be conducted in the Memorabel program.

The Memorable program provides an insight in the construction of meaning by professionals on dementia in their activities, aiming to establish a research program. In the public debate the discussions, including some of the same actors, took a different shape as will be elaborated in section 7.8.

### **7.8 Framing contests becoming public – public debate**

As discussed in Part A, framing contests arose in the public media, already before the launch of the Deltaplan Dementie (Olde Rikkert, et al., 2012), and after the government had pledged 32,5 million euro for a research program in 2013, a public debate played out in a rather polarized manner. The question then becomes: How is early diagnostics for Alzheimer's disease mobilized within the framing struggles that were addressed in Part A?

In articles that proudly announce the Deltaplan, and articles that are positive on the plan, early diagnosis pops up in relation to furthering medical research and improving health care. A medical researcher, for example, speaks of early 'molecular diagnosis' as promising medical progress: *"If we don't do anything, in 2040 half a million Dutch persons have Alzheimer's, an unimaginable number. There is still no medication, the disease is irreversible and progressive. Since recently we can make a diagnosis based on the presence of the Alzheimer protein in the brain. This is going to bring us further. We know that one third of the elderly has this protein in their brain. Who will get Alzheimer's? Can we prevent that with early treatment?"* (Interview with medical scientist in ("Ik voel me een detective; levenslessen" 2013). And a geriatric psychiatrist speaks of early diagnostics as an improvement of diagnostic practice: *"we are working hard on early diagnostics – that is also what we hope to develop further within the Deltaplan Dementie. We follow a large group of persons with memory complaints who visit our polyclinic, some of them already for more than ten years. That way we try to find out if we can predict whether persons will get troubles with self-reliance. For patients that is important to know."* (in "Hoop op genezing nog ver weg" 2013 (Algra, 2013)). In these articles early diagnostics is positioned as a knife that cuts on two sides: contributing to both progression of medical research and improving diagnostic practice for patients.

Yet, quickly other positions were voiced: A professor in long term care for dementia, for example, expresses her worries about the prominence of the medical perspective in the Deltaplan: *".. it is regrettable that the Deltaplan Dementia medicalizes that much. Dementia*

*specialists don't have much more to offer to patients than a diagnosis, uncertainty about the progression and the hope for a miracle cure. (...) We are missing the essence. As long as there is no cure against dementia, we have to take care for persons with dementia as good as we can.*" (Thé & Reerink, 2013). A politician voices the same worries: *"The plan has a largely medical perspective: how can dementia be signaled better, treated, or even cured, and how can informal caregivers be supported? That is fine of course. But I miss the attention for societal acceptance of dementia."* ("Maatschappelijke omgang met dementia verwaarloosd," 2013). Within such a polarized debate (see Part A), early diagnostics becomes part of the 'medical framing', and figures as a key element in that framing. This means it is discussed as part of a medical framing for dementia – both in terms of hopes and in terms of critiques on medicalization.

In the public debate on the Deltaplan Dementie, journalists started writing articles to characterize and understand the different stances. For example, an overview article ("Is dementie écht zo'n groot probleem? Deltaplan Dementie ontketend richtingensrijd," 2013) interviewed different experts who all felt the need to address early diagnostics: *"Another objection concerns the preference that speaks from the plan for biomedical research searching for the causes of dementia, coupled to a speedy diagnosis. That research is still at the mouse- and molecular level (...) Applications are not there yet. Than you should not give it such large importance. (...); "Emphasizing diagnosis for elderly with dementia is nonsense (...) What is the added value of a diagnosis with costly tests such as brain scans and lumbar punctures? Do people enjoy life more after that? Already more and more persons request for euthanasia after receiving an early diagnosis dementia.";* (...) *Companies invest only if there are ways to regain the investments. But that can lead to growing costs for the government. The growth of the costs in health care is mainly caused by the use of new technologies.*" Early diagnostics occurs as an issue which different experts feel that they need to address. These contestations reveal that the need for and desirability of early diagnostics is not self-evident and depends on the question: for what or for whom is it important or desirable?

These messages in the media are mainly short and not always early diagnostics appeared as a topic. To understand how the participants of the public debate construct the meaning of early diagnostics for Alzheimer's disease, individual interviews were conducted with a number of professionals who articulated their position in the media.

## **7.9 Behind the scenes of the public debate**

To deepen the understanding of the framing contests occurring in the media, additional interviews were conducted with persons who articulated their stance in the public debate. In these interviews the meanings of early diagnostics were constructed in relation to a number of interests: a timely diagnosis coupled to providing good care (7.9.1); an early diagnosis and providing clarity to persons in pre-dementia stages like MCI (7.9.2); early

diagnostics and the development of disease modifying treatment (7.9.3), and medicalization of coping with dementia (7.9.4).

### **7.9.1 A timely diagnosis as a prerequisite for good care**

Early diagnosis is often constructed as a timely diagnosis in relation to suitable care and support for persons in the early phases of dementia. The director of the Deltaplan Dementie (2014) states: *“It is important to diagnose as early as possible... I think there is consensus on this point. To diagnose as early as possible enables a. early support and b. early interventions (for as far as they are available).”*; *“In the Deltaplan early diagnosis has been almost a starting point: the earlier the better.”* He also acknowledges that how to implement early diagnosis in patient care is not straightforward. *“There are no harsh statements on that, because diagnosis is a thorny issue: should everybody have a diagnosis? Who should diagnosticate? Do you have to do a scan or can it be done in a different ways? These issues are still hanging.. In the Deltaplan it was mainly said that early diagnosis is good. The earlier the better.”* (director of Deltaplan Dementie, 2014)

While the argument that an early or timely diagnosis is ‘good’ was initially considered as common ground by the initiators of the Deltaplan Dementie, it is stressed in a number of interviews that this statement is not backed by scientific evidence. *“There is no evidence for that. Indeed, people just make these claims. They just say that. And everybody takes it at face value. But there is no evidence for it.”* (professor in geriatrics) *“The main message nowadays is ‘early diagnosis is good for you’. But that we do not quite know. For some people it is good. But they should be well-informed before they can think about what is good for them. So I think it needs to be nuanced. The complexity will become clearer. (...) I think we will say in the future ... well.. in 2014 we had too simplistic ideas.”* (professor in geriatric psychiatry, 2014).

Many interviewees elaborate a version of the argument that receiving a timely diagnosis is important for persons with dementia and their relatives to understand what is going on, to be able to cope with the symptoms of dementia and to receive care and support. For example *“It is about being close to the persons, how can you support them? (...) It is more about support of persons in that situation, and notifying them of the support options. That is what you do for persons with dementia.”* (professor in psychogeriatrics, 2014) *“While there aren’t any consequences in terms of treatment (...) there is an interest in early diagnosis because of the right to health care reimbursement based on a diagnosis. And it can be of importance for the persons involved to cope with the changes they are facing.”* (professor in long-term care, 2014). In one interview, the same reasoning – that a timely diagnosis is important to receive (reimbursement for) the care and support needed, led to the conclusion that *“That is rightly so. And completely true. And I find it terrible that we arranged access to health care in that way.”* (professor in geriatric medicine, 2014)

In interviews stressing the value of a timely diagnosis, two preconditions are mentioned. Firstly, it is stressed that proper care and support should be in place after the diagnosis. Initiatives such as meeting centers, Alzheimer Cafés, day care facilities, and case managers

are mentioned as positive examples. Secondly, the needs and wants of patients and informal caregivers should be known to provide suitable care and support. And this is (surprisingly) not the case: *“What are their true needs? What are their troubles? We should listen to their stories. People receive care that is offered by institutions and health care providers. But are we listening to what they really need?”* (professor long term care) *“We did an application for research in Memorabel to explore what people themselves want.”* (professor in geriatric psychiatry, 2014)

On the one hand, a timely diagnosis is seen to enable timely health care and support. On the other hand, for persons faced with this timely diagnosis, this also enables a timely organization of euthanasia and euthanasia requests. *“You see a lot of anticipated fear. What we see happening is.. requests of euthanasia at a very early stage of the dementia process. (..) people who are functioning well but want euthanasia, because knowing the diagnosis the future prospects can be unbearable. (...) According to the law it is allowed, and it happens. But I find it... a pity, to say the least. I have nothing against euthanasia. But it is anticipated fear and these people said: once I am demented, nobody will execute a euthanasia. Which is also allowed by law by the way.. but it is madness.. euthanasia on highly demented persons. Those persons in the early phases could still enjoy life, but because of the diagnosis there is a fear of the Sword of Damocles, and people request euthanasia.”* (professor in geriatrics, 2014)

### **7.9.2 Early diagnostics and pre-dementia stages**

Early diagnostics gains meaning as providing clarity, not only when a person has dementia, but also in pre-dementia stages such as Mild Cognitive Impairment, MCI. The research director of the Alzheimer Association for example, stresses the importance of this development: *“Most exciting is the area of MCIs, to distinguish within that group: this person has memory complaints but is not heading for dementia. To comfort those persons would be ideal. Of course you need to be certain, because if you comfort persons who needs to visit you again in two years that is tricky. (...) “this MCI group... If you arrive at a memory clinic with - in your experience - serious memory complaints, and diagnostic tests show that there is something going on, but they are not sure how to call it, I think that is hard on people. Because what to do: hope, don’t hope? It is a sword of Damocles and you don’t want it hanging above your head for three years. That is a reason to speed up research in that direction. To make this group of persons as small as possible. (...) These are persons who want to know, who want to have certainty and you have to leave them with the uncertainty. That is difficult. Anyway. If you drop the sword, you need to drop it well. Not halfway, because that is when it gets scary.”* (interview research director Alzheimer Association, 2014)

Whether biomarker tests and imaging techniques will be capable of providing such certainty is challenged in some other interviews. The promises of biomarker and imaging techniques as diagnostic tests for Alzheimer’s disease are that they will signal deviations in the brain that may eventually lead to dementia at a time when patients do not yet experience symptoms of dementia. In these interviews, the current discomfort with the diagnostic category MCI,

will apply as well to these biomarker and imaging tests that show or signal deviations in the brain. Like with Mild Cognitive Impairment, persons who show positive on these early diagnostic tests may not develop dementia in the following years. So actually, instead of speaking of an early diagnosis, a risk profile might be a more appropriate term.

Another question addressed is whether an early diagnosis is beneficial to patients. *“How timely is timely? If you have no symptoms, do you have to know that you will - maybe in five years time - have them? Should you burden persons with such knowledge? Because it might be possible to see signs earlier and earlier. So the question then becomes where to draw the line. How timely? I understand that they want to know as early as possible for research purposes to - preferably even before clinical symptoms are present – do things that may lead to delaying the onset of those symptoms. But when I consider it from my work, I would, ehmm like that people timely know to what condition their symptoms are related.(..) I think a lot of misery can be prevented that way.(..) Yes. So I do support a timely diagnosis.”* (professor in psychosocial care, 2014) Within this line of reasoning, a diagnosis should only be conducted when this has consequences: better support, knowing what is going on, enabling better ways of coping with changes. And it should be balanced with the less beneficial consequences of a diagnosis: being excluded from certain activities, and people may deem you to be less capable than you actually are because of the public image of dementia. The benefit for a person to receive such an ‘at risk label’ is not straightforward. When persons do suffer from complaints or worries there are psychosocial interventions available. However, these will only be helpful when a person experiences complaints, and a *timely diagnosis* of symptoms is sufficiently early for that.

### **7.9.3 Early diagnostics and the development of disease modifying treatment**

Beside patient care, early diagnostics gains meaning in relation to experimental medical research aiming to unravel the disease mechanisms causing Alzheimer’s disease, and to speed up the development of disease modifying treatment. *“To track persons who are at risk of developing dementia and to provide treatment on time is one of the most exciting things. Because treatments will likely have the most effect in early stages. New treatments that will hopefully also arrive eventually. But you need to be able to distinguish within the MCI group.”* (director of the Alzheimer Association)

In Part A on the framing of dementia in the Deltaplan Dementie the controversy on whether Alzheimer’s disease is a condition that can be treated with disease modifying treatment was addressed. From the position that Alzheimer’s disease is not a curable disease, the interest of medical science in early diagnostics is somewhat uncomfortable. Doubt is expressed by a professor in neuropsychiatry (2014) participating in a large project on early diagnostics (LeARN): *“I don’t think that it has yielded much (author: of the outcomes that were promised at the onset of the program). And it has yielded nothing that I expect to result in a substantial health gain for persons with dementia. (...) So it makes you wonder: Is it the aim to figure*

*something out for the patient, or do we help to keep ourselves busy for five years. I state it very negatively here. I don't mean it like that. I think it has again yielded insight. (...) It is more and more, at least for me, proving that Alzheimer's disease as a disease does not exist. That you shouldn't think in terms of 'a marker' for Alzheimer's disease."* Others wonder about priority setting in research: *"Look, everybody wants to know what causes the disease, of course. I just don't think there is one cause. So. It is very complex. And we are spending a lot of money on that. And the question is whether this is the way to find out. Maybe it is... I... I admire people who try to figure it out. But I have doubts if they will. In the meanwhile I think: care provision is only getting worse. So I wonder: what are we doing?"* (professor psychosocial care, 2014) *"I think it is interesting for scientists. And the money that circulates in that kind of medical research cannot be use in other places."* (professor in long term care. 2014)

From the perspective of doubting the possibility to find a marker for Alzheimer's disease and a disease modifying treatment, the development of biomarker tests and imaging techniques can still be valuable for the purpose of prevention. There is little knowledge on risk and protective factors for prevention (besides general advices on healthy living). Biomarkers could provide clues for that. *"We could also follow persons over a long term and find out how to age as healthy as possible. We could do that. Instead of searching for a cause of dementia."* (professor in psychosocial care, 2014)

#### **7.9.4 Medicalization of coping with dementia**

Early diagnosis gains meaning as part of a medical approach of dementia and a furthering of medical insight in the condition, which leads to shifts in diagnosis. *"Eventually the diagnosis will shift a little. The persons of which you can currently say 'yes Alzheimer, but not dementia' that is exciting. If they show Alzheimer pathology, but are functioning well clinically speaking, this is where it will shift a little. First in research, with applications in trials. But maybe it can also work in diagnostic practice."* (director Alzheimer's Association, 2014)

While some consider this as medical progress, others consider it to be a step in the further medicalization of dementia. A professor in geriatrics (2014) positioned early diagnosis within a broader societal trend of narrowing the broadband of normality. The reasoning behind that is that early diagnosis of Alzheimer's disease in older persons is an example of this trend (just like for example ADHD diagnosis in children). Diagnoses (in general) are normative, because a diagnosis draws the line between what is accepted as normal and what is considered to be deviant. While these decisions are made by a rather small group of mainly medical professionals, these decisions decrease the bandwidth of normality in society. In the case of early diagnosis of Alzheimer's disease, diagnoses are considered to result in a further medicalization of aging processes.

Other routes were discussed in interviews: *"I think that, yes, how do I say it... psychosocial doesn't cover what I mean.. The humane part... remains underexposed, and deserves research attention. (...) It is mainly the technocracy that greatly prevails, the technology. And not what it means for persons."* (professor in geriatric psychiatry, 2014) *"We are talking about health*

*care. While I am convinced that the less 'white coats' visit you, the better it is for you. We create, for a large part, our own diseases. And we are... medicalizing aging. Up to now, we have wanted to solve everything with care and medical interventions. The moment you pull it out of the medical or care domain, maybe some things will collapse. But other things might improve. The municipalities can improve welfare. If you make sure.. (..) the neighbourhood is safe, there is social cohesion. That there are social services nearby. That the human touch returns. By working with neighbourhood teams. That home care works together with social care. Then a lot of the current care consumption will prove to be unnecessary. (...) Dutch society can benefit from less medicalization. Less disease approach. When people feel well, they need less care. If people aren't lonely, they use less care.. " (employee insurance company, 2014)*

What would in this less-medicalization-way-of-thinking be an improvement in diagnostic practice? Two interviewees described the ideal situation for a diagnosis to be a kitchen table conversation. The diagnostic process does not need to be a onetime event and does not have to take place in a medical setting. A general practitioner who notices signals, can asks persons for a follow up appointment, and make a visit at home. In a kitchen table conversation it can be discussed what is going on with the persons involved, information can be provided on what kind of help is available and persons should be directed to the right places for support. Also conversations with the family should be part of this support. The general practitioner should gain a good view of what is going on and can make the diagnosis. This close involvement of general practitioners is deemed important, to be able to provide information and support that suits those persons in that situation.

One professor in geriatrics went a step further and challenged the need to formally establish a diagnosis dementia at all. Persons, he argues, visit a general practitioner because they are afraid and feel they need help. A diagnosis as such does not help to meet any of these two needs. A general practitioner should give people the right information so they understand what is going on. He/she can explain that decline comes with aging, and can show a person how he or she functions on different scales compared to other persons of their age. He/she can explain that cognitive functions decrease from the age of 35 onwards: that they are currently at a certain position on the scale, and that it will decrease. He/she can say that this is irreversible and rejuvenation is not possible. This creates a framework for persons to understand their situation. Then he/she can ask what they need to remain functioning in their daily life. This differs from saying: you have Alzheimer's disease and there is really nothing to be done about it. Since the diagnosis is just a picket pole set somewhere on the line of reduced functioning, actually both messages provide the same information. Providing a disease label, however, makes people more likely to take a sick role, while explaining the processes of aging and how these happen in their situation, enables people to stay a member of society.

The neurologist that initiated the Deltaplan Dementie considers the critiques on early diagnostics to be highly problematic. To move from considering dementia as a disease, back to considering it part of normal aging he finds a disregard of the severity of the condition. There is critique on the emphasis on early diagnostics in the Deltaplan Dementie, because the value of early diagnostics is not clear (yet) for clinical practice and the costs of health care increased due to the use of expensive diagnostic techniques such as MRI scans. His reaction to this critique is the following: *“This is a non-argument. By saying that, you deny that dementia is a disease and that it is important to diagnose it. I never said persons need to be diagnosed as early as possible, or to trace possible patients. With early diagnosis (...) I mean adequate good diagnostics when a person has complaints, in which there is a lot to gain. And it could be done cheaper. We would prefer a bloodmarker or something else to demonstrate in a simple way what is going on. But while that is not available you need to make a scan. You only need to do that once, and it is not that expensive.”* (...) *“there is a diagnostic nihilism when it comes to dementia. (...) That is a real disregard of the severity of the condition. And people experience it as disregard. If you ask patients and informal caregivers, they find good diagnostics very important. Good diagnostics, well organised, in an efficient way, for persons who experience complaints.”*

The main question of this part B is when and how ‘early diagnostics for Alzheimer’s disease’ gains meaning in the debate on how the Dutch should deal with dementia. In section 7.6. to 7.8 the meanings and valuations of early diagnostics for Alzheimer’s disease were analysed in the process of the development of the Deltaplan Dementie. The different meanings and valuations were further unravelled through in-depth interviews of which the results were presented in section 7.9.1 to 7.9.4. This analysis yielded a rich pallet of when and how the meanings of early diagnostics for Alzheimer’s disease are constructed in a debate on how the Dutch should deal with dementia.

### **7.10 Discussion and conclusion on the dynamic meanings of early diagnostics in the Deltaplan Dementie**

In Part A the framing of dementia in the Deltaplan Dementie has been addressed. In the Deltaplan Dementie and the discussions surrounding it, early diagnosis is one element (among many) in the collective action framing and the framing struggles on how the Dutch can deal with dementia. Part B highlights how early diagnostics for Alzheimer’s disease has been mobilized in relation to the challenges dementia poses on society and how to address these. This analysis has shown how different meanings of early diagnostics for Alzheimer’s disease unfolded during the process of developing the Deltaplan Dementie: (1) from the drawing of public awareness and the mobilization of resources, (2) through the merging of many different scientific domains in a research program and (3) framing contests occurring in response to the Deltaplan Dementie (4) and in interviews conducted behind the scenes of the public debate.

To draw attention and mobilize resources for the Deltaplan Dementie, the motivational framing took the shape of a disaster rhetoric and an aging-and-innovation discourse (see part A). Early diagnosis appears in relation to both discourses. In the disaster rhetoric early diagnosis was mobilized as part of the solution to the socioeconomic challenges dementia poses to society. A *timely diagnosis* could enable health care policy makers to improve the provision of care and support to persons with dementia to reduce health care costs. *Early molecular diagnosis* in terms of biomarkers and medical imaging could contribute to a 'true solution' to dementia in terms of prevention or disease modifying treatment. In relation to the aging-and-innovation discourse, imaging techniques and biomarker analysis are being mobilized as a strength of Dutch science and industry. To remain its leading position, the Netherlands should participate in the relevant European research programs. The competitive power within these innovative areas should be safeguarded and Dutch government and business are urged to invest in (amongst others) research on imaging techniques and biomarker analysis.

After the ministry of Health plead to invest in a research program, the research program Memorabel was developed in 2013. In Memorabel, Dutch dementia researchers should join hands. Different (scientific) approaches to dementia are seen as essentially complementary. Early molecular diagnostics using biomarker and imaging techniques are called a 'catalyst' for medical research, and are spoken about as *the* next step to further medical scientific research to understand and intervene in Alzheimer's disease. However, when research on early diagnostics is addressed in the realm of patient care, questions arise on the desirability and value of early diagnostics. A timely (earlier) diagnosis in clinical practice is mainly constructed as an improvement in diagnostic practice to provide clarity to patients and informal caregivers and to enable timely care and support. At the same time, it is stressed that the value of early diagnostics for Alzheimer's disease for clinical practice is not self-evident: the tests also produce false positives and negatives, the test results should be well-communicated, an (early/timely) diagnosis should be in line with the needs of patients, and the psychological and social factors should be taken into account.

In the polarized public debate on the Deltaplan Dementie (see part A) many experts participating in the debate mobilize early diagnostics somehow. So early diagnostics is an issue that is subject to debate. In this polarized debate, early diagnostics is resolutely positioned in the 'cure camp' as part of the framing of dementia as a neurodegenerative disease of which the causes should be found, which should be diagnosed early, and treated. Critiques targeting the medicalization of dementia thus also target the value of early diagnostics. Also more specific objections and worries are raised about early diagnostics for Alzheimer's disease.

In depth interviews with participants of the public debate showed that critiques stem from diagnostic and prognostic framings which put the persons with dementia and their caregivers central. The meanings of early diagnostics exceed the economic, medical research and

clinical realm (to which the meanings were confined in the announcement of the Deltaplan and the research program) and move into persons daily lives and how persons with dementia are ex- or included in society. In these framings, early diagnostics for Alzheimer's disease does not appear as a self-evident direction to pursue.

This analysis has shown the unfolding meanings of early diagnostics for Alzheimer's disease during the development of the Dutch Deltaplan Dementie. The construction of meaning of early diagnostics for Alzheimer's disease shifted and changed, depending on the stages of the development of the plan and the setting in which articulations took place. With the aim to mobilize attention and resources, early diagnostics for Alzheimer's disease was constructed as a large promise expected to progress medical science, boost economy and reduce health care costs. It was constructed as the next step to further medical research on Alzheimer's disease which aims to understand the causes and mechanisms of Alzheimer's disease, and to find possible targets for disease modifying treatment or prevention. The value of early diagnostics for clinical practice, for the well-being of patients, or for good patient care is not self-evident. Some say that it is pertinent to distinguish which persons with memory complaints will develop dementia and which won't, and do not see an earlier diagnosis as the most urgent matter to improve the care and support for persons with dementia. The development of molecular diagnostic tests is not considered to be the most pressing issue to improve clinical diagnostic practice. However, it is an issue that people need to relate to. The public debate and the interviews with participants showed that innovative diagnostic tests which are considered crucial for furthering medical research on Alzheimer's disease, do not need to be crucial for improving diagnostic practice, providing care and support, reducing health care costs, living well with dementia, or creating an improved social and cultural dealing with dementia.

Early diagnostics gains meaning in relation to different contexts and goals. Depending on the context to which it is tied, the value and prominence of early diagnostics changes. Early diagnostics gains meaning as improving diagnostic (clinical) practice; as effectively organizing health care and reducing health care costs; as improving the coping with dementia in daily life of persons by enabling timely care and support and providing clarity; as furthering medical research to understand disease mechanisms, prevention and disease modifying treatments; as shifting cultural notions of normal by moving the definition of Alzheimer's disease to earlier stages; and as stimulating the economy by generating scientific knowledge and improving the innovative position of research and industry.

A consequence of this multiplicity of meanings is that a comment such as 'early diagnosis is good' or 'we should invest in early diagnostics' can be interpreted in so many ways that it is easily agreed upon. The promise that early diagnosis can contribute to (m)any of the directions addressed above is easily made and might be true, but what is meant by early diagnosis can be very different for each individual promise.

The fact that early diagnostics is being tied to so many different interests and goals makes it difficult to understand the consequences of this development. The question whether early diagnostics for Alzheimer's disease is a desirable direction to be pursued can only be answered with a counter-question: wherefore?

This multiplicity of meanings also creates certain dynamics. Firstly, it creates a convincing argument of why early diagnostics for Alzheimer's disease is worth pursuing. Secondly, it also raises questions, such as in whose interest is early diagnostics being pursued and who will benefit in the end. Will this really be of benefit to patients, or is it just in the interest of science and industry? Thirdly, work is being done to set boundaries to responsibilities and promises, for example by stating that early diagnostics is of interest for science, and it might also eventually be of value for clinical practice. Another example is the creation of all kinds of subcategories and delineations such as that a timely diagnosis (with or without biomarker analysis and imaging techniques) is of value for patients, and a prodromal diagnosis in the MCI stage might be of interest for those persons who want to know at a very early stage of disease progression, and an early predementia diagnosis is only of value for science. Fourthly, we see that even though some stakeholders may argue that early diagnostics is only meant for research purposes, for example, the development cannot be confined to one area only. This becomes visible in amongst others the move from an early and certain diagnosis of dementia to enable timely care and support, to the same development enabling early euthanasia, or a medicalization of ageing processes.

# **DISCUSSION AND CONCLUSIONS**



# Chapter 8

## Discussion and conclusions

This thesis addresses the social and cultural implications of early diagnostics for Alzheimer's disease with the aim to contribute to responsible innovation. The approach to responsible innovation was based on two starting assumptions:

1. it is possible to empirically study the implications of an emerging technology in existing settings (technology assessment conducted 'in the wild'), and
2. there is no need to speculate on the implications of new and emergent technologies, in this case early diagnostics for Alzheimer's disease. Social and cultural implications of emerging technologies can be studied in the present.

Explorative research activities conducted in memory clinics, general hospitals, laboratories, nursing homes, day care facilities, insurance companies, research groups, and different media showed that early diagnostics has vastly different meanings, depending on the actors and the context. Moreover, also Alzheimer's disease itself was approached in multiple ways. Arguably, the diagnosis of Alzheimer's disease is highly dependent on the understanding of Alzheimer's disease itself, as has been shown in chapter 2. Based on these explorative activities the multiple meanings of early diagnostics for Alzheimer's disease were taken as the central research question in this thesis, with the assumption that this would provide insight in technology assessment going on 'in the wild'.

Based on these starting assumptions and first insights the following research question was formulated:

1. *What are the **meanings of early diagnostics** for Alzheimer's disease in different settings?*

The empirical chapters have addressed this research question extensively. Based on these chapters, this discussion chapter also reflects on the two other research questions:

2. *Does the study of meanings reveal **assessments** of early diagnostics 'in the wild' and if so, how is early diagnostics for Alzheimer's disease assessed?*
3. *What does the study of meanings imply for the notion of **responsible innovation**?*

The following three sections address these three research questions subsequently. Section 8.1 presents the meanings of early diagnostics for Alzheimer's disease in different settings. I discuss two ways to learn from these multiple meanings encountered in every setting: a narrative and a categorical way. Section 8.2. reflects on the question whether and how the study of meanings reveals assessments of early diagnostics 'in the wild'. I show three ways in which the study of meanings add to technology assessment occurring in the wild. Section

8.3. reflects on what responsible innovation would constitute, based on the outcomes of the study of multiple meanings and technology assessment in the wild. I argue that no closure is to be expected and that responsible innovation asks for humility and a constant balancing act.

## **8.1. The meanings of early diagnostics for Alzheimer's disease**

*What are the meanings of early diagnostics for Alzheimer's disease in different settings?*

A first conclusion is that multiple meanings of early diagnostics co-exist. In every setting a multitude of meanings was found. The different meanings will be discussed in this paragraph. Each setting provided a window onto the cultural repertoire of early diagnostics for Alzheimer's disease. The explication of these multiple meanings reveals the *scope* of the implications of early diagnostics for Alzheimer's disease.

The empirical chapters showed multiple meanings of early diagnostics within each setting. Comparing the meanings between settings showed overlaps and differences. This section (8.1.) discusses *what* the meanings of early diagnostics in the different settings are. *How* meanings co-exist will be discussed in section 8.2. on technology assessment 'in the wild'.

To analyse the construction of meaning of early diagnostics of Alzheimer's disease four very different settings were analysed: public media (section 8.1.1.), a health technology assessment setting (section 8.1.2.), Alzheimer Cafés (section 8.1.3.), and the development of a national dementia strategy, i.e. the Dutch Deltaplan Dementie (section 8.1.4.). These settings were chosen based on a number of factors: (1) early diagnostics is a topic of conversation (2) different actors interact in these settings, making explicit the construction of meaning, (3) the settings highly differ from one another, and (4) the settings were available and accessible.

A discursive approach was used to analyse the meanings of early diagnostics of Alzheimer's disease, inspired by literature on discourse analysis, modes of ordering and framing analysis (chapter 4). In each setting the meanings of early diagnostics for Alzheimer's disease were analysed, and each analysis had a distinct focus. In the public media, the health technology assessment, and the Alzheimer café the focus was on *the multiplicity of meanings* through delineating interpretative packages in these settings. Even though the data was collected over a longer timeframe, the analyses were more *snapshot-like*. This resulted in lists of interpretative packages in each setting, partly overlapping, partly differing. In the last setting, the Deltaplan Dementie, the data was analysed *longitudinally* to allow studying the *dynamics* that comes with the *co-existence of multiple meanings* within a setting.

The outcomes are summarized in section 8.1.1. to 8.1.4, showing the (multiple) meanings of early diagnostics in each setting. Section 8.1.5. concludes and reflects on whether the findings from the different settings can be aggregated.

### **8.1.1. Setting 1: Dutch newspaper articles**

Chapter 5 contains the analysis of the meaning of early diagnostics as constructed in newspaper articles between 1995 and 2010. Newspaper articles were analysed as an indicator of cultural repertoire (Swidler 1986), or more specific, the *issue culture* of early diagnostics for Alzheimer's disease (Gamson & Modigliani, 1989). An issue, such as early diagnostics, is usually surrounded by a number of elements that often appear grouped in clusters. This is what we referred to as 'interpretative packages'. Newspaper articles are considered as a setting that both mirrors and constitutes a cultural repertoire. As such they provide an entrance point to analyse interpretative packages, or clusters of related elements, through which the meaning of early diagnostics of Alzheimer's disease is constituted.

Nine different interpretative packages were delineated from the analysis of newspaper articles, in which early diagnostics for Alzheimer's disease gained meaning as:

- a step towards a solution of the societal challenge that dementia poses, through improving health care and decreasing health care costs (*Apocalyptic demography*),
- pushing the boundaries of brain sciences and neurosciences, increasing knowledge on Alzheimer's disease, and progression towards a medical solution or prevention of Alzheimer's disease (*Scientific progress*),
- pieces of the complex puzzle of the condition Alzheimer's disease, which is seen as the outcome of many accumulating biological, personal and social mechanisms (*Scientific complex puzzle*),
- fundamentally changing health care towards predictive medicine, and developing tests to predict the development of AD in an individual (*Technological progress*),
- an innovative product for a huge market (*Economic competitiveness*),
- enabling the timely start of a well-organized and suitable care and support trajectory for a patient and his or her family (*Health care provision*),
- increasing knowledge on risk factors of dementia and enabling measures to prevent Alzheimer's disease (*Successful aging*),
- patient information providing relief and clarity to a patient, or a doomsday scenario becoming reality (*Fear and worry*),
- a verdict enabling a self-chosen death (*Good life and death*).

The analysis of the meanings of early diagnostics for Alzheimer's disease in newspaper articles confirmed the diversity and ambiguity. Earlier studies on framing of dementia in the media emphasized the dominance of a medical framing of Alzheimer's disease and argued for alternative framings in the media. This study on the one hand acknowledged this critique by showing many articles with a medical framing of dementia. On the other hand, the analysis showed that the construction of meanings of early diagnostics for Alzheimer's disease in

public media went beyond a medical understanding of Alzheimer's disease. In the newspaper articles this promised biomedical innovation gained meaning through a multitude of understandings of dementia (see table 5.1 in chapter 5).

Secondly, the analysis showed how the diversity of the cultural repertoire on early diagnostics for Alzheimer's disease guided thinking about problems and solutions. Early diagnostics was mobilized as one element within larger narratives that relate to bigger problems or higher goals, which are referred to as 'the core' of the interpretative package. Early diagnosis itself was never at the 'core' of the interpretative package, but its meaning was always related to such a bigger problem or higher goal: face the societal challenge posed by the changing demography, find a cure against Alzheimer's disease, further scientific knowledge, develop a strong knowledge economy, keep the health care system viable and affordable, fear of aging and particularly dementia, defeat AD through aging successfully, or maintain autonomy by taking your life in your own hand.

### **8.1.2. Setting 2: a Health Technology Assessment**

Chapter 6 compares and contrasts a health technology assessment and an Alzheimer Café setting. In both settings it was analysed how the development of early diagnostics for Alzheimer's disease was entangled with specific definitions of Alzheimer's disease and articulations of problems and solutions in dealing with Alzheimer's disease in the near future. These delineated interpretative packages form the repertoire that is available and frequently used in these settings. The packages found in each setting are separately addressed in respectively 8.1.2. and 8.1.3. and the outcomes are discussed together.

The Health Technology Assessment (HTA) was conducted to assess the clinical and economic value of the early diagnostic instruments as developed by the research consortium LeARN. The HTA setting was a rather medical setting in which, among others, medical professionals, chemical analysts, and health economists work together to produce and exchange knowledge for the assessment of the societal relevance of early diagnostic instruments. The HTA assesses the value of early diagnostics in relation to the quality of life for the patient and informal caregivers, the improvement in clinical decision making and health care costs. The analysis of meanings of early diagnostics in the Health Technology Assessment setting was based on the project description of the HTA, on (draft) articles about the HTA, on interviews with the researchers involved and on participant observations in HTA meetings.

The analysis of the meaning of early diagnostics in this setting resulted in the identification of six interpretative packages through which early diagnosis gains meaning:

- *Early diagnostics as value for money.* 'Health care is expensive and is getting more costly. New technologies could potentially improve health care and increase the quality of life for patients and informal caregivers, but may also lead to an increase in costs. Therefore it has to be examined whether they are value for money. For early molecular diagnostics that is not clear yet.'

- *Early diagnostics as having uncertain consequences for (future) health care practices.* ‘Consequences of new health technologies are complex to assess. You first need to know how they will change the possibilities for diagnostic and clinical practice, and what it means for patients, informal caregivers, and the total costs of health care. It is a tremendous task, but we need to do it.’
- *Early diagnostics as innovation trajectories.* ‘Progress in health care is possible with innovation. Early diagnostics is an umbrella term for various technological developments. They are rooted in different sets of expertise. So, technologies have their own trajectories and they compete.’
- *Early diagnostics as changing the definition of Alzheimer’s disease.* ‘We are now capable of diagnosing Alzheimer’s dementia at an early stage, which changes the notion of what it means to be diagnosed with Alzheimer’s disease. But also the basis on which a diagnosis is made is shifting. The diagnosis of Alzheimer’s disease used to be on the basis of exclusion of other conditions. The importance of early diagnostics is that it can show actual traces of Alzheimer’s disease in the brain. In this way the whole notion of Alzheimer’s disease changes from symptoms to pathology. With early diagnostics we can work on better definitions for research, drug development and monitoring of patients.’
- *Early diagnostics as a step on the road to medication.* ‘Early diagnostics should lead to better medication. Progress in health care is on finding better medication. When patients are diagnosed more accurately, the matching of patients and drugs is better. Furthermore an early diagnosis enables treatment on an early stage when medication is expected to be most effective. Even when a treatment is lacking currently, it is important to anticipate its future availability.’
- *Early diagnostics as part of early management.* ‘The quality of new technologies for health care is determined by their benefit for patients. Since there is no medication for Alzheimer’s disease, early diagnostic technologies have nothing to offer in terms of cure. Instead early diagnostics should be part of management of the disease in early phases.’

### **8.1.3. Setting 3: Alzheimer Cafés**

Also in the setting of the Alzheimer Café the construction of meaning of early diagnostics was analysed. Alzheimer Cafés are set up to provide persons confronted with this condition with information and with (peer) support to better deal with their situation. I attended these cafés for one and a half year (from April 2010 to November 2012), made notes during these evenings, read the documents related to the cafés and conducted interviews with organizers and volunteers of the café. In this setting early diagnostics was an issue that only passes as a topic of conversation once in a while, and it was interwoven with specific definitions of Alzheimer’s disease.

Five interpretative packages through which early diagnostics gains meaning were identified:

- *Early diagnostics as identifying a biomedical condition.* ‘In case of worries about forgetfulness, go and see your doctor. With new diagnostic tests a diagnosis can be conducted in an increasingly early stage. Alzheimer’s disease is a disease of which forgetfulness is an important symptom. However, it is not the only cause of forgetfulness, so it is important to find out what is going on.’
- *Early diagnostics as early patient management.* ‘It is key that patients and informal caregivers make sense of early signals of dementia and can adapt their life to this new situation and related prospects. An official diagnosis should support their understanding and provide entrance to health care arrangements. The core issue of Alzheimer’s disease is how patients and caregivers can cope with it.’
- *Early diagnostics as labelling persons.* ‘Now that Alzheimer’s disease is diagnosed at an increasingly early stage, the mismatch between public perceptions related to the label dementia and the actual functioning of a person will increase. A diagnosis Alzheimer’s disease attaches a label to a person. When this happens it has various profound social consequences.’
- *Early diagnosis as a life event putting things in an ‘Alzheimer perspective’.* ‘Being diagnosed as having Alzheimer’s disease is a life changing event. It requires a deep existential response and changes a person’s past and future. Do you really want to know this in an early stage?’
- *Early diagnostics as reducing health care costs.* ‘A timely diagnosis can reduce health care costs by preparing caregivers and thus allowing patients to stay at home longer. In an aging society, patients with Alzheimer’s disease are a burden. Demographic trends will run to financial and nursing limits.’

In both the HTA and the Alzheimer Cafés a multiplicity of meanings of early diagnostics for Alzheimer’s disease co-existed. This finding is similar to the findings from the public media setting.

A second finding is that multiple meanings are juxtaposed in documents and by persons. The exchanges in the HTA and Alzheimer Cafés setting are much more elaborate as compared to newspaper articles, which tend to be short and fragmented. In the more elaborate exchanges in meetings, conversations, interviews, and documents it was notable that multiple packages are juxtaposed and that single persons can draw upon and move between packages. Each interpretative package appeared as a ‘bead’, and every story or conversation as a unique ‘necklace’.

A comparison of the outcomes of the HTA and Alzheimer Café setting reveals differences and overlaps between the interpretive packages in both settings. The delineation of multiple packages creates a sensitivity to the politics at work in particular situations or in discussions taking place, and it enables the identification of issues that have become invisible or backgrounded.

#### **8.1.4. Setting 4: Deltaplan Dementie**

National dementia strategies are being developed worldwide and also in the Netherlands. A part of a Dutch national dementia strategy is the 'Deltaplan Dementie', initiated in 2012. The analysis of the previous settings (paragraph 8.1.1, 8.1.2., 8.1.3.) showed that strategies to deal with dementia are entangled with specific understandings of dementia. In part A of chapter 7 on the Deltaplan Dementie, the co-existence of multiple framings of dementia was analysed, and in part B the co-existing meanings of early diagnostics. The analysis was different from the previous chapters because it showed (part of) a dynamic process of meaning making – whereas the other chapters were more 'snapshot-like'. To do so, the method of collective action framing was used for the analysis of meaning, including the concepts of motivational, diagnostic and prognostic framing. Firstly the framing of dementia during the Deltaplan Dementia will be discussed, followed by the meanings of early diagnostics for Alzheimer's disease.

##### ***Framing of dementia***

In part A of chapter 7 the framing of dementia in the Deltaplan Dementie was analysed. To gather attention and resources and mobilize collective action, the motivational framing of the Deltaplan Dementie consisted of two rather standard framing strategies: a) the use of an apocalyptic demography, predicting a national disaster to be averted, and b) an innovation discourse, stating that investing in science and business will not only avert the national disaster, but also boost the economy and help elderly at the same time. Both framing strategies have proven to be effective to mobilize attention and resources, while the drawbacks generated by these types of framing are also generally known.

Within the research program Memorabel, which was the part of the Deltaplan Dementia that was funded first, the diagnostic and prognostic framing of dementia as a societal challenge could be analysed. Dementia was mainly framed as a disease of which all aspects should be addressed, by a wide range of mainly medical researchers. The problem of dementia was redefined into four research themes following a highly medical framing of dementia (Downs et al., 2006): causes and mechanisms of disease, diagnosis, treatment and prevention, and effective care and support. These different aspects were further specified into research topics. The main idea was that covering all aspects will lead to a full-fledged research program to address the societal challenge.

In the public media a stream of articles emerged during the development and after the launch of the Deltaplan Dementie: articles announcing the plan, critical articles and journalistic articles aiming to provide an overview of the discussions. Discussions played out in an antagonistic fashion with participants being addressed as either protagonists or antagonists, and different schools of thought were being delineated.

Further interviews were conducted to trace the diagnostic and prognostic framings underlying the critique in the media. The critiques stemmed from framings of dementia as a

syndrome, which is a heterogeneous complex condition overlapping with normal aging processes leading to a rather uniform set of symptoms known as dementia, and as a condition of a person stressing that the person should be central. These diagnostic framings led to other strategies to deal with dementia. Rather than battling or curing dementia, preventing dementia and living well with dementia became the aims to strive for. Medical research had a much more humble position in these prognostic framings.

### ***Meanings of early diagnostics for Alzheimer's disease***

Early diagnosis for Alzheimer's disease gained multiple meanings within the process of developing a Deltaplan Dementie. In the motivational framing for a Deltaplan Dementie, early diagnosis was mobilized in relation to the disaster rhetoric of dementia and an innovation discourse. Early diagnosis played a triple role in averting dementia as a national disaster. A timely diagnosis was presented as an improvement in care and support for 'the patient of today' in terms of: (1) improving the quality of care for persons with dementia and their relatives, and (2) reducing health care costs. Early molecular diagnostics were considered to (3) contribute to a 'true solution' to dementia by speeding up research on prevention and disease modifying treatment, which, in the end, would reduce the number of persons with dementia in the future. In the innovation discourse early molecular diagnostics gained meaning as an important area for research and innovation in which the Netherlands excels. Investments in research on early molecular diagnostics for Alzheimer's disease would enable the Netherlands to maintain and confirm its leading competitive position in the innovation race between countries.

In the research program Memorable early diagnosis gained different meanings, depending on whether it was related to medical research or to application in clinical care. In the form of biomarker and imaging techniques, it gained meaning as a catalyst for medical research and as the next step to further medical research. However, in the realm of patient care the value of biomarker and imaging techniques was not self-evident and questions arose on the desirability, value and applicability of such novel tests. A timely diagnosis gained meaning as a possible improvement of clinical practice, but only when it would take into account the psychological and social factors and the needs of patients and informal caregivers.

In the polarized public debate on the Deltaplan Dementie the meaning of early diagnosis exceeded the medical and clinical domain. It was either positioned as an important research area, or it was subject to a wide range of objections and worries and considered as a symbol of the ongoing medicalization of dementia. These objections arose from an assessment of early diagnostics from the context of persons' daily lives and the in/exclusion of persons with a label Alzheimer's disease in society.

The setting of the Deltaplan Dementia showed that the efforts to collectively tackle the challenges of dementia unleashed a multitude of framings. A struggle occurred over who got to define what a dementia strategy should constitute. The reconstruction showed different

models on how framings were considered to co-exist: one model in which different framings co-exist as parts of whole. A second model in which framings co-exist as antagonistic positions and a third model in which framings co-exist as moving in different directions. I argued that it is important to reflect on which model is most appropriate in which situations and I illustrated the political consequences of the model that was used in the design of the dementia research program Memorabel.

### **8.1.5. Subconclusions: meanings of early diagnostics for Alzheimer's disease**

My efforts to answer the first research question "*What are the meanings of early diagnostics for Alzheimer's disease in different settings?*" revealed a multiplicity of meanings. In every setting interpretative packages show overlap and similarities with the packages described in other settings. In the methodological section (Chapter 4) it was explained that the outcomes of the analysis of meanings of early diagnostics were (1) empirical findings on how meanings are constructed in practices, and (2) the result of the ordering work conducted by the analyst.

Due to the settings and also due to the bottom up, inductive method of data gathering, every analysis generated a new list of interpretative packages. This raises the question whether it might be possible and worthwhile to aggregate findings from the different settings into a limited number of packages through which early diagnostics gains meaning (for example to come up with, say, three discourses, or six frames). In other words: how much more ordering work should I as an analyst do in this concluding section?

#### ***To aggregate or not to aggregate?***

The strategy to further aggregate findings implies certain assumptions: (1) the meaning of early diagnostics for Alzheimer's disease can be caught in a limited number of packages, to be recognized in the different settings and (2) the robustness of the analysis can be confirmed, or can be validated by triangulation of the outcomes of analyses in different settings.

Yet, this is not what I found. The interpretative packages as delineated in the four settings are not set in stone. If I would have studied different settings, or even the same settings a few years earlier or later, different packages would have been delineated. Probably these would partly overlap with the ones currently delineated, maybe new packages would have surfaced and new elements would have appeared in the packages. The packages delineated in different settings show many similar elements, but these are arranged slightly differently and the emphasis is different. This would render an aggregation in terms of a limited number of frames as a construct by the analysts and an artificial move. Therefore I refrained from further aggregation. Instead, I will reflect on what it implies that from each setting a different list of interpretative packages emerges.

In the settings I did find actors aggregating different meanings into large clusters. In the Deltaplan Dementia setting, for example, this happened. With the aim to understand

discussions about what a Deltaplan Dementia should constitute, opponents and proponents of the plan were constructed. At the same time, the actors involved in the discussion knew (as became clear from the in-depth interviews conducted) that the “for or against”, “cure versus care”, or “we versus them” kind of discussions were not doing right to the richness and nuances of reality. In-depth interviews showed much more nuance and overlap than such polarized discussions suggest. While aggregation occurs from time to time and place-to-place, these provide an interesting dynamic to be observed, rather than to be celebrated as clever aggregations of the different meanings.

What, then, could be the merit of not aggregating? Instead of merely focussing on the often repeated interpretative packages, the conclusion can also focus on the flexibility in each specific construction of meaning. In each setting, and even in every articulation, meanings are constructed in a specific way. What is made visible and invisible, foregrounded and backgrounded and which elements will be mobilized can differ in each articulation. Emphasizing this would value the ambiguity and messiness of the social world and show the richness, flexibility and nuance in social reality. The abundance of ways to construct meanings and that no meaning is set in stone, then becomes clear.

This strategy of stressing multiplicity would emphasize the politics of limitations. If there are repetitive similar articulations then this is a reproduction of meaning and this is an act. For example, if there would be a hegemonic situation, where early diagnostics is only understood through one discourse, then a focus on flexibility would immediately make clear that this apparent self-evidence is actually a rather remarkable outcome of power. By emphasizing the multiplicity of phenomena, the politics of the construction of meaning becomes visible again. Things could have been and can be different. There are many ways to understand early diagnostics for Alzheimer’s disease, and many ways to (en)act. And each construction of meaning is a political act.

Thus, by creating such aggregated frames I, as an analyst, would perform an act. I would divide the blurry, flexible, messy social world into big blocks. By doing this I would emphasize and reinforce a certain structure, which makes the world more ‘solid’ than the findings in the different settings show. Making big blocks can help to explain and understand recurrent patterns, while leaving out the (specific, flexible, playful, creative) not-repetitive parts of social reality.

In contrast, focussing on the flexibility of the data and the differences of meaning-making in each setting, would do justice to social reality and would emphasize the richness of social reality. It creates a focus on the agency and politics present in each articulation. By highlighting the complexity, messiness and blurriness of social reality the conclusions do justice to this reality.<sup>21</sup> Based on these considerations I will refrain from aggregating these

---

<sup>21</sup> In retrospect, the method chosen at the start of the research steers the conclusions. In chapter 4 I started by explaining the networked nature of meaning and the methodological choice to analyse medium-sized

outcomes into larger packages *as a conclusion*. However, *as a tool*, it might be useful to do so.

### ***Sensitivity through narrative knowledge***

Travelling between settings allows better understanding the next situation (see chapter 4 on the method for the tourist metaphor for conducting research). It reveals the narrative patterns that are commonly used in each setting (Bruner, 1986) and through which early diagnostics gains meaning within these settings. This type of research leads to a kind of knowledge generation similar to conducting multiple case studies: *“each setting helps to expand and refine our collective abilities to recognize what may be the case in this or that site or situation. Each new case will better equip us to understand (...) in the next site or situation – while remaining open to what so far has not been noticed. For what is irrelevant in one situation may be striking in another. What has been remarked upon in one case is subsequently a lot easier to recognise ones more.”* (Heuts & Mol, 2013, p. 139) A researcher following the tourist approach, sees, hears and is part of many unfolding stories. This creates a sensitivity of what is at stake and how everything is intertwined. Sharing these insights in this thesis in the form of interpretative packages, and highlighting what is at stake in each setting, showing the way different elements are interrelated with the issue of early diagnostics for Alzheimer’s disease, can equip stakeholders to navigate within the messiness and complexity. This type of knowledge is also described as narrative knowledge rather than as categorical knowledge (Bruner, 1986; Polkinghorne 2006) and can be compared to the knowledge generated from case histories in the medical field.

### ***Categorical knowledge, a radar as a tool***

Even though the different packages cannot be reduced to one another, there is a value in reducing the complexity to a limited number of frames. Such a limited overview could function as a ‘checklist’ or tool to be aware of what is foregrounded and backgrounded, what is included and what is omitted, what is made salient and what is silenced. I have made a radar (Figure 2) of the domains with stakes in early diagnostics for Alzheimer’s disease, as a tool to (at least) scan the scope of an argument, a research proposal, a discussion, a newspaper article, etcetera, and see which domains are foregrounded and which are backgrounded. The radar shows the minimum of areas that are influenced by (promises of) early diagnosis. If all of these domains are covered in a discussion, this does not mean that all is taken into account. The aggregation of a limited number of interpretative packages is a simplification. Yet, there is an instrumental value in simplifying – to recognize and understand

---

networks of elements that are articulated together. Therefore the concept ‘interpretative packages’ of clusters of elements that are articulated in relation to each other was introduced to analyse the different settings. By doing so, a certain level of aggregation was chosen, which steers the conclusions.

patterns in discussions. While simplifying can make things clear, Alfred Whitehead’s (1919) advice ‘seek simplicity and distrust it’ applies to the checklist/ radar offered.



Figure 8. 2 Radar of the domains with stakes in early diagnostics for Alzheimer’s disease

## 8.2. Technology assessment ‘in the wild’

*Does the study of meanings show **assessment** of early diagnostics ‘in the wild’ and if so, how is early diagnostics for Alzheimer’s disease assessed?*

Section 8.1. summarized the outcomes of the different settings, showed lists of interpretative packages in each setting and discussed how packages relate to each other. This section addresses if and how the study of the multiplicity of meanings shows assessment of early diagnostics for Alzheimer’s disease ‘in the wild’. Section 8.2.1. explains the use of the term ‘technology assessment’ as acts of assessment, rather than as formal procedures conducted by specialized agencies. In section 8.2.2. it is argued each interpretative package can be seen as a limited assessment, spanning the scope of implications of early diagnostics for Alzheimer’s disease, including assessment criteria, and showing discussions on the appreciation of early diagnostics on these criteria. Section 8.2.3. shows how each setting studied has invited specific threads of assessment. It is argued that how early diagnostics for Alzheimer’s disease is assessed depends on the stakes in particular settings. In section 8.2.4. shows technology assessment through recurring narratives across settings. The argument is that this is part of the cultural repertoire on early diagnostics for Alzheimer’s disease that are to be expected and dealt with. Section 8.2.5. goes back to the research question and provides the answers this thesis yielded.

### 8.2.1. Acts of assessment

As explained in Chapter 1 the notion of technology assessment ‘in the wild’ diverts from the conventional idea of technology assessment as a formal procedure conducted through specialized agencies. The assessment of technologies also takes place in interactions and sense-making outside of these procedures. (Rip, 1986, 1987; van Est & Brom, 2012)

Technology assessment as an act involves various elements, including *identifying* the scope of the development and who and what is involved; *valuating* the different implications according to specific criteria; *appreciation* or judgement of the implications of that technology; and pointing out possible directions for intervention. These acts of technology assessment are not confined to TA specialists and take place ‘in the wild’ all the time.

The empirical chapters focussed on the construction of meaning in interaction. These interactions always also include acts of (partial) technology assessment. The scope and the implications of early diagnostics for Alzheimer’s disease come forward via the multitude of webs of relations through which early diagnostics gains meaning. In each setting **acts of assessments** take different routes. Depending on what is at stake in each settings, meanings not only co-exist differently, the **evaluation** also takes place along different threads. The study shows recurrent discussions and narratives. There are **recurrent dynamics** between interpretative packages. The outcomes also show all kinds of dynamics occurring within and between the delineated meanings of early diagnostics for Alzheimer’s disease. These recurrent dynamics are to be expected when navigating in the field of early diagnostics for Alzheimer’s disease. Furthermore these dynamics show how implications of early diagnostics do not follow mechanistic cause-consequence routes. (Section 8.2.2.)

### **8.2.2. The scope of implications**

The scope and the implications of early diagnostics for Alzheimer's disease come forward via the multiplicity of interpretative packages through which early diagnostics gains meaning. The interpretative packages are webs of relations, consisting of clusters of elements that are connected to early diagnostics. Every individual interpretative package can be considered as a limited assessment in itself. For example, the interpretative package of early diagnostics as value for money, leads to evaluations in terms of '*does early diagnostics lead to increased or decreased quality of life and to increased or decreased health care costs?*' The interpretative package of early diagnostics as a life event, leads to evaluations in terms of '*how does early diagnostics fit into a person's life as a life event and is this a life event that suits a persons' life?*' Early diagnostics as part of an apocalyptic demography leads to evaluations as '*does early diagnosis lead to less persons with dementia?*' and '*does it lead to less health care costs?*'. Early diagnostics as scientific progress leads to evaluations in terms of '*is early diagnostics the direction to be pursued to understand Alzheimer's disease or to develop a treatment?*' Each interpretive package provides a limited number of unambiguous assessment criteria (valuations). The appreciation of early diagnostics on these criteria may not be easy and can differ. One may disagree on whether early diagnostics is the right direction to be pursued for scientific progress, or whether it leads to increased quality of life. Individual interpretative packages span the scope of implications of early diagnostics for Alzheimer's disease, include assessment criteria, and show discussions on the appreciation of early diagnostics on these criteria.

Throughout the empirical chapters it became clear that these interpretative packages do not co-exist as loose sand. In Chapter 6, analysing the HTA and Alzheimer Cafes settings, I used the metaphor of beads on a necklace to describe how meanings are lined up. The co-existence of meanings does not appear to be random. Some patterns have already been touched upon in the individual chapters, such as the aging-and-innovation discourse, a 'cure versus care' discussion, or the fragmented character of framing in newspaper articles. For this discussion I discern two types of patterns shaping the co-existence of multiple meanings of early diagnostics:

- a) patterns *within* settings. Every settings invites a particular way to deal with the co-existence of meanings. (addressed in section 8.2.3.)
- b) patterns *between* interpretative packages recurring *across* settings. There are larger narratives that re-occur in the different settings. These can thus be considered as part of the cultural repertoire, where early diagnostics is understood through narratives that are historically and culturally rooted. (addressed in section 8.2.4.)

### **8.2.3. Patterns *within* settings: Threads of assessment**

From comparing the outcomes of the different settings, it becomes clear that how meanings co-exist depends on *where* the analysis is conducted. Newspaper articles are generally relatively short and do not necessarily relate to one another, which leads to a fragmentation of meanings. The health technology assessment is a building activity where all data should accumulate and merge into one large assessment, with the aim to produce clear and solid

outcomes based on the best available evidence. In the Alzheimer Café setting, multiple meanings of early diagnostics co-exist next to each other. Multiple meanings side by side, provide a rich variety for the persons visiting the café from which they can use what applies to them and suits best to make sense of and improve their specific situation. In the Deltaplan Dementie first a strong story was constructed to draw attention and join forces, all meanings are said to exist side by side, while at the same time there is a political struggle going on as to who gets the power to define, which directions should be pursued, which issues should gain more or less priority, attention and funding, what exactly the problem is and which solutions are viable. There are strategic moves from actors trying to get attention for their work and to get their specific solution as a main priority of the plan.

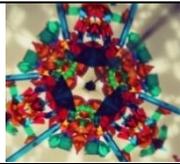
Each setting invites particular types of narratives, depending on the nature of that setting. There is a reason that people write newspaper articles, conduct a health technology assessment, organise or visit an Alzheimer Café, or get involved in (a discussion on a) national dementia strategy. There is something at stake. Newspaper articles report on issues that are considered of public relevance leading to narratives on why something is important, for what and for whom? Early diagnosis is mainly mobilized as contributing to solving bigger problems or achieving higher goals. In newspaper articles early diagnostics relates to benefits to society, science, economy and business, patients, and to the aging population. Also the question of in interest (who benefits?) comes to the fore. The main aim of the Health Technology Assessment is to achieve more certainty on the cost/benefit ratio of early diagnostics for Alzheimer's disease with the aim to provide evidence to policy makers on whether specific technologies should be used in standard clinical practice. It assesses the value of early diagnostics in terms of quality of life of patients and informal caregivers and its costs. To make a solid claim on the value of early diagnostics for Alzheimer's disease, a HTA model is built and clinical trials are conducted. This is a building activity where all data should accumulate and merge into one large assessment, with the aim to produce clear and solid outcomes based on the best available evidence. In the Alzheimer Cafés on the other hand all kinds of stories are told, to apprehend specific situations and to better cope with these situations. The central aim here is enabling persons to *tinker* (Mol, Moser, & Pols, 2010) in their specific situation to create a liveable and valuable daily life with dementia. The Deltaplan Dementie aims to unite forces to deal with dementia as society and mobilize resources to do so. This setting revolves around drawing public and political attention, and struggles between actors on which directions to pursue. In each setting, different meanings do not co-exist randomly, but are directed towards what is at stake in that setting.

I already referred to packages as 'beads' and conversations, meetings, or documents as 'necklaces'. Staying with the necklace metaphor, each setting offers a specific thread, stringing the beads in a particular way. Early diagnostics is mobilized in these settings, gains meaning and is assessed in line with these stakes.

To summarize: The multiple meanings of early diagnostics for Alzheimer's disease co-exist in particular ways, namely (1) fragmented, (2) as building blocks that should be in- or excluded, (3) as tools for tinkering and sense-making, and (4) as competing for the power to define. This is related to what is at stake in each setting. In this case this is (1) the potential relevance

or benefits to society, (2) evidence of its value and of the different technological options compared to each other, (3) how it contributes to help persons cope with real life experiences in their daily lives, and (4) power and politics in defining the problems to be solved and directions to be pursued and mobilizing attention and resources to do so. See table 8.2. for an overview.

**Table 8.2 Co-existence of meaning in different settings, depending on what is at stake**

Setting	Thread What is at stake	Co-existence of meaning	Image/metaphor
Dutch Newspaper articles	<i>Relevance / Benefits</i>	Fragmentation	
Health Technology Assessment	<i>Evidence</i>	Building blocks Inclusion, exclusion	
Alzheimer Cafés	<i>Experience / Coping</i>	Tools for tinkering, Telling many stories	
National Dementia plan	<i>Politics / Prioritizing</i>	Competing power to define Strengthening / weakening Foregrounding / backgrounding	

It thus becomes clear that the social and cultural value of early diagnostics for Alzheimer’s disease has been evaluated along the threads discussed above. How early diagnostics for Alzheimer’s disease is assessed depends on the stakes in that particular setting. This is a good reminder that technology assessment is never self-evident, objective or neutral, since a technology is always assessed along particular threads in relation to particular stakes. This also pre-structures the type of interactions (or mutual responsiveness in terms of Von Schomberg, 2011) that will occur. When it comes to assessing early diagnostics for Alzheimer’s disease, at least four threads matter:

Relevance: What is the (societal) relevance of this technology and whose interest does it serve?

Evidence: What is the (scientific) evidence of the potential value?

Experience: How will it fit into person’s daily lives/ practices and how will it improve these?

Politics and power: What problems are solved, which directions are pursued and which are not, which experts are considered authorities, where to are attention and resources directed?

#### **8.2.4. Patterns *between* interpretative packages recurring across settings: Meanings co-exist, but do not accommodate every arrangement**

A first way in which the study of the multiplicity of meanings shows assessment of early diagnostics 'in the wild' was through spanning the scope of implications (8.2.2.). The second way is through the threads of assessment (8.2.3). There is a third way in which the study of meanings shows assessment of early diagnostics 'in the wild'. The previous paragraph described different ways in which meanings co-exist *within* particular settings. Looking *across* the different settings allows the tracing of recurrent patterns in arrangements of interpretative packages. These recurrent dynamics between interpretative packages show the discussions and narratives that are to be expected when it comes to early diagnostics for Alzheimer's disease. Interpretative packages co-exist, but some arrangements are better accommodated than other arrangements.

These recurring patterns have been touched upon in the individual empirical chapters (Chapter 5 through 7). Examples are the mutually strengthening 'strategic marriages' of packages, such as in the apocalyptic demography narrative, or the aging-and-innovation discourse; relations of a rival nature such as the polarized cure versus care discussions; or the controversial relations between packages in the medical controversy on the nature of Alzheimer's disease.

The recurrence of these patterns in the empirical data (as well as in scientific literature), indicate that these are patterns which play out time and again. These are 'standard' narratives which are very likely to occur when it comes to early diagnostics for Alzheimer's disease. A sense of the kind of patterns between packages is a prerequisite to understand what responsible innovation might entail in the case of early diagnostics for Alzheimer's disease.

A list of recurring patterns is offered in this section, without claiming to provide a full overview of all (possible) patterns cutting through packages. While they play out slightly different in each instance, they show similarities and follow approximately the same route. For each pattern I (1) describe the recurrent dynamics between packages and characterize the relationship, (2) provide examples of occurrences in the settings studied, and (3) point to literature in which these relations are also identified. These are discussions and strategic alignments that can be expected to occur when it comes to early diagnostics for Alzheimer's disease.

The recurrent patterns that were observed throughout the different settings are:

- Scientific controversy
- Split between future promise and present developments
- Happy marriages

- Two sides of the same coin
- Tricky entanglements
- Polarization

### ***Pattern 1: Scientific controversy***

A medical controversy roams the scientific study of Alzheimer's disease. A controversy is a situation in which opposing views are expressed and the disagreement is strong. The controversy is about whether Alzheimer's disease should be considered a 'disease' for which the causes can be found and treated, called the *reductionist theory* by Lock (2013), or a 'syndrome' consisting of a cluster of symptoms of which the causes are diverse and highly intertwined with normal aging processes, called the *entanglement theory* by Lock (2013). This controversy has accompanied the medical study of Alzheimer's disease since the introduction of the term Alzheimer's disease (see also Chapter 2).

In the different settings this controversy played out a number of times. Interestingly this controversy was not explicitly present in the newspaper articles analysed up to 2010. In the HTA setting, discussions occurred about the disease model: whether Alzheimer's disease is a disease that should be defined according to pathological features, or a syndrome that should be defined according to the cluster of symptoms (interpretative package 4 in section 6.4.1.). These discussions were critical and made the predominantly reductionist assumptions of HTA (and the LeARN research program) explicit. In the Alzheimer Café setting, where Alzheimer's disease is dealt with as a condition of a person, the medical controversy did not play out. There is respect for medical specialists and gratitude towards scientists who work hard to come up with a treatment. In the Deltaplan Dementie setting, in contrast, the controversy heated up. Medical specialists publicly disagreed on the medical models to understand Alzheimer's disease and the subsequent research agendas to strive for.

Early diagnostics for Alzheimer's disease has a paradoxical position within this controversy. Early diagnostic instruments enable the tracing of changes in the brain and the body and are expected to lead to an earlier and more certain diagnosis. However, early diagnostic instruments do not necessarily lead to more certainty. We see that more detailed insight in the functioning of the brain and the body is accompanied by uncertainty about what these observations mean. Are they a symptom? Are they the pathology? Are they protective? Rather than leading to in depth knowledge, early diagnostics lead to increasing unknowns and uncertainties. This paradox was also observed by Burri, Carusi, & Asprakdaki (2014) for medical imaging techniques in general.

There is a huge amount of medical literature on this controversy (see also section 2.2.4.). Chapter 2 already presented two articles that appeared during the writing of this thesis that are highly illustrative for this controversy, namely Richards and Brayne (2010) and Selkoe (2012), see table 2.3. These articles start from the same observation that despite tremendous effort no disease modifying treatment of Alzheimer's disease has been found. Depending on the medical model adhered to, they come to totally different conclusions on the way to deal with Alzheimer's disease in society and the meaning of early diagnostics to serve these goals. The first article of Richards and Brayne (2010), adhering to the

*entanglement theory*, shows public health scientists arguing for a move away from precision in diagnostic classification, and towards a pragmatic approach to the needs of persons with dementia and their families and an emphasis on reduction of risk factors throughout life (Richards & Brayne, 2010). The second article of Selkoe (2012), adhering to the *reductionist theory*, argues for the moral obligation to never quit the quest to find a treatment and to make success from failure (Selkoe, 2012).

Early diagnostics gains meaning within this controversy and the controversy heats up when it comes to the issue of early diagnostics. This controversy is likely to remain playing out time and again when it comes to early diagnostics for Alzheimer's disease as it has played out during the last decades.

### ***Pattern 2: Split between future promise and present developments***

While the innovation of early diagnostics for Alzheimer's disease is made relevant through promises about better care in *the future*, in *the present* budget cuts are being made in public health care. This leads to a tricky split between on the one hand the future promises of early diagnostics and on the other hand current developments in health care. The development of early diagnostics is accompanied by promises that it enables timely care and support. These promises seem to presume the availability and accessibility of formal care and support in the (nearby) future. However, precisely that is becoming a matter of concern in the Netherlands. Health care policy is geared towards reducing formal care provision with policies emphasizing self-reliance, informal caregiving and staying at home as long as possible. Hence, the promises of early diagnostics to enable timely care and support become problematic. The relevance of early diagnostics for Alzheimer's disease for patients depends not only on how well these tests perform in a clinical setting, but also on developments in the health care system in which they will be embedded.

This split is particularly present in the public media setting, where in the packages 'apocalyptic demography' and 'health care provision' early diagnostics is deemed necessary to maintain a viable health care system, by allowing patients and families to prepare more effectively for what is ahead. This would enable persons with dementia to stay at home longer and thus reduce health care costs. Within this line of reasoning, early diagnostics are turned into a solution for the reduced availability of formal care. While the focus on self-reliance and informal caregiving may reduce health care costs, in the packages 'successful aging' and 'good life and death' this situation is explained as elderly having to fend for themselves and a moral bankruptcy of society that fails to organise health care in a reassuring way. In the Health Technology Assessment setting (Chapter 6) the worry about the availability of care is turned into a prerequisite for innovation. It is emphasized that early diagnosis should be part of management of the disease in the early phases. This package is a response to the worry that early diagnostics became too much a goal in itself. In the Deltaplan Dementie early diagnosis is also coupled to improving health care, but through another route. In the *research program* the label 'Alzheimer's disease' enables, when it is provided to patients at an early stage, health care policy makers to trace persons with dementia through the health care system and thus to optimize the system as a whole in

terms of health care costs. This could help in maintaining a viable health care system. In the *public debate* on the plan the emphasis on research on the causes of dementia and a speedy diagnosis are questioned, and it is stated that more attention is needed for care provision. In sum: while future promises of early diagnostics include enabling care and support at a timely stage, in the present the accessibility and quality of public health care are becoming a matter of concern.

### ***Pattern 3: Happy marriages***

Besides frictions between packages, there are also happy marriages between packages – packages that strengthen each other and together form a convincing narrative. A happy marriage repeatedly occurring throughout this thesis is the following:

- A huge societal problem is arising. The numbers of persons with dementia is expected to increase drastically, while at the same time the number of persons to provide care for the elderly is decreasing. Both are demographic changes due to the aging society. This will lead to a crisis in health care and economy. Action needs to be taken to prevent a crisis.
- Dementia is a horrible condition. It is our moral imperative to do something about it. We cannot leave these persons suffering.
- To solve these problems (investments in) research and innovation are urgently needed.

This happy marriage is particularly present in the Deltaplan Dementie setting (Chapter 7), and also a repetitive narrative in the newspaper articles studied in chapter 5. Within the Health Technology Assessment setting this happy marriage was not explicitly articulated, although it served as a legitimation of the LeARN consortium as a whole. Also in the Alzheimer Cafés it was not prominently articulated or addressed, yet sometimes entered when for examples persons visiting the café were worried about being a burden to society. This narrative appears in the legitimation of funding for research and innovation and in public discussion and debate and less so outside of these realms. In chapter 6 the political effect of the ‘aging and innovation discourse’ has been discussed. It backgrounds among others difficult questions on how early diagnostic tests will become part of good patient management, uncertainties about the value for money, worries about budget cuts in care provision and reimbursements, the (social) effects of the label Alzheimer’s disease for a person, the life event this signifies, and how this changes the definition of Alzheimer’s disease.

The happy marriage of looming disaster, a moral imperative to do something about it and science as a solution is a strong narrative which has repeatedly been described in different strands of literature on dementia and aging studies, as well as in literature in the field of science and technology studies. I will address a number of related concepts that have discussed the same (kind of) narrative. This narrative is referred to as, amongst others, the ‘health politics of anguish’ (Chaufan et al., 2012) and ‘apocalyptic demography’ (Robertson, 1990). These are described in Chapter 2. These are strategies that have been used to put

Alzheimer's disease on the public agenda. Over the past decades, these strategies have proven to be successful in drawing attention and mobilizing resources. In Science and Technology Studies the same narrative is seen in general amongst innovation for the elderly. Mort refers to this narrative as the 'crisis account of aging' (Mort & Roberts, 2010; Ney, 2009).

Neven showed the presence of an 'aging-and-innovation discourse' (Neven, 2011) as general legitimation for research funding, emphasizing the need for research and innovation to deal with the aging society. Neven explains that this narrative is attractive because of the triple-win situation it suggests. Elderly win, by maintaining an independent lifestyle and well-being and by reducing the load on informal caregivers. Society wins, by delaying or eliminating the need to live in expensive care facilities, reducing the burden on the health care system. Economy (business, science) wins because the innovations can serve an enormous market due to the rising costs of health care, manpower shortage and the aging population.

Early diagnostics in this happy marriage can also be understood as part of the 'aging enterprise' (Estes, 1993), a term that has also been used since the 1980s, to delineate a happy marriage between the aging population and health care provision. The term 'aging enterprise' refers to the increasing number of aging persons (or in this case persons with dementia) framed as a problem to be dealt with by designated care professionals, medical researchers and industry. Within dementia studies the same coalitions have been described following the disaster rhetoric (e.g. Robertson, 1990; Robertson, 1997). Robertson describes an over-servicing of health care due to provider-induced demand for health care services. She explicitly refers to the widening of the diagnostic category dementia and the expansion of what is referred to as Alzheimer's disease as creating a 'medical space' where the medical profession is the authority and health care services are the providers. However, while the care for elderly is a growth sector for health care services and industry, many of what they service may not be health problems at all.

Metaphors are important framing devices in this happy marriage and are omnipresent in newspaper articles and the Deltaplan Dementia (e.g. Diesfeldt, 2014). These include many disaster metaphors, such as a flood, or a 'tsunami of persons with dementia', but also the 'epidemic of the future'. The persons with dementia are 'victims', 'stricken by dementia', and dementia is 'the enemy of the people'. This is illustrated by dramatical personal stories of patients with dementia and informal caregivers. Following this disaster rhetoric, the heroes arise to save us. In this context 'hope' and 'fate' are repeatedly used words.

Fear for catastrophes and hope for salvation have always accompanied technological development. The prediction of catastrophes has a paradoxical moral dimension. Grunwald, an expert in vision assessment, points to the duty to expect the catastrophe in order to prevent the catastrophe (Grunwald, 2007). However, while the proclamation of possible future catastrophes can boost developments in a desirable direction, it can also "*intensify the impression of disorientation and uncertainty*" (Grunwald, 2007, p. 386). Longino, a professor in sociology of aging, argues that this kind of framing is not very constructive: "*When a crisis is manageable, it is managed. When a crisis is overwhelming, as in the case of*

*the demographic imperative, it is only depressing” (Longino, 2005, p. 81). Furthermore, Longino has made a strong case against this apocalyptic picture of demography, not only because it is depressing, but because this kind narrative puts the well-being of older people at risk and is ageist as well: “They are not people anymore; they are ‘the burden’. From this negative point of view, these elderly people are not capable of contributing creative solutions to meeting their own needs. They have no agency. They are inert, the burden. The sky is falling, and it is falling because there are too many elderly people” (Longino, 2005, p. 79).*

These happy marriages form a strong coalition and provide a successful strategy to mobilize attention and resources for Alzheimer’s disease. Its performativity, however, is problematic in at least three ways. Firstly, it is problematic in what it leaves out, namely the medical controversy on the nature of the condition and whether science is the way to solve the problem. Secondly, this narrative uses and instigates fear to boost investments in research and innovation. This is a morally questionable strategy. Thirdly, through the metaphors used, this narrative literally creates victims. All in all, the question arises whether the purpose justifies the means (Van Gorp, Vercruyssen, & Van den Bulck, 2012).

#### ***Pattern 4: Two sides of the same coin***

Early diagnostics gains meaning as providing relief for the fear and worry for dementia, as well as contributing to the desire to *not* get dementia. The fear for dementia and the strive towards successful aging appear as two sides of the same coin. While terms such as successful aging, healthy aging, or active aging point into the desired direction of growing old without complaints, Alzheimer’s disease becomes symbolic for a failure to do so.

In the public media setting, the packages on successful aging and on fear and worry about dementia form two sides of the same coin, as different expressions of the desire to keep Alzheimer’s disease at bay. The interpretative package ‘early diagnostics as identifying a biomedical condition’ in the Alzheimer Café setting expresses that comforting persons who are overly worried is one of the reasons why an early diagnosis for Alzheimer’s disease is important and why persons visit a memory clinic. Also in the discussions surrounding the Deltaplan Dementie the Deltaplan was criticized for playing onto the fear for dementia to gain funding for a medical research program. Furthermore it was observed that public debates about dementia revolve around either euthanasia or a better diagnosis and treatment. This has led to the call for a different societal strategy to dementia, namely a strategy geared towards acceptance and inclusion, enabling persons to live well *with* dementia.

The strive towards successful aging and the fear for dementia, present in interpretative packages on early diagnostics for Alzheimer’s disease, show different responses to the same wish: to keep dementia at bay. While most research on how early diagnostics affects quality of life focusses on persons undergoing such diagnostic tests (in memory clinics, or in clinical research), early diagnostics for Alzheimer’s disease also affects the lives of elderly without complaints and without undergoing these tests, by feeding into their fears or hopes. Elderly who are very alert on symptoms of dementia (‘the worried well’ (Corner & Bond, 2004)) are the key subject in this narrative.

This phenomenon is referred to as ‘anticipatory dementia’ (Cutler & Hodgson, 1996) or ‘dementia worry’ (Kessler, Bowen, Baer, Froelich, & Wahl, 2012): the emotional response to the perceived threat of developing dementia. The worry whether age associated memory changes are an early warning signal or a harbinger of dementia in the future “*may represent another potential threat to psychological well-being*” (Cutler & Hodgson, 1996, p. 663) that is generally not taken into account in studies on interventions for dementia.

The development of early diagnostic instruments, and terms such as MCI, early Alzheimer’s disease, or pre-symptomatic Alzheimer’s disease, strengthen the image of Alzheimer’s disease as a creeping condition that may already be doing its destructive work within a person, without the person noticing it. This means that while early diagnostics may contribute to the goals of successful aging, it will simultaneously contribute to an increased fear and worry for the situation when aging occurs not as successfully as hoped for – for failing to age well. This dynamic suggests that early diagnostics feeds into the same problem it aims to solve. Early diagnostics appears as a snake that bites its own tail: on the one hand the promises of early diagnostics for Alzheimer’s disease include offering comfort to overly worried persons, while on the other hand they are feeding into the fear for having Alzheimer’s disease and thus create even more ‘worried well’ seeking comfort.

#### ***Pattern 5: Tricky entanglements***

End of life discussions have been a recurring topic in Dutch society over the last years and particularly end of life discussions in the case of dementia. In these discussions tricky entanglements occur between different interpretative packages. In principle, a medical diagnosis enables persons to anticipate the expected disease progression and prepare for it. This can include choosing for available medical or psychosocial treatment, organize care provision and living conditions, or write a testament. However, it also means that persons can wish to *not* advance into dementia and organise their end of life.

In the public media setting (chapter 5) the euthanasia issue is an important element in the package on ‘good life and death’, where it is also stressed that this is a precarious issue because of the entanglements with expectations of aging, and fear of an impoverished health care system. In the Alzheimer Café settings I visited these entanglements were not addressed, although reportedly end of life issues were addressed in other Alzheimer Cafés in the Netherlands. In the Health Technology Assessment setting the end of life discussions are not present in the packages. The topic was addressed in meetings, but a self-chosen death does not fit with the assumptions of the HTA models. For example it does not fit the ‘quality adjusted life years’ scale where death means the lowest quality of life. Furthermore, while a self-chosen death results in a reduction of health care costs, it is not a desirable direction to pursue in health care policy. In the public debate on the Deltaplan Dementie, the increasing number of vital elderly signing advanced directives and persons with early Alzheimer’s requesting for euthanasia and assisted suicide were a matter of concern (chapter 7 part B). The promises of early diagnostics are entangled with the public portrayal of dementia as a horrible disease and a burden to society, the fear of elderly to develop dementia and the

strive for successful aging (see 8.3.3.), news about budget cuts in health care provision and impoverishment of elderly care (see 8.3.2.) and a widening of the regulations for euthanasia.

A reason to seek an early diagnosis is the *'temptation of beneficent euthanasia'* (Johnstone 2013, p. 40). Early diagnostics for Alzheimer's disease can enable a person to request for euthanasia at a moment in life where one is still considered to be mentally capable of such decisions. *"The assumption here is that patients in a very early stage of dementia can still have enough awareness to suffer unbearably from the prospect of increasing mental decline. Put differently: the earlier a diagnosis can be established, the greater the chance to have one's (still competent) request (...) complied (...)"* (Hertogh et al., 2007, p. 51). This only makes a more certain and accurate diagnosis at an earlier stage more important. Because if a person decides for a pre-empted death based on this diagnosis, it has to be absolutely certain that the diagnosis is accurate.

This 'beneficent euthanasia' is highly related to a general discomfort with dementia in western hypercognitive (Post 2000) individualized societies. *"Nothing is as fearful as Alzheimer's Disease because it violates the spirit of self-control, independence, economic productivity and cognitive enhancement that defines our dominant image of human fulfilment"* (Post 2000, p. 245). Many elderly in society fear the prospect of dementia and are looking for means to avert the mental decline caused by dementia. It is quite telling that participants in the public debate on euthanasia in the case of (early stage) dementia *"are mainly vital seniors who are fearful of developing dementia, while the voice of people with dementia themselves is totally absent in this arena"* (Hertogh et al. 2007, p. 53). This is in line with the dynamic addressed in the paragraph on fear and hope (Section 8.3.3.). This desire to be spared a life with dementia feeds into the desire for 'a pill' to cure or prevent dementia, as well as into the desire for a self-chosen death. Johnstone refers to euthanasia, physician-assisted suicide and advanced directives as 'terror management': a symbolic defence against this fear. *"Euthanasia and physician-assisted suicide is framed and expressed in a way that, paradoxically, offers individuals reassurance and protection (terror management) against their death-related anxieties (...)"* (Johnstone, 2013, p. 389).

In the Netherlands there is a long history of discussions on euthanasia. Euthanasia in the case of dementia emerged as a public issue in the 1980s: the time in which public attention for dementia increased and dementia was labelled 'Alzheimer's disease', and in which the new generation of vital elderly referred to as the 'third generation' or the 'leisure generation' emerged (see chapter 2). Initially debates in the Netherlands focussed on advanced directives and on late stage dementia - both problematic and hardly ever granted. (For a full overview of the Dutch debate on euthanasia/assisted suicide in dementia cases up to 2007 see Hertogh, de Boer, Dröes, & Eefsting, 2007.) Yet with the development of an early or earlier diagnosis of Alzheimer's disease new discussion arises. Persons for whom the prospect of dementia leads to unbearable suffering seek an early diagnosis to request for euthanasia. Yet, due to the tricky entanglements, this suffering may be the result of many factors: fear for the illness, a desire to maintain autonomy up to death, but also the negative public representations of dementia, a fear for neglect in formal care, or because people don't want to be a burden to their family or society. Studies that were conducted on the experience

of persons with early stage dementia reveal that the experience of dementia involves not only the mental and physical complaints and the prospect of progression. Persons are often deeply affected by the negative treatment they get, the effects of social exclusion, and the representations of dementia as a devastating disease, more than by the actual symptoms at that moment. The question is whether an early diagnosis coupled to requests for early euthanasia are an acceptable and desirable way to cope with dementia. These discussions are usually followed by a plea to manage Alzheimer’s disease with compassion and care and the use of other terms and metaphors to enable more constructive representations of dementia.

**Pattern 6: Polarization**

When stakeholders compete with each other over attention, money or power, discussions about Alzheimer’s disease and early diagnostics tend to polarize and proceed in a predictable manner. Stakeholders get ordered according to whether they are, say, in the ‘cure’ or in the ‘care’ camp, or whether stakeholders chose for the strategy of *battling* dementia or *living with* dementia.

**Table 8.3. Polarized ordering of positions to deal with dementia**

Cure	Care
Battling	Living with
Dementia is a real disease	Dementia is part of aging
We cannot leave these persons suffering	Accept
Need for medical interventions	Need for cultural changes, social work, care and psychosocial interventions
Investments in early diagnosis and treatment	Investments in care and support
Horrible disease	There is value in life with dementia
Burden to society, stigma	Part of society, inclusion

The meanings of early diagnostics found in the Health Technology Assessment setting and the Alzheimer Café setting were related to the cure versus care discussion in chapter 6. Both settings did not show the polarization as such. One of the reasons was that the promises of early diagnostics for Alzheimer’s disease address both the ‘cure’ and the ‘care’ strategies of dealing with dementia. Another reason is that the analysis did not show just two lines of reasoning in which early diagnostics gains meaning, but a patchwork of meanings, interests, and goals. While ‘cure’ and ‘care’ are terms that are related to treating patients (through curing or caring) the meanings of early diagnostics are broader than merely treating patients, such as the organisation of the health care system, medical research agendas, business and economy and persons with a life (contrary to patients with a medical condition). The cure-versus-care dichotomy did surface from time to time, but only when either allocation of research budgets or the attraction of patients (clients) by health care providers were at stake. The dichotomy was then used in argumentations to mobilize allies or resources.

In the public media setting earlier studies analysed media messages as either contributing to a medical framing of dementia or not – taking the dichotomy as the starting point of analysis. The approach to framing analysis in this thesis showed that in newspaper articles early diagnostics was understood through a multitude of framings. This shows a more diverse picture than a dichotomy, including elements that are related to the ‘cure’ and the ‘care’ side of the polarization.

The Deltaplan Dementie setting showed a perfect example of the polarization pattern, particularly in the public debate where stakeholders were positioned as ‘for’ or ‘against’ and positions were simplified when competing for attention, allies, or resources. The phenomenon is well-known in the literature (see for example Chaufan et al., 2012; Kitwood, 1990; Lock, 2013). A recent publication of Manthorpe and Iliffe (Manthorpe & Iliffe, 2016) provides an interesting analysis of the polarization in the dementia debate and the consequences of this dialectic on dementia policy.

### **8.2.5. Subconclusions: technology assessment ‘in the wild’**

The second research question was: *Does the study of meanings show assessment of early diagnostics ‘in the wild’ and if so, how is early diagnostics for Alzheimer’s disease assessed?* The short answer is: yes, this study has shown assessments of early diagnostics ‘in the wild’.

In fact, each interpretative package contains a limited technology assessment in the wild. The multitude of interpretative packages that we encountered in the four settings spans the scope of the implications of early diagnostics for Alzheimer’s disease. Moreover, each individual interpretive package provides a limited number of assessment criteria (valuations), and thus shows a limited assessment in itself (section 8.2.2.).

We could add that in each setting early diagnostics is assessed along particular threads. These threads, particular for each setting, structure the co-existence of meanings. Each setting invited a particular way of dealing with the co-existence of interpretative packages: through fragmentation, inclusion/exclusion, as tools for tinkering, and competing with each other. This is related to what is at stake in a setting, which structures the co-existence of meanings along different ‘threads’: the potential relevance or benefits to society, evidence of its value, how it helps to cope with the real life problems of dementia, the power and politics defining problems to be solved and directions to be pursued. How early diagnostics is assessed depends on the stakes in each setting.

Finally, technology assessment in the wild takes place through recurring narratives and discussions that are part of the cultural repertoire. Across settings recurrent dynamics between interpretive packages were found. The recurrent dynamics between interpretative packages include a controversy, a split between developments in the present and promises for the future, a happy marriage, two sides of the same coin, tricky entanglements and a polarization. These narratives and discussions show that implications of early diagnostics follow many routes. These are patterns that play out time and again, are known in the field, and are to be expected to play out again. They are standard narratives and discussions that are to be expected and dealt with.

### **8.3. Responsible innovation**

*What does the study of meanings imply for the notion of **responsible innovation**?*

Thus far, we encountered the multiplicity of meanings of early diagnostics of Alzheimer's disease and we studied the kaleidoscopic multiplicity of meanings. The different ways in which meanings co-exist in the four settings (section 8.2.) also showed how the co-existence of meanings depends on the stakes in a setting (paragraph 8.2.3. Table 8.2). Finally I identified a number of recurring patterns that characterise the dynamics of co-existence and that can be anticipated (section 8.2.4). I argued that these findings are forms of technology assessment occurring in the wild. The last step of this thesis, then, is to reflect on what these findings imply for the notion of responsible innovation.

First of all, we should acknowledge that the ambition of this research to contribute to responsible innovation is not straightforward. Yes, some would claim that acknowledging the complexity (Stirling, 2010) and the uncertainties and ambiguities (M. Hajer & Laws, 2009) surrounding the development of early diagnostics for Alzheimer's disease would allow for a reflective way of acting on early diagnostics for Alzheimer's disease. Yet, an initial reflection (in chapter 3) also yielded several 'quandaries' of responsible innovation: problematic, difficult and ambiguous conditions that somehow require fundamental and practical decisions. After the explorations of early diagnostics of Alzheimer's disease in literature (chapter 2) and after studying meaning making in practice, we are now in a position to reflect on what this route through the quandaries of responsible innovations has yielded.

Below I will argue that the tourist detour of this thesis yielded the following contributions to the theory and practice of responsible innovation:

- 1) An awareness of different modes of thought about implications of new technologies that surfaced throughout this thesis: a linear, a network, and a patchwork mode (section 8.3.1).
- 2) The importance of 'the benefit of the doubt' (section 8.3.2.), including:
  - a plea for sensitivity of interrelatedness and awareness of the fringes;
  - the statement that reducing side-effects is quite impossible without affecting many other relations;
  - the problem with solving problems;
  - an argument for humility;
  - the need for balancing acts.

#### **8.3.1. Understanding implications of early diagnostics for Alzheimer's disease**

How does a technological development relate to its implications? This whole thesis has been written from the premise that early diagnostics gains meaning within networks of relations and as a result it is part of what could be referred to as a '*patchwork understanding*' of

implications of early diagnostics for Alzheimer's disease. This contrasts with two dominant alternatives that were encountered in this study: a *linear understanding* in which causes and consequences are like domino blocks, and a *network* understanding that stresses interrelatedness and interdependence.

In this section I will discuss these three and argue that *patchwork understanding* of implications, which emerges from the approach of this thesis, does more justice to the multiplicity of meanings.

### ***Linear understanding***

Consequences of early diagnostics in this model are constructed as following a linear sequence. The sources of the changes are the diagnostic instruments developed in the lab, which will impact diagnostic practice once they are implemented, and will then have consequences for the patients, informal caregivers and wider society. This linear model is at the heart of the health technology assessment setting. Also in the research program of the Deltaplan Dementie the linear notion of consequences of innovation was visible.

Characteristic within this understanding are the boundaries or restrictions between the subsequent steps. Formal procedures are in place to determine whether early diagnostics are allowed to progress to the next step. There is boundary work about where early diagnostics for Alzheimer's disease should be implemented, with characteristic sentences such as 'this is still in the research phase', 'it is meant for research purposes only', 'early diagnostics are meant to improve care provision, not as a ticket for euthanasia'.

This linear understanding shows a rather mechanical version of implications of early diagnostics for Alzheimer's disease. Within this narrative for example medical research is the source of knowledge and innovation and different consequences of this innovation follow each other, like billiard balls or domino-blocks. The term 'impact' suits this reasoning – there is a cause and an effect and effects only happens when there is physical contact.

In literature on innovation this understanding of implications is resembled by the ever present linear model of innovation (Godin, 2006). In medical research the concept of 'translational research' relates to this understanding of consequences (see for example Van der Laan & Boenink, 2015 for a discussion of these concepts). Within this linear understanding, consequences of innovation are mainly linked to the implementation of the technology, and to restrictions or criteria for implementation.

### ***Network understanding***

Another understanding that was present in the different settings suggests that diagnostic innovation is intertwined with many other processes such as changes in diagnostic categories and cultural images of dementia. In the HTA setting, for example, in the package 'early diagnostics as changing the definition of Alzheimer's disease', or in the Alzheimer Café in the package 'early diagnostics as labelling persons' it is observed that the public understanding of Alzheimer's disease may no longer coincide with the functioning of persons diagnosed as such. In the Deltaplan Dementie setting critiques arose on the medicalization of dementia,

arguing against the dominance of the medical side, and discussions unfolded on the medical, psychological and social aspects of early diagnostics. This dynamic also appeared in the theory chapter (chapter 2) as the disease-illness-sickness triad, which suggests that changes in one of the three concepts affect the other two. The disease-illness-sickness model shows that you cannot change a disease definition without it affecting the illness- and the sickness-side.

This is a rather organic approach to implications of early diagnostics for Alzheimer's disease. Changes in one area influence other areas directly and consequences of early diagnostic instruments are mentioned without them even being implemented. And more precisely that one package cannot be isolated from the other in terms of the creation of consequences. While the implementation of the technology may be restricted from entering other practices, this network understanding stresses that consequences are not restricted to the use of technology in a particular practice.

The historian of technology Thomas P Hughes (Hughes, 1986) coined the term 'seamless web' to describe the same phenomenon of the network understanding. He describes two types of understanding of the relationship between technological development and so-called contextual factors (social, political, economic, and so on). He refers to a mechanical, analytical way of thinking (what I referred to as the 'linear understanding') and a systematic, organic and holistic way of thinking (here referred to as 'network understanding'). He also states that when shifting from a linear model to an organic model, "*the background merges into foreground*" (pg. 290). Technological systems are developed in a social or political background, which is reflected, or embodied, by the technology. This immediately shows the difficulty with any such distinction. Also Actor Network Theory provides a network understanding of science and innovation. In Actor Network Theory (Latour, 1987) scientific objects are considered to become more 'real' as they become entangled in webs of cultural significance, material practices and theoretical derivations. The same holds for technological developments (Latour, 1996). This means that the image of new scientific findings impacting on society is not correct. The entanglements are crucial.

For responsible innovation the mode of understanding used for determining implications of early diagnostics for Alzheimer's disease matters. In the linear understanding a new technology or scientific knowledge is developed or even invented in a laboratory and then impacts society. The mere question 'what are the implications of early diagnostics for Alzheimer's disease?' seems to imply a linear sequence.

This thesis shows a less linear and more networked understanding of implications of new technologies: all is relational. The research and development of biomarker and imaging techniques to enable an early diagnosis of Alzheimer's disease is shaped by numerous social processes and adds to the shaping of numerous social processes, because it is entangled with them.

### ***A patch-work understanding***

The packages delineated in the settings reveal webs of relations. Yet, on closer inspection, the term 'seamless' fits less well. The creation of meaning through webs of relations (interpretative packages), show a patchwork of webs of relations partly overlapping, partly differing, partly strengthening each other, and partly causing friction.

The investigations for this thesis started from different settings where early diagnostics enters the conversations going on in there. Note that there was no a priori assumption on where reality is constructed, and no place was privileged to define what matters of concern are. The study of settings shows a multiplicity of realities in progress, and points to the webs of relations in which they are produced, and how these interfere with each other (through happy marriages, controversies, frictions, etcetera). It shows how specific settings make some meanings more visible and other meanings less visible, and how each setting has its own dynamic of how meanings interrelate. These outcomes are in line with the work that Ingunn Moser conducted on dementia (Moser 2008; 2011) and Mol's work on ontologies in medical practice (Mol, 2002).

For the notion of responsible innovation these different models point in different directions. The next section will elaborate on what a patchwork understanding of consequences of early diagnostics implies for the notion of responsible innovation.

### **8.3.2. The benefit of the doubt**

#### ***Sensitivity of interrelatedness & awareness of the fringes***

The constant outcome in every chapter of this thesis has been that wherever you look, early diagnostics for Alzheimer's disease gains multiple meanings. Wherever you start, whatever entrance is chosen, a web of relations expands from there, with crosslinks and overlaps between interpretative packages and between settings. We found that early diagnostics gains meaning through *a patchwork* of webs of relations, and that *interrelatedness* is key to understanding social implications of early diagnostics for Alzheimer's disease.

We also found that in each conversation, interview, meeting, document, setting (and also in each interpretative package) particular elements are highlighted and other elements are less visible. The word 'side-effect', for example, already reveals that there are a lot of backgrounded aspects. Clearly, any narrative on this technology has its boundaries, and, that travelling across settings, as done in this thesis, reveals a broader view of what is at stake, what is included and what is left out in specific practices or discussions, and whether this is okay or not.

There are some lessons to be learned for responsible innovation from these insights. Firstly, the notion of interrelatedness stresses that responsible innovation means more than legitimizing an innovation with a particular construction of meaning. It invites to be aware of

the multiplicity of meanings used and to be sensitive to how words, interpretations and actions influence each other. It might be possible to *think* in boxes, but not to *act* in boxes.

Secondly, how to think of reducing negative (side-)effects of a new technology when everything is connected and when negative effects cannot be easily reduced without causing other effects? Aiming to optimize one issue will affect other issues. Rather than resolving, this asks for a continuous balancing act.

Thirdly, while simplification is a necessity in a complex world, it is also vulnerable to manipulation. Leibing argued how oversimplification takes place in the form of shortcuts in argumentation to get to the desired conclusion, leaving out considerations that may have led to a different conclusion (Leibing, 2016). A story that tucked away the fringes and leaves you with barely any food for thought has polished away considerations. Good stories, round stories are to be distrusted. If something sounds too good to be true – it probably is. Reality is messy and there are multiple meanings, ambiguities, controversies, uncertainties and loose ends. The message remains “keep it complex” (Stirling, 2010). By creating awareness of considerations that have disappeared from the surface, I hope to enable actors to reflect on the choices that are made, and can be made in every situation, again and again.

### ***Intervention in complex networks of relations***

Because everything is connected somehow, just reducing one effect will be a hard thing to do. The dynamics discussed in paragraph 8.2.4. reveal patterns of implications that differ from cause-effect relations, such as:

- *A means to an end*: early diagnostics for Alzheimer’s disease often figured in interpretative packages as a means to an end, a bigger problem or a higher goal (see 8.1.1.). Addressing the undesirable consequences or implications of early diagnostics thus probably also involves reconsideration of the end, the bigger problem or the higher goal.
- *Start of a river*: the development of early diagnostics for Alzheimer’s disease fits into a trend of biomarker research, a general aim to prevent diseases rather than to cure them, the rise of a generation of elderly that expect to age actively, and so on. This resembles the start of a river from many little streams, with early diagnostics for Alzheimer’s disease as one of the little streams. This means that the sequence of implications and consequences cannot be related back directly and causally to the development of early diagnostics for Alzheimer’s disease alone.
- *Two sides of the same coin*: aiming for one desirable outcome may simultaneously lead to less desirable consequences elsewhere. An example is the relation between successful aging and the worry about dementia. The aim for successful aging is inherently connected with the fear of failing to age successfully.
- *Positive feedback loops*: there are also mutually reinforcing relations, as we have seen in the combination between the challenge that dementia poses on society, the

promises of scientific research and technological development and the desire for economic growth.

- *Attenuating consequences*: relations that weaken implications also exist, as with the 'care' pole of the polarized debate which aims to reduce the force of the 'cure' pole that deals with dementia through predominantly medical intervention.
- *Pulling the blanket*: when you pull the blanket on a two person bed with one small blanket to keep you warm, the other person will react by also pulling the blanket to keep warm, and so on. This seesaw dynamic is visible in the polarization patterns that occur.

It is very difficult, if not impossible, to change one aspect without affecting many other relations.

### ***The problem with solving problems***

The search for responsible innovation typically brings phrasings about innovation solving problems. The research program on responsible innovation that funded this thesis says, for example: "*When it comes to solving global problems (...), people have great expectations from technology and science*" and "*considering the solutions that technological and scientific know-how is capable to offer to societal issues and problems, it is important to examine their ethical and societal aspects*" (NWO, 2008). In other words, science and technology could offer solutions to societal problems, but since they can also have undesirable consequences, these should be anticipated and averted for the technology to be societally acceptable. At the end of this thesis, this does not appear to be the most obvious vocabulary to address responsible innovation.

Following the results this thesis, responsible innovation is not about an innovation 'as such' being acceptable or not, and it is not about reducing negative, undesirable or unintended consequences. It is all about multiplicity and relations. Early diagnostics does not simply appear as a solution to a problem, but as another element taken up in a multitude of practices, gaining many meanings. These observations link to the concepts of 'tinkering' (Mol et al., 2010), 'bricolage' (Strauss, 1962) or even 'jugaad' (Sekhasaria, 2013). Bricolage refers to the skill to put pre-existing materials together to make something new with whatever is at hand. The term 'tinkering' is used to argue that care in practice involves persons, technologies, knowledges and so on. All these things need 'tinkering' to provide good care. So knowledge and technologies, like early diagnostics for Alzheimer's disease, are not merely functional tools for those dealing with Alzheimer's disease in practices, but something to be tinkered with persistently to provide care in practice. Unfortunately, many work on dementia consists of 'jugaad' innovation. Jugaad, an Indian word, refers to improvising solutions with scarce resources.

Some problems can be solved, others should be dealt with. Early diagnostics for Alzheimer's disease was introduced as one of the promising innovations to find (partial) solutions for

dementia as a large societal problem. Alzheimer's disease is likely to remain an issue that should be dealt with medically, individually, as a family, societally, economically, and so on. Early diagnostics for Alzheimer's disease then represents another option, another tool at hand for those dealing with Alzheimer's disease. This dealing with involves constant processes of bricolage, tinkering or jugaad, to suit a specific situation.

### ***Humility***

To think of technological solutions to solve global problems seems haughty. A problem like dementia is not a problem that can be 'fixed', but asks for an open mind and a look around to see what is at hand to deal with it within the confines. The developments in early diagnostics for Alzheimer's disease might be helpful, tricky, or not very helpful after all. Jasanoff (Jasanoff, 2003a; 2007) addressed this point in her distinction between 'technologies of hubris' and 'technologies of humility'. She states that "*Real problems in the real world are infinitely complex, and for any given problem, science offers only part of the picture.*" (Jasanoff, 2007, p. 33). Furthermore, she argues that knowledge gained by science usually opens up new uncertainties. She wonders: "*How should policy makers deal with these layers of ignorance?*" And she continues "*the short answer is with humility, about both the limits of scientific knowledge and about when to stop turning to science to solve problems*" (Jasanoff, 2007, p. 33). Responsible innovation asks for a sense of humility.

### ***Balancing act***

All kinds of questions are related to responsible early diagnostics of Alzheimer's disease: how to support persons in the best way? How to increase quality of life while keeping health care costs from rising? How to keep a viable health care system? What is the best way to conduct clinical trials? How should you talk about early diagnostics to 'the public'? For whom is early diagnostics helpful, *qui bono*? What leans towards false promises and self-interest? And so on. These stakes and issues cannot be dealt with in one move, as aiming to optimize one issue will affect other issues and since the ongoing discussion will not be resolved once and for all. Rather than resolving, this asks for a continuous balancing act.

There are many balancing acts occurring already. In the chapter on the Deltaplan Dementie, for instance, we have seen how a 'fighting Alzheimer's disease' discourse was balanced with a 'living with Alzheimer's disease' discourse. In the meantime the 'living with' discourse has gained foothold, leading to new balancing acts. Critiques on the 'living with' discourse start to appear because there is 'too much' emphasis on the positive view on dementia, which suggests that you can also live badly with dementia (Bartlett, et al., 2017).

While balancing acts take place, there are also persistent (and known) imbalances. Two persistent imbalances appeared in this thesis in particular. The first is the lack of voice of persons with Alzheimer's disease, and the second is the playing on hope and fear as a driver for innovation. The fear for dementia makes Alzheimer's disease such a huge issue and one to be averted (e.g. Corner & Bond, 2004). Predicting a catastrophe is a proven strategy to get dementia on the public or political agenda. The fear of elderly persons developing dementia may be a driver of early diagnostics and treatment. However, the strategies playing on these

fears have painful and unwanted consequences. It is ethically questionable to draw on or even play on the fear of dementia (or the fear of catastrophes) as a driver for innovation. Even though fear is a strong driver (Kahneman, 2013), it is a bad councillor. There have to be more creative ways to draw attention and create a sense of urgency (Van Gorp et al., 2012). This thesis aligns with the earlier observation of Clarke in her article 'the case of the missing person' (Clarke, 2006) that persons with Alzheimer's disease are mostly spoken for. Yes, they had a voice in Alzheimer Cafés, but even there it were mostly the informal caregivers who did the talking. In the Deltaplan Dementie, the research agenda of Alzheimer Nederland was based on patient and informal caregiver consultation. Overall persons with dementia are spoken for by medical experts, informal caregivers, formal care providers, and politicians. This issue has been addressed for a long time (Cotrell & Schulz, 1993) but remains relevant: persons with Alzheimer's disease should have a voice as well.

In this thesis I made the issue of culture around early diagnostics for Alzheimer's disease and the dynamics that occur in this field explicit. Since this is not an area of innovation where a closure is to be expected, a challenge for all involved actors is to assess the implications of early diagnostics for Alzheimer's disease and how to act responsibly. Because of the long and rich history of dealing with dementia and Alzheimer's disease, many possible imbalances played out in the past, and there is a repertoire available to build upon for ongoing balancing acts.

#### **8.4 To conclude**

In this last section I reflected on the question how this empirical study of multiple meanings can contribute to responsible innovation. The specific approach taken on responsible innovation in this thesis was that it is possible to conduct technology assessment 'in the wild' without using specific technology assessment or foresight tools, and that the assessment of new and emerging technologies can be empirically studied in the present. It is not necessary to imagine future situations to assess consequences. This approach has made the multiple meanings of early diagnostics for Alzheimer's disease explicit, which in itself is a contribution to responsible innovation. It has shown that the co-existence of multiple meaning depends on the setting and that settings invite particular patterns of co-existence, based on the stakes in these settings. This articulation, contestations and interaction of meanings can be considered as acts of technology assessment in the wild. Even though the dynamics differ per setting, patterns of co-existence are to be expected and learned from. I distinguished three models to understand the implications of novel technologies: a linear, a network and a patchwork understanding. The patchwork understanding of implications of novel technologies that emerged from this thesis leads to an approach to responsible innovation which I summarized as 'the benefit of the doubt'. This boils down to an urge for sensitivity of interrelatedness and awareness of fringes, to the recognition that we should in many instances *deal* with problems (rather than aim to *solve* problems), and that we cannot escape from balancing acts. Above all, 'the benefit of the doubt' asks for humility in the face of dramatic diseases, loud solutions and a bewildering multiplicity of meanings.





# Appendices

## **Appendix 1: A non-exhaustive list of explorations in the dementia landscape**

### Memory centers in academics hospitals

- Memory Day Center of Radboud medical center.
  - Participant observation in April 2010 and between July and September 2010. Following three persons with suspicion of Alzheimer's disease through the whole diagnostic procedure. Interviews with geriatrics, nurse practitioners, neuropsychologists, MRI laboratory personnel and informal conversations with patients and informal caregivers.
- Memory clinic academic hospital Maastricht
  - Participant observation May 2011, two days at the memory clinic.

### General hospital

- Tilburg Hospital
  - Interview case manager, interview psychiatrist, discussions on early diagnostics for Alzheimer's disease during a team meeting of the geriatric department following a presentation of my colleague Anna Laura van der Laan. Participant observation of ambulant work of psychiatrist.

### Nursing homes

- De Posten, Enschede
  - Participant observation in November 2010 and in September 2012; Informal conversations with all the personal on the psychogeriatric ward and the residents; Report on experiences and reflection with policy maker, head of psychogeriatric ward, psychologist; Interviews on (early) diagnosis of Alzheimer's disease and expectations for the future way of dealing with Alzheimer's disease
- Joachim and Anna, Nijmegen
  - Participant observation and conversations with the clients and care professionals.

### Home care and welfare

- Participant observation during evenings for public education on dementia organised by GGZ and ZZG zorggroep.
- Interviews with welfare organisations in Nijmegen (Pro Persona) and Utrecht (Stichting Stade, U-Centraal), home care organisation, day care facility (SWON), volunteer organisations and Alzheimer Café regional president in Nijmegen.
- Various interviews within GGZ Nijmegen

### Patient organisation

- Interviews with research director of Alzheimer Nederland, reading policy documents of Alzheimer Nederland
- Visiting various Alzheimer Cafés and attending a course for volunteers in the Alzheimer Cafés, reading about the rationale behind the cafés in books of the founding father Bere Miesen.

### Insurance companies

- Interview on early diagnostics in insurance policy (Achmea)

### Informal caregivers

- Conversations with informal caregivers acquainted to me.

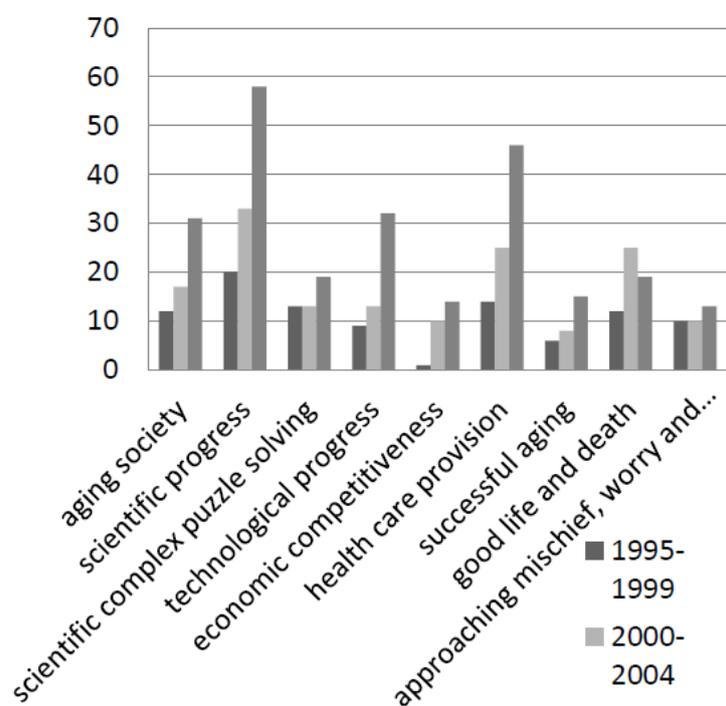
### Public media

- Visiting public screening of documentaries such as 'Mam', 'Verdwaald in het geheugenpaleis' and theater plays such as 'Heb ik Alzheimer' and discussions taking place there and in media afterwards
- Exploration of representations of dementia in movies (a.o. Away from her, De zaak Alzheimer, Son of the Bride, Savages, The iron lady, Friends with benefits, Il y a longtemps que je t'aime, The rise of the planet of the apes, The notebook, Iris, It runs in the family, Win Win, The curious care of Benjamin Button)
- Exploration of representation of dementia in books (i.e. Hersenschimmen - Bernlef, De Zaak Alzheimer – Jef Geeraerts, Dan wappert mijn hart naar je toe , liefde in tijden van alzheimer – Janne Harmsen de Boer, De oude koning in zijn rijk – Arno Geiger, Rimpels – Paco Roca, Gevoel en belevenis – Ben Wikkers, Ik heb Alzheimer, Het verhaal van mijn vader – Stella Braam)
- Following public media messages (e.g. television and newspaper articles) on dementia

### LeARN

- Annual meetings of the LeARN consortium; observations and presenting

## Appendix 2A : Number of articles related to interpretative packages



## Appendix 2B: Search strings used in LexisNexis

(((((Alzheimer! OR dement!) AND (Biomarker! OR bloedtest! OR hersen-vocht! OR CSF! OR lumbaal! OR ruggenmerg! OR ruggenprik! OR vroegdiagn! OR “vroegdiagn!” OR “vroegsign!” OR “vroeg sign!” OR MRI! OR “PET scan!” OR “vroeg opsporing” OR “voorspell!” OR “beeldvormende techn!” OR beelddiagn! OR “vroegtijdige diagn!” OR “moleculaire diagn!” OR “molecular imag!” OR SPECT OR marker! OR detect!))))))

## Appendix 2C

*De Telegraaf*: (398) 1/3/2007

*NRC Handelsblad*: (244) 11/7/2009; (340) 8/3/2008; (344) 16/2/2008; (352) 25/1/2008; (386) 30/6/2007; (457) 12/11/2005; (484) 20/11/2004; (549) 2/11/2002; (584) 2/6/2001; (723) 10/10/1996; (733) 8/3/ 1996

*Trouw*: (387) 5/6/2007; (395) 22/3/2007; (554) 27/9/2002

*Het Financieel Dagblad*: (376) 1/10/2007; (471) 7/5/2005



# References

- Adelman, E.E., J.H.T. 2003. Ignoring the controversies: Newspaper reports on Alzheimer's disease treatment. *Journal of the American Geriatrics Society* 51 (12): 1821-1822.
- Albert, M. S., S.T. DeKosky, D. Dickson, B. Dubois, H.H. Feldman, N.C. Fox, .... and C.H. Phelps. 2011. The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's and Dementia* 7 (3): 270-279
- Algra, W. 2013. Hoop op genezing nog ver weg. p. 9. 8 April 2013 *De Verdieping, Trouw*.
- Alzheimer's Association. New diagnostic criteria and guidelines for Alzheimer's disease. [http://www.alz.org/research/diagnostic\\_criteria/](http://www.alz.org/research/diagnostic_criteria/). Accessed 11 July 2011.
- Baarda D.B., M.P.M. de Goede, J. Teunissen. 2005. Basisboek Kwalitatief Onderzoek. Leiden, The Netherlands: Stenfert Kroese
- Ballenger, J. F. 2000. Beyond the characteristic plaques and tangles: Mid-twentieth-century U.S. psychiatry and the fight Against senility. In *Concepts of Alzheimer Disease - Biological, Clinical, and Cultural Perspectives*. ed. Whitehouse, P.J., K. Maurer and J. F. Ballenger, 83–103. Baltimore, United States of America: The John Hopkins University Press.
- Ballenger, J. F. 2006. *Self, senility, and Alzheimer's disease in modern America*. Baltimore, United States of America: John Hopkins University Press.
- Ballenger, J. F., P.J. Whitehouse, C.G. Lyketsos, P.V. Rabins, and J.H.T. Karlawish. 2009. *Treating dementia, do we have a pill for it?* Baltimore, United States of America: The John Hopkins University Press.
- Bartlett, R., L. Windemuth-Wolfson, K. Oliver, and T. Dening. 2017. Suffering with dementia: the other side of "living well". *International Psychogeriatrics* 29 (2), 177–179.
- Batsch, N. L., and M.S. Mittelman, 2012. Overcoming the stigma of dementia, World Alzheimer Report 2012. London, United Kingdom: Alzheimer's Disease International (ADI).
- Battista, R.N., and M.J. Hodge. 1999. The evolving paradigm of health technology assessment: reflections for the millennium. *Canadian Medical Association* 160 (10), 1464–1467.
- Beard, R.L. 2004. Advocating voice: organisational, historical and social milieux of the Alzheimer's disease movement. *Sociology of Health & Illness* 26 (6): 797–819.
- Beard, R.L. 2004. In their voices: Identity preservation and experiences of Alzheimer's disease. *Journal of Aging Studies* 18 (4): 415–428.
- Beard, R.L., and P.J. Fox. 2008. Resisting social disenfranchisement: Negotiating collective

- identities and everyday life with memory loss. *Social Science and Medicine* 66 (7): 1509–1520.
- Beard, R.L., and T.M. Neary. 2013. Making sense of nonsense: experiences of mild cognitive impairment. *Sociology of Health & Illness* 35 (1): 130–146.
- Behuniak, S.M. 2011. The living dead? The construction of people with Alzheimer's disease as zombies. *Ageing and Society* 31 (1), 70–92.
- Benford, R.D., and D.A. Snow. 2000. Framing Processes and Social Movements: An Overview and Assessment. *Annual Review of Sociology* 26: 611–639.
- Berchtold, N.C., and C.W. Cotman. 1998. Evolution in the conceptualization of dementia and Alzheimer's disease: Greco-Roman period to the 1960s. *Neurobiology of Aging* 19 (3): 173–189.
- Bijker, W.E. 1995. *Of Bicycles, Bakelites, and Bulbs: Toward a Theory of Sociotechnical Change*. (Inside Technology). Cambridge Mass. and London England: MIT Press.
- Bijker, W.E., T.P. Hughes, and T. Pinch. 1989. *The Social Construction of Technological Systems*. Cambridge Massachusetts and London England: MIT Press.
- Birks, M., and J. Mills. 2011. *Grounded Theory: A Practical Guide*. Londen, United Kindom: Sage.
- Blennow, K. (2010). Biomarkers in Alzheimer's disease drug development. *Nature Medicine* 16 (11): 1218–1222.
- Blom, M., and B. Miesen, B. 2000. Handleiding Alzheimer Café. Amersfoort, Nederland: Stichting Alzheimer Nederland.
- Boenink, M. 2016. Biomarkers for Alzheimer's disease: Searching for the missing link between biology and clinic. In *Emerging Technologies for Diagnosing Alzheimer's Disease, innovating with care*. ed. Boenink, M., H. Van Lente, and E. Moors, 63–82. London, United Kingdom: Palgrave Macmillan.
- Boenink, M. 2017. Gatekeeping and trailblazing: The role of biomarkers in novel guidelines for diagnosing Alzheimer's disease. *BioSocieties* 13 (1): 213–231.
- Boer, M. E., R.M. Dröes, C. Jonker, J.A. Eefsting, and C.M.P.M. Hertogh. 2010. De beleving van beginnende dementie en het gevreesde lijden. *Tijdschrift Voor Gerontologie En Geriatrie* 41 (5): 194–203.
- Bortolotti, L., and H. Widdows. 2011. The right not to know: the case of psychiatric disorders. *Journal of Medical Ethics* 37 (11): 673–676.
- Borup, M., N. Brown, K. Konrad, and H. van Lente. 2006. The sociology of expectations in science and technology. *Technology Analysis & Strategic Management* 18 (3): 198–285.
- Botton, A. de. 2007. *De kunst van het reizen*. Amsterdam, The Netherlands: Olympus.
- Braak, H., and E. Braak. 2000. Neurofibrillary changes, the hallmark of Alzheimer Disease. In *Concepts of Alzheimer Disease - Biological, Clinical, and Cultural Perspectives*. ed. Whitehouse, P.J., K. Maurer, and J. F. Ballenger, 53–71. Baltimore, United States of

- America: The John Hopkins University Press.
- Brayne, C. 2007. The elephant in the room - healthy brains in later life, epidemiology and public health. *Nature Reviews Neuroscience* 8: 233–239.
- Brink, M. van den. 2010. *Rijkswaterstaat on the Horns of a Dilemma*. PhD Thesis. RU Radboud Universiteit Nijmegen. Delft, The Netherlands: Eburon.
- Brouselle, A., and C. Lessard. 2011: Economic evaluation to inform health care decision-making. Promise, pitfalls and a proposal for an alternative path. *Social Science and Medicine* 72 (6): 832-839.
- Brown, N., and M. Michael. 2003. A sociology of expectations: Retrospecting prospects and prospecting retrospects. *Technology Analysis & Strategic Management* 15 (1): 3–18.
- Brown, N., A. Rip, and H. van Lente. 2003. Expectations in & about science and technology, a background paper for the “expectations” workshop of 13-14 June 2003, Accessed december 2013  
<https://www.york.ac.uk/satsu/expectations/Utrecht%202003/Background%20paper%20version%2014May03.pdf>.
- Brown, P. 1995. Naming and Framing: The Social Construction and Illness. *Journal of Health and Social Behavior* 35 (Extra issue: Forty Years of Medical Sociology: The State of the Art and Directions for the Future): 34–52.
- Bruner, J.S. 1986. *Actual minds, possible worlds*. Cambridge Massachuchetts and London England: Harvard University Press.
- Buchem, M.A. van, B.N.A. van Berckel, et al. (2007), *Project description Leiden Alzheimer Research Netherlands*. Eindhoven: CTMM.
- Buckholtz, N.S. 2011. Perspective: In search of biomarkers. *Nature* 475 (S8, 14 July 2011).
- Burri, R.V., A. Carusi, and A.A. Asprakdaki. 2014. Visualising bodies within and beyond laboratories and clinics. *TECNOSCIENZA Italian Journal of Science & Technology Studies* 5 (1): 165–189.
- Carpenter, B.D., C. Xiong, E.K. Porensky, M.M. Lee, P.J. Brown, M. Coats, ... and J.C. Morris. 2008. Reaction to a dementia diagnosis in individuals with Alzheimer’s disease and mild cognitive impairment. *Journal of the American Geriatrics Society* 56 (3): 405–412.
- Carpenter, B., and J. Dave. 2004. Disclosing a dementia diagnosis: A review of opinion and practice, and a proposed research agenda. *The Gerontologist* 44 (2): 149–158.
- Center for Translational Molecular Medicine. 2006. Business plan. <http://www.ctmm.nl/pro1/general/start.asp?i=2&j=0&k=0&p=0&itemid=52&folder=About%20CTMM&title=Business%20Plan>. Accessed 11 July 2011
- Chaufan, C., B. Hollister, J. Nazareno, and P.J. Fox. 2012. Medical ideology as a double-edged sword: The politics of cure and care in the making of Alzheimer’s disease. *Social Science and Medicine* 74 (5): 788–795.
- Claassen, J. 2011. Diagnose dementie moet eerder. *Medisch Contact* 66 (49): 3048–3051.

- Clarke, J.N. 2006. The case of the missing person: Alzheimer's Disease in mass print magazines 1991-2001. *Health Communication* 19 (3): 269–276.
- Clifford, R.J.Jr, M.S. Albert, D.S. Knopman, F.M. McKahnn, R.A. Sperling, M.C. Carillo, B. Thies, and C.H. Phelps. 2011. Introduction to the recommendations from the national institute on aging and the Alzheimer's association workgroup on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia* 7 (3): 257-262.
- Cohen, L. 1995. Toward an anthropology of senility: anger, weakness, and Alzheimer's in Banaras, India. *Medical Anthropology Quarterly* 9 (3): 314–334.
- Comer, M. 2008. Early Alzheimer's disease diagnostics: Wait! Wait! Don't tell me! *Alzheimer's and Dementia* 4 (5): 368-370.
- Corner, L., and J. Bond. 2004. Being at risk of dementia: Fears and anxieties of older adults. *Journal of Aging Studies* 18 (2): 143–155.
- Corner, L., and J. Bond. 2006. The impact of the label of mild cognitive impairment on the individual's sense of self. *Philosophy, Psychiatry & Psychology* 13 (1): 3-12.
- Cornett, P. F., and J.R. Hall. 2008. Issues in disclosing a diagnosis of dementia. *Archives of Clinical Neuropsychology* 23 (3): 251–256.
- Cotrell, V., and R. Schulz. 1993. The perspective of the patient with Alzheimer's Disease: A neglected dimension of dementia research. *Gerontologist* 33 (2): 205–211.
- Cuijpers, Y. 2016. Dikes and dementia: How multiple framings of dementia co-exist during the development of a national dementia strategy. In *Emerging Technologies for Diagnosing Alzheimer's Disease, Innovating with Care*. ed. Boenink, M., H. van Lente and E. Moors, 185–204. London, United Kingdom: Palgrave Macmillan.
- Cuijpers, Y., and H. van Lente. 2015a. The meanings of early diagnostics for Alzheimer's disease in Dutch newspapers. A framing analysis. In *Popularizing Dementia. Public Expressions and Representations of Forgetfulness*. ed. Swinnen, A., and M. Schweda. p. 295-314. Bielefeld, Germany: Transcript.
- Cuijpers, Y., and H. van Lente. 2015b. Early diagnostics and Alzheimer's disease: Beyond 'cure' and 'care'. *Technological Forecasting and Social Change* 93: 54-67.
- Cutler, S. J., and L.G. Hodgson. 1996. Anticipatory dementia: a link between memory appraisals and concerns about developing Alzheimer's disease. *The Gerontologist* 36 (5): 657–664.
- Dehue, T. 2008. *De Depressie-Epidemie*. Amsterdam-Antwerpen, The Netherlands-Belgium: Augustus.
- Deltaplan tegen dementie, VUmc Alzheimercentrum waarschuwt voor epidemie. 2012. April 11. *De Telegraaf*.
- Derksen, E.W.C. 2011. *Diagnostic disclosure: a basic intervention in dementia care*. PhD Thesis. Radboud University Nijmegen, The Netherlands.
- Derksen, E.W.C., M. Vernooij-Dassen, F. Gillissen, M. Olde-Rikkert, and P. Scheltens. 2005.

- The impact of diagnostic disclosure in dementia: a qualitative case analysis. *International Psychogeriatrics / IPA* 17 (2): 319–326.
- Dewulf, A., B. Gray, L. Putnam, R. Lewicki, N. Aarts, R. Bouwen, and C. van Woerkum. 2009. Disentangling approaches to framing in conflict and negotiation research: A meta-paradigmatic perspective. *Human Relations* 62 (2): 155–193.
- Diesfeldt, H. 2014. 'Een dam opwerpen tegen dementie' Beeldspraak in het publieke debat. *Denkbeeld* 26 (1): 12–15.
- Dillmann, R.J.M. 2000. Alzheimer Disease: Epistemological Lessons from History? In *Concepts of Alzheimer Disease - Biological, Clinical, and Cultural Perspectives*. ed. Whitehouse, P.J., K. Maurer, and J.F. Ballenger, 129–157. Baltimore, United States of America: The John Hopkins University Press.
- Doyle, C.J., D.R. Dunt, A. Dare, S. Day and B.S. Wijesundara. 2012. Media Reports on Dementia: Quality and Type of Messages in Australian Media. *Australasian Journal on Ageing* 31(2): 96-101.
- Downs, M. 2000. Ageing update. Dementia in a socio-cultural context: An idea whose time has come. *Ageing and Society* 20 (3): 369–375.
- Downs, M., L. Clare, and J. MacKenzie. 2006. Understandings of dementia; explanatory models and their implications for the person with dementia and therapeutic effort. In *Dementia, mind, meaning, and the person*. ed. Hughes, J.C., S.J. Louw, and S.R. Sabat, 235–258. Oxford, United Kingdom: Oxford University Press.
- Dröes, R.M. 2007. Insight in coping with dementia: Listening to the voice of those who suffer from it. *Ageing & Mental Health* 11 (2): 115–118.
- Dröes, R.M. 2010. Omgaan met de gevolgen van dementie: Het psychosociale perspectief. Inaugural lecture, VU Amsterdam, The Netherlands.
- Dubois, B., H.H. Feldman, C. Jacova, J.L. Cummings, S.T. DeKosky, P. Barberger-Gateau, ... P. Scheltens. 2010. Revising the definition of Alzheimer's disease: A new lexicon. *The Lancet Neurology* 9 (11): 1118-1127.
- Dubois, B., H.H. Feldman, C. Jacova, S. T. DeKosky, P. Barberger-Gateau, J. Cummings, ... P. Scheltens. 2007. Research criteria for the diagnosis of Alzheimer's disease: revising the NINCDS–ADRDA criteria. *The Lancet Neurology* 6 (8): 734–746.
- Dubois, B., A. Padovani, P. Scheltens, A. Rossi, and G.D. Agnello. 2016. Timely diagnosis for Alzheimer's Disease: A literature review on benefits and challenges. *Journal of Alzheimer's Disease* 49 (3): 617–631.
- Dungen, P. van den., H.W.M. van Marwijk, H.E. van der Horst, E. P. Moll van Charante, J. MacNeil Vroomen, P.M. van de Ven, and H.P.J. van Hout. 2012. The accuracy of family physicians' dementia diagnoses at different stages of dementia: a systematic review. *International Journal of Geriatric Psychiatry* 27 (4): 342–354.
- Entman, R.M. 1993. Framing: Toward Clarification of a Fractured Paradigm. *Journal of Communication* 43 (4): 51–58.

- Est, R. van, and F.W.A. Brom. 2012. Technology assessment as an analytic and democratic practice. In *Encyclopedia of Applied Ethics (2<sup>nd</sup> edition)*. ed. R. Chadwick, 306-320. San Diego, United States of America: Academic Press.
- Estes, C.L. 1993. The 1992 Kent Lecture. The aging enterprise revisited. *The Gerontologist*, 33 (3): 292–298.
- European Union Joint Programme Neurodegenerative Disease Research. 2012. JPND Research Strategy: Tackling the Challenge of Alzheimer’s and Other Neurodegenerative Diseases in Europe. Swindon and London, United Kingdom: Medical Research Council.
- Fairclough, N.L. 2003. *Analysing Discourse: Textual analysis for social research*. London United Kingdom and New York United States of America: Routledge Taylor & Francis Group.
- Fisher, E., and R.L. Mahajan. 2006. Midstream modulation of nanotechnology research in an academic laboratory. Proceedings of ICEME2006 ASME International Mechanical Engineering Congress and Exposition, [http://csid.unt.edu/files/Fisher\\_MM\\_IMECE-06%20\\_.pdf](http://csid.unt.edu/files/Fisher_MM_IMECE-06%20_.pdf). Accessed 6 July 2011.
- Fisk, J.D., B.L. Beattie, M. Donnelly, A. Byszewski, and F.J. Molnar, F. J. 2007. Disclosure of the diagnosis of dementia. *Alzheimer’s and Dementia* 3 (4): 404-410.
- Förstl, H. 2000. Contributions of German neuroscience to the concept of Alzheimer Disease. In *Concepts of Alzheimer Disease - Biological, Clinical, and Cultural Perspectives*. ed. Whitehouse, P.J., K. Maurer, and J.F. Ballenger, 72–82. Baltimore, United States of America: The John Hopkins University Press.
- Fox, P.J. 1989. From senility to Alzheimer’s disease: the rise of the Alzheimer’s disease movement. *The Milbank Quarterly* 67 (1): 58–102.
- Fox, P.J. 2000. The Role of the Concept of Alzheimer Disease in the Development of the Alzheimer’s Association in the United States. In *Concepts of Alzheimer Disease - Biological, Clinical, and Cultural Perspectives*. ed. Whitehouse, P.J., K. Maurer, and J.F. Ballenger, 209-233. Baltimore, United States of America: The John Hopkins University Press.
- G8. 2013. G8 Dementia Summit Declaration. Policy paper RDD/10495. Published 11 September 2013.
- Gamson, W.A., and K.E. Lash. 1983. Political Culture of Welfare Policy. In *Evaluating the Welfare State*. Ed. S.E. Spiro and E. Yuchtman-Yaar. 397-415. New York, United States of America: Academic Press.
- Gamson, W.A., and A. Modigliani. 1989. Media discourse and public opinion on nuclear power: A constructionist approach. *American Journal of Sociology* 95 (1): 1–37.
- Gamson, W.A., D. Croteau, W. Hoynes, and T. Sasson. 1992. Media Images and the Social Construction of Reality. *Annual Review of Sociology* 18: 373-393.
- Garud, R., and D. Ahlstrom. 1997. Technology assessment, a socio-cognitive perspective.

*Journal of Engineering and Technology Management* 14 (1): 25-48.

- Gauthier, S., A. Leuzy, E. Racine, and P. Rosa-Neto. 2013. Diagnosis and management of Alzheimer's disease: Past, present and future ethical issues. *Progress in Neurobiology* 110: 102–113.
- George, D.R., S.H. Qualls, C.J. Camp, and P.J. Whitehouse. 2013. Renovating Alzheimer's: "Constructive" reflections on the new clinical and research diagnostic guidelines. *Gerontologist* 53 (3): 378-387.
- George, D.R., P.J. Whitehouse, and J.F. Ballenger. 2011. The evolving classification of dementia: Placing the DSM-V in a meaningful historical and cultural context and pondering the future of "Alzheimer's." *Culture, Medicine and Psychiatry* 35 (3): 417–435.
- George, D.R., and P.J. Whitehouse. 2009. The Classification of Alzheimer's Disease and Mild Cognitive Impairment: Enriching therapeutic models through moral imagination. In *Treating Dementia, Do We Have a Pill for It?* ed. Ballenger, J.F., P.J. Whitehouse, C.G. Lyketsos, P.V. Rabins, and J.H.T. Karlawish, 5–25. Baltimore, United States of America: The John Hopkins University Press.
- Gertz, H.-J, and A. Kurz. 2011. Diagnosis without therapy - early diagnosis of Alzheimer's disease in the stage of mild cognitive impairment. *Nervenarzt* 82 (9): 1151-1159.
- Godin, B. 2006. The Linear Model of Innovation, The Historical Construction of an Analytical Framework. *Science Technology & Human Values* 31 (6): 639-667.
- Gordon, R.S. 1983. An operational classification of disease prevention. *Public Health Reports* 98 (2): 107–109.
- Gorp, B. van. 2007. Het reconstrueren van frames via inductieve inhouds-analyse: uitgangspunten en procedures. *KWALON* 35 (2): 13–18.
- Gorp, B. van. 2007. The Constructionist Approach to Framing: Bringing Culture Back In. *Journal of Communication* 57 (1): 60-78.
- Gorp, B. van. 2010. Strategies to take subjectivity out of framing analysis. In *Doing News Framing Analysis: Empirical and Theoretical Perspectives*. ed. D'Angelo, P., and J.A. Kuypers, 84-109. New York and Oxon, United States of America and United Kingdom: Routledge.
- Gorp, B. van, and T. Vercruyse. 2012. Frames and counter-frames giving meaning to dementia: A framing analysis of media content. *Social Science and Medicine* 74 (8): 1274–1281.
- Gorp, B. van, T. Vercruyse, and J. van den Bulck. 2012. Toward a more nuanced perception of Alzheimer's disease: designing and testing a campaign advertisement. *American Journal of Alzheimer's Disease and Other Dementias* 27 (6): 388–396.
- Grey, A. de., and M. Rae. 2008. *Ending aging : the rejuvenation breakthroughs that could reverse human aging in our lifetime*. New York, United States of America: St. Martin's Press.

- Grundmeijer, H.G.L.M. 2011. Vroegdiagnostiek naar dementie: niet doen. *Nederlands Tijdschrift voor Geneeskunde* 155 (A3821)
- Grunwald, A. 2004. Paper 5: Vision assessment as a new element of the FTA toolbox. Paper presented at EU-US Seminar: New Technology Foresight, Forecasting & Assessment Methods, Seville, Spain.  
<http://forera.jrc.ec.europa.eu/fta/papers/Session%204%20What's%20the%20Use/Vision%20Assessment%20as%20a%20new%20element%20of%20the%20FTA%20toolbox.pdf>. Accessed 11 July 2011.
- Grunwald, A. 2007. Converging technologies: Visions, increased contingencies of the conditio humana, and search for orientation. *Futures* 39 (4): 380–392.
- Grunwald, A. 2010. From speculative nanoethics to explorative philosophy of nanotechnology. *NanoEthics* 4 (2): 91-101.
- Gurevitch, M., and M.R. Levy. 1985. *Mass Communication Review Yearbook* 5. Beverly Hills, United States of America: Sage.
- Guston, D.H., and D. Sarewitz. 2002. Real-time technology assessment. *Technology in Society* 24 (1-2): 93-109.
- Guston, D.H., E. Fisher, A. Grunwald, R. Owen, T. Swierstra, and S. van der Burg. 2014. Responsible innovation: motivations for a new journal. *Journal of Responsible Innovation* 1(1): 1–8.
- Gutman, A., and D. Thompson. 1996. *Democracy and disagreement*. Cambridge, United States of America: Harvard University Press.
- Hajer, M.A. 2006. Doing discourse analysis: coalitions, practices, meaning. In *Words matter in policy and planning, discourse theory and method in the social sciences*. ed. M. van den Brink and T. Metzke, Netherlands Geographical Studies Series 344: 65-74. Utrecht, The Netherlands: Koninklijk Nederlands Aardrijkskundig Genootschap.
- Hajer, M., and D. Laws. 2009. Ordering through Discourse. In *The Oxford Handbook of Public Policy* 3. ed. Moran, M., M. Rein, R. E. Goodin, 251-268, New York, United States of America: Oxford University Press.
- Halley, E., Boulton, R., McFadzean, D., Moriarty, J. 2005: The Poppy Café: a multi-agency approach to developing an Alzheimer Café. *Dementia* 4 (4): 592-594.
- Hampel, H., R. Frank, K. Broich, S.J. Teipel, R.G. Katz, J. Hardy, ... , and K. Blennow. 2010. Biomarkers for alzheimer's disease: Academic, industry and regulatory perspectives. *Nature Reviews Drug Discovery* 9: 560-574.
- Handels, R.L.H., P. Aalten, C.A.G. Wolfs, M. OldeRikkert, P. Scheltens, P.J. Visser, ..., and F.R.J. Verhey, 2012. Diagnostic and economic evaluation of new biomarkers for Alzheimer's disease: the research protocol of a prospective cohort study. *BMC Neurology* 12: 72.
- Hansen, E.C., C. Hughes, G. Routley, and A.L. Robinson. 2008. General practitioners' experiences and understandings of diagnosing dementia: Factors impacting on early

- diagnosis. *Social Science and Medicine* 67 (11): 1776–1783.
- Harman, G., and L. Clare. 2006. Illness representations and lived experience in early-stage dementia. *Qualitative Health Research* 16 (4): 484–502.
- Harris, P.B. 2012. Maintaining friendships in early stage dementia: Factors to consider. *Dementia* 11 (3): 305–314.
- Harris, P.B., and J. Keady. 2008. Wisdom, resilience and successful aging: Changing public discourses on living with dementia. *Dementia* 7 (1): 5–8.
- Henwood, F., S. Wyatt, A. Hart, and J. Smith. 2003. 'Ignorance is bliss sometimes': Constraints on the emergence of the 'informed patient' in the changing landscapes of health information. *Sociology of Health and Illness* 25 (6): 589-607.
- Hertogh, C.M.P.M., M.E. de Boer, R.-M. Dröes, and J.A. Eefsting. 2007. Would we rather lose our life than lose our self? Lessons from the Dutch debate on euthanasia for patients with dementia. *The American Journal of Bioethics : AJOB* 7 (4): 48–56.
- Hippel, E. von. 1976. The dominant role of users in the scientific instrument innovation process. *Research Policy* 5 (3): 212-39.
- Hisschemöller, M., and R. Hoppe. 1995. Coping with intractable controversies: The case for problem structuring in policy design and analysis. *Knowledge and Policy* 8 (4): 40–60.
- Hofmann, B. 2002. On the Triad Disease, Illness and Sickness. *Journal of Medicine and Philosophy* 27 (6): 651–673.
- Holstein, M.B. 1996. *Negotiating Disease: Senile Dementia and Alzheimer's Disease, 1900-1980*. PhD Thesis. University of Texas Graduate School of Biomedical Sciences, Galveston, United States of America.
- Holstein, M.B. 2000. Aging, Culture and the Framing of Alzheimer Disease. In *Concepts of Alzheimer Disease - Biological, Clinical, and Cultural Perspectives*. ed. Whitehouse P.J., K. Maurer, and J.F. Ballenger, 158–180. Baltimore, United States of America: The John Hopkins University Press.
- Holwerda, T.J., D.J.H. Deeg, A.T.F. Beekman, T.G. Van Tilburg, M.L. Stek, C. Jonker, and R.A. Schoevers. 2014. Feelings of loneliness, but not social isolation, predict dementia onset: Results from the Amsterdam Study of the Elderly (AMSTEL). *Journal of Neurology, Neurosurgery and Psychiatry* 85 (2): 135–142.
- Hoven, J. van den, N. Doorn, T. Swierstra, B.J. Koops, and H. Romijn. 2014. *Responsible innovation 1: Innovative solutions for global issues*. *Responsible Innovation 1: Innovative Solutions for Global Issues*. Dordrecht, The Netherlands: Springer.
- Hughes, T.P. 1986. The Seamless Web: Technology , Science , Etcetera , Etcetera. *Social Studies of Science* 16 (2): 281–292.
- Humpel, C. 2011. Identifying and validating biomarkers for Alzheimer's disease. *Trends in Biotechnology* 29 (1): 26-32.
- Hyman, B. T., C.H. Phelps, T.G. Beach, E.H. Bigio, N.J. Cairns, M.C. Carrillo, ..., and T.J. Montine.

- (2012). National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association* 8 (1): 1–13.
- Ik voel me een detective; levenslessen. 2013, April 6. *NRC Handelsblad*.
- Iliffe, S., J. Manthorpe, and A. Eden, 2003. Sooner or later? Issues in the early diagnosis of dementia in general practice: A qualitative study. *Family Practice* 20 (4): 376–381.
- Innes, A. (2009). *Dementia Studies: A social science perspective*. London, United Kingdom: Sage Publications.
- Innes, A., and J. Manthorpe. 2012. Developing theoretical understandings of dementia and their application to dementia care policy in the UK. *Dementia* 12 (6): 682-696.
- Is dementie écht zo'n groot probleem? Deltaplan Dementie ontketent richtingenstrijd. 2013, April 19. *NRC Handelsblad*.
- Jack, C.R., M.S. Albert, D.S. Knopman, G.M. McKhann, R.A. Sperling, M.C. Carrillo, ..., and C.H. Phelps. 2011. Introduction to the recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's and Dementia* 7 (3): 257-262.
- Jack, C.R., D.S. Knopman, W.J. Jagust, L.M. Shaw, P.S. Aisen, W. Weiner, W., ..., and J.Q. Trojanowski, 2010. Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade. *Lancet Neurology* 9 (1): 1–20.
- Jack, C.R., D.S. Knopman, W.J. Jagust, R.C. Petersen, M.W. Weiner, P.S. Aisen, ... , and J.Q. Trojanowski. 2013. Update on hypothetical model of Alzheimer's disease biomarkers. *Lancet Neurology* 12 (2): 207–216.
- Jasanoff, S. 2003. Technologies of humility: citizen participation in governing science. *Minerva*, 41 (3): 223–244.
- Jasanoff, S. 2007. Technologies of humility. *Nature* 450: 33.
- Johnson, Deborah G. 2007. Ethics and technology 'in the making': An essay on the challenge of nanoethics. *NanoEthics* 1 (1): 21-30.
- Johnstone, M.-J. 2013. Metaphors, stigma and the “Alzheimerization” of the euthanasia debate. *Dementia* 12 (4): 377–393.
- Jonker, C., J.P.J. Slaets, and F.R.J. Verhey, 2009. *Handboek dementie, laatste inzichten in diagnostiek en behandeling*. Houten, The Netherlands: Bohn Stafleu van Loghum.
- Jorgensen, M., and L.J. Phillips. 2002. *Discourse Analysis as Theory and Method*. London, United Kingdom: Sage Publications.
- Jutel, A. 2009. Sociology of diagnosis: A preliminary review. *Sociology of Health and Illness* 31 (2): 278-299.
- Jutel, A. 2011. Classification, disease, and diagnosis. *Perspectives in Biology and Medicine* 54 (2): 189–205.

- Jutel, A., and A. Nettleton. 2011. Towards a sociology of diagnosis: reflections and opportunities. *Social Science & Medicine* 73 (6): 793–800.
- Kabinet investeert extra in bestrijding dementie; “Deltaplan” moet kosten tot 2020 met 3 mld verlagen. 2013, April 4. *NRC Handelsblad*.
- Kahneman, D. 2013. *Thinking fast and slow*. New York, United States of America: Farrar, Straus and Giroux.
- Kapasi, A., C. DeCarli, and J.A. Schneider. 2017. Impact of multiple pathologies on the threshold for clinically overt dementia. *Acta Neuropathologica* 134 (2): 171-186.
- Karlawish, J. 2011. Addressing the ethical, policy, and social challenges of preclinical Alzheimer disease. *Neurology* 77 (15): 1487–1493.
- Katz, J., M. Aakhus, H.D. Kim, and M. Turner. 2002. Young user's attitudes toward ICTS: A comparative semantic differential study of the mobile telephone. *Annales Des Telecommunications/Annals of Telecommunications* 57 (3-4): 225-37.
- Katz, S. 2013. Dementia, personhood and embodiment: what can we learn from the medieval history of memory? *Dementia* 12 (3): 303-314.
- Katzman, R. 1976. Editorial: The prevalence and malignancy of Alzheimer's disease: A major killer. *Archives of Neurology* 33 (4): 217-218.
- Katzman, R., and K.L. Bick. 2000. The Rediscovery of Alzheimer Disease During the 1960s and 1970s. In *Concepts of Alzheimer Disease - Biological, Clinical, and Cultural Perspectives*. ed. Whitehouse P.J., K. Maurer, and J.F. Ballenger, 104–124. Baltimore, United States of America: The John Hopkins University Press.
- Kessler, E.M., C.E. Bowen, M. Baer, L. Froelich, and H.W. Wahl. 2012. Dementia worry: A psychological examination of an unexplored phenomenon. *European Journal of Ageing* 9 (4): 275–284.
- Kirkman, A.M. 2006. Dementia in the news: The media coverage of Alzheimer's disease. *Australasian Journal on Ageing* 25 (2): 74-79.
- Kitwood, T. 1990. The Dialectics of Dementia: With Particular Reference to Alzheimer's Disease. *Ageing & Society* 10 (2): 177-196.
- Kitwood, T. 1997. *Dementia Reconsidered: the person comes first*. Buckingham, United Kingdom and Philadelphia, United States of America: Open University Press.
- Kitwood, T., and K. Bredin. 1992. Towards a Theory of Dementia Care: Personhood and Well-being. *Ageing & Society* 12 (3): 269-287.
- Koch, T., and S. Iliffe. 2010. Rapid appraisal of barriers to the diagnosis and management of patients with dementia in primary care: A systematic review. *BMC Family Practice* 11: 52.
- Koch, T., and S. Iliffe. 2011. Dementia diagnosis and management: a narrative review of changing practice. *The British Journal of General Practice: The Journal of the Royal College of General Practitioners* 61 (589): e513-25.

- Kraepelin, E. 1910. *Psychiatrie: Ein Lehrbuch für Studierende und Ärzte*. 8. Leipzig, Germany: Auflage, Barth.
- Kuhn, T. 1970. *The Structure of Scientific Revolutions*. Chicago, United States of America: University of Chicago Press, University of Chicago.
- Kutschenko, L.K. 2012. Diagnostic misconceptions? A closer look at clinical research on Alzheimer's disease. *Journal of Medical Ethics* 38 (1): 57–59.
- Laan, A.L. van der, and M. Boenink. 2015. Beyond bench and bedside: disentangling the concept of translational research. *Health Care Analysis* 23 (1): 32–49.
- Laclau, E., and C. Mouffe. 1985. *Hegemony and Socialist Strategy*. London, United Kingdom: Verso.
- Laslett, P. 1987. The emergence of the Third Age. *Ageing and Society* 7: 133-160.
- Latour, B. 1987. *Science in Action*. Cambridge, United States of America: Harvard University Press.
- Latour, B. 1996. *Aramis, or, The love of technology*. Cambridge, United States of America: Harvard University Press.
- Law, J. 1994. *Organizing Modernity*. Oxford, United Kingdom: Blackwell Publishers.
- LeARN. 2010. Public Summary, In vivo molecular diagnostics in Alzheimer's Disease – LeARN. <http://www.ctmm.nl/pro1/general/start.asp?i=0&j=0&k=0&p=0&itemid=78>. Accessed 4 August 2010. Leiden, The Netherlands: Alzheimer Research Nederland.
- Leibing, A. 2002. Flexible hips? On Alzheimer's disease and aging in Brazil. *Journal of Cross-Cultural Gerontology* 17 (3): 213–232.
- Leibing, A. 2016. On Short Cuts. The Complexity of Studying the Early Diagnosis and Prevention of Alzheimer's Disease. In *Emerging Technologies for Diagnosing Alzheimer's Disease. Innovating with Care*. ed. Boenink, M., H. van Lente, and E. Moors. 41-61. London, United Kingdom: Macmillan.
- Lente, H. van. 1993. *Promising Technology, The Dynamics of Expectations in Technological Development*. PhD. Thesis. University of Twente, Enschede.
- Lente, H. van. 2015. *De ruimtetoerist - vragen over technologie en toekomst*. Inaugural Lecture, Maastricht University.
- Lente, H. van, and S. Bakker. 2010. Competing expectations: The case of hydrogen storage technologies. *Technology Analysis and Strategic Management* 22 (6): 693-709.
- Leuzy, A., and S. Gauthier, 2012. Ethical issues in Alzheimer's disease: an overview. *Expert Review of Neurotherapeutics* 12 (5): 557–567.
- Lock, M. 2013. Detecting amyloid biomarkers: Embodied risk and Alzheimer prevention. *BioSocieties* 8 (2): 107–123.
- Lock, M. 2013. *The Alzheimer Conundrum, entanglements of dementia and aging*. Princeton, United States of America: Princeton University Press.

- Longino, C.F. J. 2005. The Future of Ageism: Baby Boomers at the Doorstep. *Generations*, 3 (Fall): 79–84.
- Lucivero, F., T. Swierstra, and M. Boenink. 2011. Assessing expectations: Towards a toolbox for an ethics of emerging technologies. *NanoEthics* 5 (2): 129-141.
- Lüthje, C., C. Herstatt, and E. von Hippel. 2005. User-innovators and "local" information: The case of mountain biking. *Research Policy* 34 (6): 951-65.
- Lyketsos, C.G., C.A. Szekely, M.M. Mielke, P.B. Rosenberg, and P.P. Zandi. 2008. Developing new treatments for Alzheimer's disease: The who, what, when, and how of biomarker-guided therapies. *International Psychogeriatrics* 20 (5): 871–889.
- Lyman, K. A. 1989. Bringing the social back in: A critique of the biomedicalization of dementia. *The Gerontologist* 29 (5): 597-605.
- Maatschappelijke omgang met dementia verwaarloosd. 2013, May 19. *Nederlands Dagblad*.
- Manthorpe, J., and S. Iliffe. 2016. *The dialectics of dementia*. London, United Kingdom: Kings College London.
- Manthorpe, J., S. Iliffe, and A. Eden. 2003. The implications of the early recognition of dementia for multiprofessional teamworking: Conflicts and contradictions in practitioner perspectives. *Dementia: The International Journal of Social Research and Practice* 2 (2): 163-179.
- Mast, B.T. 2009. Uncertainties in Dementia: What Do People with Dementia Experience?. *Generations* 33(1): 30–36.
- Mattson, N., D. Brax, and H. Zetterberg. 2010. To Know or Not to Know: Ethical Issues Related to Early Diagnosis of Alzheimer's Disease. *International Journal of Alzheimer's Disease* 10 (Article ID 841941).
- Mattsson, N., H. Zetterberg, and K. Blennow. 2010. Lessons from Multicenter Studies on CSF Biomarkers for Alzheimer's Disease. *International Journal of Alzheimer's Disease*, 2010 (Article ID 610613).
- Maurer, K., S. Volk, and H. Gerbaldo. 2000. Auguste D.: The History of Alois Alzheimer's First Case. In *Concepts of Alzheimer Disease - Biological, Clinical, and Cultural Perspectives*. ed. Whitehouse P.J., K. Maurer, and J.F. Ballenger, 5–29. Baltimore, United States of America: The John Hopkins University Press.
- McKhann, G., D. Drachman, M. Folstein, R. Katzman, D. Price, and E.M. Stadlan. 1984. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 34 (7): 939–944.
- McKhann, G. M., D.S. Knopman, H. Chertkow, B.T. Hyman, C.R. Jack, C.H. Kawas, ..., and C.H. Phelps. 2011. The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's and Dementia* 7 (3): 263-269.

- McParland, P., F. Kelly, & A. Innes. 2017. Dichotomising dementia: is there another way? *Sociology of Health & Illness* 39 (2): 258–269.
- Miesen, B. 2002. *Het Alzheimer Cafe*. Houten, The Netherlands: Bohn Stafleu van Loghum.
- Miller, G. 2010. Alzheimer's Biomarker Initiative Hits Its Stride. *Science* 326 (5951): 386–389.
- Miller, G. 2012. Stopping Alzheimer's before it starts. *Science* 337 (6096): 790-792.
- Milne, A. 2010. Dementia screening and early diagnosis: The case for and against. *Health, Risk & Society* 12 (1): 65–76.
- Ministerie van Volksgezondheid, Welzijn en Sport (VWS). 2012. *Deltaplan Dementie 2012-2020*. Eindversie 19 augustus 2012.
- Mol, A. 2002. *The body multiple: ontology in medical practice*. Durham and London, United Kingdom: Duke University Press.
- Mol, A. 2008. *The Logic of Care, Health and the Problem of Patient Choice*. London and New York, United Kingdom and United States of America: Routledge.
- Mol, A., I. Moser, and J. Pols. 2010. *Care in practice, on tinkering in clinics, homes and farms*. Bielefeld, Germany: Transcript.
- Möller, H.-J., and M.B. Graeber. 2000. Johann F.: The Historical Relevance of the Case for the Concept of Alzheimer Disease. In *Concepts of Alzheimer Disease - Biological, Clinical, and Cultural Perspectives*. ed. Whitehouse P.J., K. Maurer, and J.F. Ballenger, 30–46. Baltimore, United States of America: The John Hopkins University Press.
- Moreira, T., J.C. Hughes, T. Kirkwood, T., C. May, I. McKeith, and J. Bond, 2008. What explains variations in the clinical use of mild cognitive impairment (MCI) as a diagnostic category? *International Psychogeriatrics* 20 (4): 697–709.
- Moreira, T. 2010. Now or Later? Individual disease and care collectives in the memory clinic. In *Care in Practice, on Tinkering in Clinics, Homes and Farms*. ed. Mol, A., I. Moser, and J. Pols. 119-140. Bielefeld, Germany: Transcript Verlag.
- Mort, M., and C. Roberts. 2010. At home with Machines: technology in/dependence and ageing. In *Paper presented at the EASST 2010 conference: practicing science and technology performing the social, september 2-4-2010* Trento, Italy.
- Moser, I. 2008. Making Alzheimer's disease matter. Enacting, interfering and doing politics of nature. *Geoforum* 39 (1): 98–110.
- Moser, I. 2011. Dementia and the Limits to Life: Anthropological Sensibilities, STS Interferences, and Possibilities for Action in Care. *Science, Technology & Human Values* 36 (5): 704–722
- Mueller, S. G., M.W. Weiner, L.J. Thal, R.C. Petersen, C.R. Jack, W. Jagust, ..., and L. Beckett. 2005. Ways toward an early diagnosis in Alzheimer's disease: The Alzheimer's Disease Neuroimaging Initiative (ADNI). *Alzheimer's & Dementia* 1 (1): 55–66.
- Nagel, T. 1989. *The view from nowhere*. Oxford, United Kingdom: Oxford University Press.

- Nederlandse Organisatie voor Wetenschappelijk Onderzoek. 2008a. *Maatschappelijk Verantwoord Innoveren, Ethische en Maatschappelijke Verkenning van Wetenschap en Technologie, MVI Programma notitie april 2008*. Accessed december 2009 from [http://www.nwo.nl/files.nsf/pages/NWOA\\_7E2FMH/\\$file/MVI\\_programmanotitie\\_april\\_2008.pdf](http://www.nwo.nl/files.nsf/pages/NWOA_7E2FMH/$file/MVI_programmanotitie_april_2008.pdf)
- Nederlandse Organisatie voor Wetenschappelijk Onderzoek. 2008b. *Maatschappelijk verantwoord innoveren, ethische verkenning van wetenschap en technologie, beschrijving themaprogramma*.
- Neumann, M., and R. Cohn. 1953. Incidence of Alzheimer's Disease in a Large Mental Hospital: Relation to Senile Psychosis and Psychosis with Cerebral Arteriosclerosis. *Archives of Neurology and Psychiatry* 69 (5): 615-636.
- Neuvel, K. 2014. *Alzheimer, biografie van een ziekte*. Amsterdam, The Netherlands: Podium B.V.
- Neven, L.B.M. 2011. *Representations of the old and ageing in the design of the new and emerging, assessing the design of ambient intelligence technologies for older people*. PhD Dissertation. Twente University, Enschede, The Netherlands.
- Ney, S. 2009. *Resolving Messy Policy Problems: Handling conflict in environmental transport, health and ageing policy*. London, United Kingdom: Earthscan.
- Nordmann, A. 2007. If and then: A critique of speculative nanoethics. *NanoEthics* 1 (1): 31–46.
- Nordmann, A. 2014. Responsible innovation, the art and craft of anticipation. *Journal of Responsible Innovation* 1 (1): 87-98
- Nordmann, A., and A. Rip. 2009. Mind the gap revisited. *Nature Nanotechnology* 4 (5): 273-4.
- Olde Rikkert, M., M. Verbeek, F. Verhey, and M. de Vugt. 2012, April 11. De ziekte van Alzheimer bestaat niet. *NRC Handelsblad*.
- Oudshoorn, N., and T. Pinch. 2003. *How users matter: The co-construction of users and technologies*. Cambridge, United States of America: MIT press.
- Perneczky, R., and A. Kurz. 2012. Dealing with uncertainty: Biomarkers for the early detection of Alzheimer's disease. *International Psychogeriatrics* 24 (10): 1533–1535.
- Perry, M., I. Drasković, T. van Achterberg, G.F. Borm, M.I.J. van Eijken, P. Lucassen, ..., and M.G.M. Olde Rikkert (2008). Can an EASYcare based dementia training programme improve diagnostic assessment and management of dementia by general practitioners and primary care nurses? The design of a randomised controlled trial. *BMC Health Services Research* 8: 71.
- Petersen, R. C., B. Caracciolo, C. Brayne, S. Gauthier, V. Jelic, and L. Fratiglioni. 2014. Mild cognitive impairment: a concept in evolution. *Journal of Internal Medicine* 275 (3): 214–228.

- Polkinghorne, D.E. 1995. Narrative configuration in qualitative analysis. *International Journal of Qualitative Studies in Education* 8 (1): 5-23.
- Portacolone, E., C. Berridge, J.K. Johnson, and S. Schicktanz. 2014. Time to reinvent the science of dementia: the need for care and social integration. *Aging & Mental Health* 18 (3), 269–275.
- Post, S. G. 2000. The concept of Alzheimer's disease in a hyper-cognitive society. In *Concepts of Alzheimer Disease - Biological, Clinical, and Cultural Perspectives*. ed. Whitehouse P.J., K. Maurer, and J.F. Ballenger, 245-256. Baltimore, United States of America: The John Hopkins University Press.
- Pratt, R., and H. Wilkinson. 2003. A Psychosocial Model of Understanding the Experience of Receiving a Diagnosis of Dementia. *Dementia* 2 (2): 181–199.
- Querfurth, H. W., and F.M. Laferla. 2010. Alzheimer's disease: mechanism of disease. *The New England Journal of Medicine* 362 (4): 329–344.
- Quinn, J. F. 2013. Biomarkers for Alzheimer's disease: Showing the way or leading us astray? *Journal of Alzheimer's Disease* 33 (Suppl. 1): S371–S376.
- Renshaw, J., P. Scurfield, L. Cloke, and M. Orrell. 2001. General practitioners' views on the early diagnosis of dementia. *The British Journal of General Practice : The Journal of the Royal College of General Practitioners* 51 (462): 37–38.
- Reuzel, R., and G.J. Van der Wilt. 2000. Technology Assessment in the Health Care Area: A Matter of Uncovering or of Covering Up? In *Vision Assessment: Shaping Technology in 21st Century Society*. ed. Grin J. and A. Grunwald, 53–70. Berlin Heidelberg, Germany and New York, United States of America: Springer-Verlag.
- Reuzel, R.P.B.2001. Health technology assessment and interactive evaluation: different perspectives. PhD thesis. Katholieke Universiteit Nijmegen, The Netherlands. Enschede, The Netherlands: Ipskamp.
- Richard, E., B. Schmand, P. Eikelenboom, R.G. Westendorp, and W.A. Van Gool. 2012. The Alzheimer myth and biomarker research in dementia. *Journal of Alzheimer's Disease*, 31 (Suppl. 3): S203–S209.
- Richards, M., and C. Brayne. 2010. What do we mean by Alzheimer's disease? *The British Medical Journal* 341: c4670.
- Rip, A. 1986. Societal Processes of Technology Assessment. In *Impact Assessment Today*. ed. Becker, H.A. and A. L. Porter, 415–434. Utrecht, The Netherlands: Uitgeverij Jan van Arkel.
- Rip, A. 1987. Controversies as Informal Technology Assessment. *Knowledge: Creation, Diffusion, Utilization* 8 (2): 349–371.
- Rip, A., and R. Kemp. 1998. Technological change. In *Human Choice and Climate Change*. ed. S. Rayner and E.L. Malone, 327–399. Columbus, United States of America: Battelle Press.
- Robertson, A. 1990. The politics of Alzheimer's disease: a case study in apocalyptic

- demography. *International Journal of Health Services: Planning, Administration, Evaluation* 20 (3): 429–442.
- Robertson, A. 1997. Beyond Apocalyptic Demography: Towards a Moral Economy of Interdependence. *Ageing and Society* 7 (4): 425–446.
- Robinson, L., E. Tang, and J.P. Taylor. 2015. Dementia: Timely diagnosis and early intervention. *BMJ* 350: h3029.
- Rosow, K., A. Holzapfel, J.H. Karlawish, M. Baumgart, L.J. Bain, and A.S. Khachaturian. 2011. Countrywide strategic plans on Alzheimer's disease: developing the framework for the international battle against Alzheimer's disease. *Alzheimer's & Dementia* 7 (6): 615–621.
- Rossum, I.A. van, S. Vos, R. Handels, and P.J. Visser. 2010. Biomarkers as predictors for conversion from mild cognitive impairment to Alzheimer-type dementia: Implications for trial design. *Journal of Alzheimer's Disease* 20 (3): 881–891.
- Rothschild, D. 1947. The Practical Value of Research in the Psychoses of Later Life. *Diseases of the Nervous System* 8 (4): 123–128.
- Rothschild, D., and M.L. Sharp. 1941. The Origin of Senile Psychoses: Neuropathologic Factors and Factors of a More Personal Nature. *Diseases of the Nervous System* 2: 49–54.
- Sabat, S. R., and R. Harré, The Construction and Deconstruction of Self in Alzheimer's Disease. *Ageing & Society* 12 (4): 443–461.
- Samsi, K., C. Abley, S. Campbell, J. Keady, J. Manthorpe, L. Robinson, ..., and J. Bond. 2013. Negotiating a labyrinth: experiences of assessment and diagnostic journey in cognitive impairment and dementia. *International Journal of Geriatric Psychiatry* 29 (1), 58–67.
- Schermer, M. 2013. Old age is an incurable Disease—or is it? In *Ethics, Health Policy and (Anti-) Aging: Mixed Blessings*. ed. M. Schermer, and W. Pinxten, 209–224. Dordrecht, The Netherlands: Springer.
- Schermer, M., and W. Pinxten. 2013. *Ethics, Health Policy and (Anti-) Aging: Mixed Blessings*. Dordrecht, The Netherlands: Springer.
- Schneider, J. A., Z. Arvanitakis, W. Bang, and D.A. Bennett. 2007. Mixed brain pathologies account for most dementia cases in community-dwelling older persons. *Neurology* 69 (24): 2197–2204.
- Schomberg, R. von. 2011. Prospects for Technology Assessment in a framework of responsible research and innovation. In *Technikfolgen Abschätzen Lehren: Bildungspotenziale Transdisziplinärer Methoden*. ed. Dusseldorf, M. and R. Beecroft, 39–61. Wiesbaden, Germany: VS Verlag für Sozialwissenschaften.
- Schomberg, R. von. 2013. A Vision of Responsible Research and Innovation. In *Responsible Innovation: Managing the Responsible Emergence of Science and Innovation in Society*. ed. Owen, R., B. Bessant and M. Heintz, 51–74. Hoboken, United States of America: John Wiley & Sons.
- Schön, D. A., and M. Rein. 1995. *Frame Reflection: Toward The Resolution Of Intractable Policy Controversies*. New York, United States of America: Basic Books.

- Scodellaro, C., and S. Pin. 2013. The ambiguous relationships between aging and Alzheimer's disease: a critical literature review. *Dementia* 12 (1): 137–151.
- Sekhasaria, P. 2013. Jugaad as a conceptual and materials commons. *Common Voices* 8, 21–23.
- Selkoe, D. J. 2012. Preventing Alzheimer's disease. *Science* 337 (6101): 1488–1492.
- Shulman, M.B., K. Harkins, R.C. Green, and J. Karlawish. 2013. Using AD biomarker research results for clinical care: A survey of ADNI investigators. *Neurology* 81 (13): 1114-1121.
- Smits, R.E.H.M., and W.P.C. Boon. 2008. The role of users in innovation in the pharmaceutical industry. *Drug Discovery Today* 13 (7-8): 353-9.
- Snowdon, D.A. 1997. Aging and Alzheimer's Disease: Lessons From the Nun Study. *The Gerontologist* 37 (2): 150–156.
- Sperling, R.A., P.S. Aisen, L.A. Beckett, D.A. Bennett, S. Craft, A.M. Fagan, ..., and C.H. Phelps. H. 2011. Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's and Dementia* 7 (3): 280-292.
- Steeman, E., J. Tournoy, M. Grypdonck, J. Godderis, and C. de Dierckx. 2013. Managing identity in early-stage dementia: Maintaining a sense of being valued. *Ageing and Society* 33 (2): 216–242.
- Stilgoe, J., R. Owen, P. Macnaghten, J. Stilgoe, M. Gorman, ... , and Guston, D. 2013. Developing a framework for responsible innovation. *Research Policy* 42 (9): 1568-1580.
- Stirling, A. 2010. Keep it complex. *Nature* 468 (7327): 1029–1031.
- Strauss, C. L. 2009. *Het wilde denken*. Amsterdam, The Netherlands: J.M. Meulenhoff.
- Swaab, D. 2010. *Wij zijn ons brein. Van baarmoeder tot Alzheimer*. Amsterdam, The Netherlands, Antwerpen, Belgium: Atlas Contact.
- Sweeting, H., and M. Gilhooly. 2008. Dementia and the phenomenon of social death. *Sociology of Health & Illness* 19 (1): 93–117.
- Swidler, A. 1986. Culture in Action: Symbols and Strategies. *American Sociological Review* 51 (2): 273-286.
- Tewksbury, D., and D. Scheufele. 2007. Special issue on framing, agenda setting, & priming: Agendas for theory and research. *Journal of Communication* 57 (1): 8.
- Thé, A.M., and A. Reerink. 2013, April 11. Dementie vooral gebaat bij meer levenskwaliteit. *De Volkskrant*.
- Thomas, L. 1981. The Problem of Dementia. Reprinted in 1983 *Late Night Thoughts on Listening to Mahler's Ninth Symphony*, 121. New York, US: Viking.
- Twaddle, A.C. 1994. Disease, illness and sickness revisited. In *Disease, Illness and Sickness*:

- Three Central Concepts in the Theory of Health*. ed. L. Nordenfelt and A. Twaddle, 18th ed., 1–18. Linköping, Sweden: Studies on Health and Society.
- Vann, A.S. 2011. Ten things you should do when the diagnosis is Alzheimer's. *American Journal of Alzheimer's Disease and Other Dementias* 26 (2): 93–96.
- Vermeiren, H. 2012. *Dementie, het blikveld verruimd, Introductie in Persoonsgerichte zorg en Dementia Care Mapping*. Antwerpen-Apeldoorn, Belgium-The Netherlands: Garant.
- Vernooij-Dassen, M. 2006. Receiving a diagnosis of dementia: The experience over time. *Dementia* 5 (3): 397–410.
- Vernooij-Dassen, M.J.F.J., E.D. Moniz-Cook, R.T. Woods, J. de Lepeleire, A. Leuschner, O. Zanetti, ..., and S. Iliffe. 2005. Factors affecting timely recognition and diagnosis of dementia across Europe: From awareness to stigma. *International Journal of Geriatric Psychiatry* 20 (4): 377–386.
- Vugt, M.E. de, and F.R.J. Verhey. 2013. The impact of early dementia diagnosis and intervention on informal caregivers. *Progress in Neurobiology* 110: 54-62.
- Weick, K. E. 1995. *Sensemaking in Organizations*. London, United Kingdom: Sage.
- Wetherell, M., and J. Potter. 1992. *Mapping the Language of Racism: Discourse and the Legitimation of Exploitation*. Hemel Hempstead, United Kingdom: Harvester Wheatsheaf.
- Whitehead, A.N. 1919. *The Concept of Nature*, The Tarner Lectures Delivered in Trinity College, November 1919, e-book #18835 released in 2006, [www.gutenberg.org](http://www.gutenberg.org)
- Whitehouse, P.J., A.D. Gaines, H. Lindstrom, and J.E. Graham. 2005. Anthropological contributions to the understanding of age-related cognitive impairment. *The Lancet Neurology* 4 (5): 320–326.
- Whitehouse, P.J., and D. George. 2008. *The myth of Alzheimer's, what you aren't being told about today's most dreaded diagnosis*. New York, United States of America: St. Martin's Press.
- Wilson, D. 1955. The Pathology of Senility. *American Journal of Psychiatry* 111 (2): 902–906.
- Winblad, B., P. Amouyel, S. Andrieu, C. Ballard, C. Brayne, H. Brodaty, ..., and H. Zetterberg. 2016. Defeating Alzheimer's disease and other dementias: a priority for European science and society. *The Lancet Neurology* 15 (5): 455–532.
- World Health Organization and Alzheimer's Disease International. 2012. *Dementia: a public health priority*. Geneva, Switzerland: WHO Press.
- World Health Organization. 2015. First WHO Ministerial Conference on Global Action Against Dementia, 16-17 March 2015. Geneva, Switzerland.
- ZonMw. 2013. *Memorabel, Programmavoorstel Onderzoeks- en innovatieprogramma Dementie*. Den Haag, The Netherlands.

Zuccherro, R.A., E. Hooker, and S. Larkin. 2010. An interdisciplinary symposium on dementia care improves student attitudes toward health care teams. *International Psychogeriatrics* 22 (2): 312-320.

# Summary



# Meanings and Multiplicity

## *Assessing Early Diagnostics for Alzheimer's Disease*

### INTRODUCTION

This study contributes to responsible innovation through an empirical study of the meanings of early diagnostics for Alzheimer's disease in a number of settings as a technology assessment 'in the wild'.

In aging societies such as the Netherlands, the number of persons with Alzheimer's disease is growing and expected to continue to grow. There have been increasing investments in science and innovation to find (partial) solutions to deal with dementia in society. One of the innovations in which money and hope is invested are early diagnostic tests for Alzheimer's disease with the use of biomarkers, promising to enable a more reliable and earlier identification of Alzheimer's disease at a stage with mild symptoms or even before symptoms occur. The value of these diagnostic tests are not uncontested and questions are raised on many issues, such as for example: What is the use of such tests when disease modifying treatment is lacking? Are these tests only interesting for research purposes, or also for clinical practice? Are early diagnostic tests medicalizing normally aging persons? Shouldn't more attention be paid to social, cultural and psychological aspects of dementia? This is why responsible innovation of early diagnostics for Alzheimer's disease deserves critical scrutiny.

Because dementia is a hot topic in aging societies, even though it is an emergent technology, early diagnostics for Alzheimer's disease is already part of conversations. This has led to a specific approach to responsible innovation, based on two starting assumptions:

1. Social and cultural implications of emerging technologies can be studied 'in the wild', without the use of specific TA or foresight tools.
2. Social and cultural implications of emerging technologies can be studied in the present. There is no need to speculate on the implications of, in this case, early diagnostics for Alzheimer's disease.

Explorative activities showed that early diagnostics gained vastly different meanings, depending on the actors and the contexts visited. Moreover, Alzheimer's disease itself was approached in multiple ways. The multiple meanings of early diagnostics for Alzheimer's disease are the central research topic of this thesis.

The following research questions were formulated:

1. *What are the **meanings of early diagnostics** for Alzheimer's disease in different settings?*
2. *Does the study of meanings reveal **assessments** of early diagnostics 'in the wild' and if so, how is early diagnostics for Alzheimer's disease assessed?*

3. *What does the study of meanings imply for the notion of **responsible innovation**?*

## SETTING THE STAGE

### **Chapter 2 Thinking about early diagnostics for Alzheimer's disease: history, diagnosis, ailment**

This chapter provides background literature on the different ways in which early diagnostics for Alzheimer's disease, Alzheimer's disease itself, and diagnosis and ailments in general, are understood.

A historical reconstruction of the concept of dementia shows that the understanding of Alzheimer's disease has shifted with over time, influenced by scientific, technological, and social developments. Discussions arising on early diagnostics for Alzheimer's disease in the present have their roots in a long tradition of similar discussions.

In medical literature the early signalling of biomarkers for Alzheimer's disease through early diagnostic instruments is considered key to force a breakthrough in research on the disease mechanisms causing Alzheimer's disease and to speed up the development of disease modifying treatment. Promises of early diagnostics for Alzheimer's disease also include the provision of more certainty to persons experiencing (cognitive) problems that might be a foretoken of dementia, and a reduction of the societal health care costs. These promises are not uncontested in the medical domain and there is a fundamental recurring discussion about underlying disease models.

In clinical literature an important question when it comes to early diagnostics is whether a diagnosis is a desirable intervention for a patient and at which moment in time. In psychosocial studies, the implications of an (early) diagnosis Alzheimer's disease for a patients are researched. The sociology of diagnosis considers a diagnosis a social agreement that some condition is in need of a diagnostic label, which works as an ordering device in many different domains.

The section on thinking about dementia and ailment in general shows different understandings of dementia: dementia as part of normal aging, as a medical condition, as a (bio)psychosocial process, from a social gerontological perspective and spiritual explanations for dementia. Finally analytical model to conceptualize ailments and an approach towards understanding how diseases are enacted in practice are presented.

### **Chapter 3 Quandaries of responsible innovation: The case of Alzheimer's disease**

Responsible innovation is a concept that has become fashionable in the last decade amongst policy makers, firms and researchers. At the start of this study on the possibilities of responsible innovation in the case of new molecular early diagnostics for Alzheimer's disease we came across a various basic questions concerning the ambition assumptions an approaches of responsible innovation. We have labelled these questions 'quandaries': problematic, difficult and ambiguous conditions that somehow require fundamental and practical decisions. We identified six quandaries. (1) Where to start - a technocentric or multi-

actor view on innovation? (2) Where to end – singular or multiple futures? (3) With whom – developers or stakeholders? (4) What's the goal - process or outcome? (5) What to question – speculation or plausibility? (6) Responsible for whom – responsibility for the future or the present? These considerations fed into the choice for the specific approach to responsible innovation taken in this thesis (see introduction for the description of the approach).

#### **Chapter 4 Research approach: studying the meaning of early diagnosis**

A discursive approach was used to analyse the meanings of early diagnostics of Alzheimer's disease, inspired by literature on discourse analysis, modes of ordering and framing analysis. The meanings of early diagnostics for Alzheimer's disease are traced and analysed in four different settings: public media, a health technology assessment setting, Alzheimer Cafés, and the development of a national dementia strategy, i.e. the Dutch Deltaplan Dementie. In each setting the meanings of early diagnostics for Alzheimer's disease were analysed, and each analysis had a distinct focus. In the public media, the health technology assessment, and the Alzheimer café the focus was on *the multiplicity of meanings*. Even though the data was collected over a longer timeframe, the analyses were more *snapshot-like*. In the last setting, the Deltaplan Dementie, the data was analysed *longitudinally* to allow studying the *dynamics* that comes with the *co-existence of multiple meanings* within a setting.

### **STAGING THE SETTING**

The empirical chapters provide answers to the first research question: *What are the meanings of early diagnostics for Alzheimer's disease in different settings?* Each setting provided a window onto the cultural repertoire of early diagnostics for Alzheimer's disease. The explication of these multiple meanings reveals the *scope* of the implications of early diagnostics for Alzheimer's disease. Comparing the meanings between settings showed overlaps and differences on *what* meanings of early diagnostics are constructed in the different settings are and *how* these meanings co-exist.

**Chapter 5** contains the analysis of the meaning of early diagnostics as constructed in newspaper articles between 1995 and 2010. Newspaper articles were analysed as an indicator of cultural repertoire (Swidler 1986), or more specific, the *issue culture* of early diagnostics for Alzheimer's disease (Gamson & Modigliani, 1989). Newspaper articles are considered as a setting that mirrors as well as constitutes a cultural repertoire and as such provide an entrance point to analyse interpretative packages (clusters of related elements), through which the meaning of early diagnostics of Alzheimer's disease is constituted. Nine different interpretative packages are delineated from the analysis of newspaper articles, in which early diagnostics for Alzheimer's disease gained meaning as:

- *Apocalyptic demography*. A step towards a solution of the societal challenge that dementia poses, through improving health care and decreasing health care costs.

- *Scientific progress.* Pushing the boundaries of brain sciences and neurosciences, increasing knowledge on Alzheimer's disease, and progression towards a medical solution or prevention of Alzheimer's disease.
- *Scientific complex puzzle.* Pieces of the complex puzzle of the condition Alzheimer's disease, which is seen as the outcome of many accumulating biological, personal and social mechanisms.
- *Technological progress.* Changing health care towards predictive medicine, and developing tests to predict the development of Alzheimer's disease in an individual.
- *Economic competitiveness.* An innovative product for a huge market.
- *Health care provision.* Enabling the timely start of a well-organized and suitable care and support trajectory for a patient and his or her family.
- *Successful aging.* Increasing knowledge on risk factors of dementia and enabling measures to prevent Alzheimer's disease.
- *Fear and worry.* Patient information providing relief and clarity to a patient, or a doomsday scenario becoming reality.
- *Good life and death.* A verdict enabling a self-chosen death.

The analysis of newspaper articles confirmed the diversity and ambiguity of the meanings of early diagnostics for Alzheimer's disease, which went beyond a medical understanding of Alzheimer's disease. Early diagnosis always gained meaning in relation to a bigger problem or higher goal: face the societal challenge posed by the changing demography, find a cure against Alzheimer's disease, further scientific knowledge, develop a strong knowledge economy, keep the health care system viable and affordable, provide comfort to patients, defeat Alzheimer's disease through aging successfully, or maintain autonomy by taking your life in your own hand.

**Chapter 6** compares and contrasts a health technology assessment and an Alzheimer café setting. In both settings it was analysed how the development of early diagnostics for Alzheimer's disease was entangled with specific definitions of Alzheimer's disease and articulations of problems and solutions in dealing with Alzheimer's disease in the near future.

The Health Technology Assessment (HTA) was conducted to assess the clinical and economic value of the early diagnostic instruments as developed by the medical research consortium LeARN. The analysis of the meaning of early diagnostics in this setting resulted in the identification of six interpretative packages through which early diagnosis gains meaning:

- *Early diagnostics as value for money.* 'Health care is expensive and is getting more costly. New technologies could potentially improve health care and increase the quality of life for patients and informal caregivers, but may also lead to an increase in costs. Therefore it has to be examined whether they are value for money. For early molecular diagnostics it is not clear yet.'
- *Early diagnostics as having uncertain consequences for (future) health care practices.* 'Consequences of new health technologies are complex to assess. You first need to know

how they will change the possibilities for diagnostic and clinical practice, and what it means for patients, informal caregivers, and the total costs of health care. It is a tremendous task, but we need to do it.'

- *Early diagnostics as innovation trajectories.* 'Progress in health care is possible with innovation. Early diagnostics is an umbrella term for various technological developments. They are rooted in different sets of expertise. So, technologies have their own trajectories and they compete.'
- *Early diagnostics as changing the definition of Alzheimer's disease.* 'We are now capable of diagnosing Alzheimer's dementia at an early stage, which changes the notion of what it means to be diagnosed with Alzheimer's disease. But also the basis on which a diagnosis is made is shifting. The diagnosis of Alzheimer's disease used to be on the basis of exclusion of other conditions. The importance of early diagnostics is that it can show actual traces of Alzheimer's disease in the brain. In this way the whole notion of Alzheimer's disease changes from symptoms to pathology. With early diagnostics we can work on better definitions for research, drug development and monitoring of patients.'
- *Early diagnostics as a step on the road to medication.* 'Early diagnostics should lead to better medication. Progress in health care is on finding better medication. When patients are diagnosed more accurately, the matching of patients and drugs is better. Furthermore an early diagnosis enables treatment on an early stage when medication is expected to be most effective. Even when a treatment is lacking currently, it is important to anticipate its future availability.'
- *Early diagnostics as part of early management.* 'The quality of new technologies for health care is determined by their benefit for patients. Since there is no medication for Alzheimer's disease, early diagnostic technologies have nothing to offer in terms of cure. Instead early diagnostics should be part of management of the disease in early phases.'

Alzheimer Cafés are set up to provide persons confronted with this condition with information and with (peer) support to better deal with their situation. Five interpretative packages through which early diagnostics gains meaning were identified:

- *Early diagnostics as identifying a biomedical condition.* 'In case of worries about forgetfulness, go and see your doctor. With new diagnostic tests a diagnosis can be conducted in an increasingly early stage. Alzheimer's disease is a disease of which forgetfulness is an important symptom. However, it is not the only cause of forgetfulness, so it is important to find out what is going on.'
- *Early diagnostics as early patient management.* 'It is key that patients and informal caregivers make sense of early signals of dementia and can adapt their life to this new situation and related prospects. An official diagnosis should support their understanding and provide entrance to health care arrangements. The core issue of Alzheimer's disease is how patients and caregivers can cope with it.'
- *Early diagnostics as labelling persons.* 'Now that Alzheimer's disease is diagnosed at an increasingly early stage, the mismatch between public perceptions related to the label

dementia and the actual functioning of a person will increase. A diagnosis Alzheimer's disease attaches a label to a person. When this happens it has various profound social consequences.'

- *Early diagnosis as a life event putting things in an 'Alzheimer perspective'.* 'Being diagnosed as having Alzheimer's disease is a life changing event. It requires a deep existential response and changes a person's past and future. Do you really want to know this in an early stage?'
- *Early diagnostics as reducing health care costs.* 'A timely diagnosis can reduce health care costs by preparing caregivers and thus allowing patients to stay at home longer. In an aging society, patients with Alzheimer's disease are a burden. Demographic trends will run to financial and nursing limits.'

In both the HTA and the Alzheimer Cafés multiple meanings of early diagnostics for Alzheimer's disease co-existed. Single persons or documents draw upon and move between packages. Each interpretative package appeared as a 'bead', and every story or conversation as a unique 'necklace'.

A comparison of the outcomes of the HTA and Alzheimer Café setting reveals differences and overlaps between the interpretive packages in both settings. The delineation of multiple packages creates a sensitivity to the politics at work in particular situations or in discussions taking place, and it enables the identification of issues that have become invisible or backgrounded.

**Chapter 7** analyses the strategies to deal with dementia as part of a national dementia strategy. National dementia strategies are being developed worldwide and also in the Netherlands. A part of a Dutch national dementia strategy is the 'Deltaplan Dementie', initiated in 2012.

Within this setting we see that the efforts to collectively tackle the challenges of dementia has unleashed a multitude of framings of dementia. A struggle occurred over who got to define what a dementia strategy should constitute. The reconstruction showed different models on dementia were considered to co-exist: as parts of whole, as antagonistic positions and as moving in different directions. I argued that it is important to reflect on which model is most appropriate in which situations.

The analysis of the meanings of early diagnostics again showed a multiplicity of meanings, and some of the dynamics this multiplicity creates. Firstly, it creates a convincing argument of why early diagnostics for Alzheimer's disease is worth pursuing. Secondly, it raises questions, such as in whose interest is early diagnostics is being pursued and who will benefit in the end. Will this really be of benefit to patients, or is it just in the interest of science and industry? Thirdly, actors set boundaries to responsibilities and promises, for example by stating that early diagnostics is of interest for science, and it might also eventually be of value for clinical practice. Another example is the creation of all kinds of subcategories and delineations such as that a timely diagnosis is of value for patients, and a prodromal diagnosis

in the MCI stage might be of interest for those persons who want to know at a very early stage of disease progression, and an early predementia diagnosis is only of value for science. Fourthly, we see that the development cannot be confined to the boundaries actors set. This becomes visible in amongst others the move from an early and certain diagnosis of dementia to enable timely care and support, to the same development enabling early euthanasia, or a medicalization of ageing processes.

## DISCUSSION AND CONCLUSIONS

How does an empirical study of multiple meanings contribute to responsible innovation? The specific approach taken on responsible innovation in this thesis is that it is possible to conduct technology assessment 'in the wild' without using specific technology assessment or foresight tools, and that the assessment of new and emerging technologies can be empirically studied in the present. It is not necessary to imagine future situations to assess consequences.

### **What are the meanings of early diagnostics for Alzheimer's disease in different settings?**

Every setting contained a multiplicity of meanings of early diagnostics for Alzheimer's disease, with overlaps and differences between settings (see summary chapter 5 to 7). Analysing different settings builds a sensitivity for the specificities of each situation, while at the same time becoming aware of what is made salient and what is backgrounded in each situation.

### **Does the study of meanings reveal assessments of early diagnostics 'in the wild' and if so, how is early diagnostics for Alzheimer's disease assessed?**

The short answer is: yes, this study has shown assessments of early diagnostics 'in the wild' in three ways.

The multitude of interpretative packages that were encountered in the four settings span the scope of the implications of early diagnostics for Alzheimer's disease. Each interpretative package contains a limited technology assessment in itself, by providing a limited number of assessment criteria (valuations).

In each setting early diagnostics is assessed along particular threads. These threads, particular for each setting, structure the co-existence of interpretative packages: through fragmentation, inclusion/exclusion, as tools for tinkering, and competing with each other. This is related to what is at stake in a setting: the potential relevance or benefits to society, evidence of its value, how it helps to cope with the real life problems of dementia, the power and politics defining problems to be solved and directions to be pursued. How early diagnostics is assessed depends on the stakes in each setting.

Furthermore, technology assessment in the wild takes place through recurring narratives and discussions that are part of the cultural repertoire. Across settings recurrent dynamics between interpretative packages were found. The recurrent dynamics between interpretative

packages include a controversy, a split between developments in the present and promises for the future, a happy marriage, two sides of the same coin, tricky entanglements and a polarization. These narratives and discussions show that implications of early diagnostics follow many routes. These are patterns that play out time and again, are known in the field, and are to be expected to play out again. They are standard narratives and discussions that are to be expected and dealt with.

### **What does the study of meanings imply for the notion of responsible innovation?**

The patchwork understanding of implications of novel technologies that emerged from this thesis leads to an approach to responsible innovation which I summarized as ‘the benefit of the doubt’. This boils down to an urge for sensitivity of interrelatedness and awareness of the fringes, to the recognition that we should in many instances deal with problems (rather than aim to solve problems), and that we cannot escape from balancing acts. Above all, ‘the benefit of the doubt’ asks for humility in the face of dramatic diseases, loud solutions and a bewildering multiplicity of meanings.

# Samenvatting



# Twijfeltocht door Alzheimerland

## *Betekenenissen van vroegdiagnostiek van de ziekte van Alzheimer*

### INLEIDING

Met een empirisch onderzoek naar de betekenissen van vroegdiagnostiek voor de ziekte van Alzheimer en hoe deze geëvalueerd worden 'in het wild', beoogt deze studie bij te dragen aan maatschappelijk verantwoord innoveren.

In vergrijzende samenlevingen zoals Nederland, groeit het aantal mensen met dementie. Ook de investeringen in wetenschap en innovatie stijgen, om (gedeeltelijke) oplossingen te vinden voor de problemen die dit met zich meebrengt. Een van de innovaties waarop hoop is gevestigd en veel onderzoek naar gedaan wordt zijn tests voor vroegdiagnostiek van de ziekte van Alzheimer, die gebruik maken van biomarkers en imaging technieken. De verwachting is dat deze tests de ziekte van Alzheimer kunnen vaststellen in een fase waarin een persoon slechts milde symptomen heeft, of zelfs voordat symptomen van de ziekte van Alzheimer optreden. De waarde van dergelijke tests is niet onomstreden en roept allerlei vragen op zoals bijvoorbeeld: Wat is het nut van dergelijke testen als de ziekte niet geremd, gestopt of genezen kan worden? Zijn deze testen ook interessant voor de klinische praktijk, of alleen voor onderzoeksdoeleinden? Is vroegdiagnostiek van de ziekte van Alzheimer niet eigenlijk een vorm van medicalisering van veroudering? Zou er niet meer aandacht besteed moeten worden aan de sociale, culturele en psychologische aspecten van dementie? Deze en andere vragen zijn aanleiding voor dit onderzoek naar wat maatschappelijk verantwoorde vroegdiagnostiek van de ziekte van Alzheimer in zou kunnen houden.

Dementie is een onderwerp waar veel aandacht voor is in vergrijzende samenlevingen. Vandaar dat, alhoewel vroegdiagnostische tests voor de ziekte van Alzheimer opkomend technologieën zijn, deze wel al onderwerp zijn van gesprek. Dit heeft geleid tot twee aannames waarmee dit onderzoek naar verantwoord innoveren begonnen is:

1. Sociale en culturele implicaties van opkomende technologieën kunnen bestudeerd worden 'in het wild' zonder gebruik van specifieke instrumenten voor technology assessment of toekomstverkenningen.
2. Sociale en culturele implicaties van opkomende technologieën kunnen bestudeerd worden in het heden. Er is geen reden om te speculeren over de implicaties van, in dit geval, vroegdiagnostiek van de ziekte van Alzheimer.

Tijdens de verkennende onderzoeksactiviteiten werd duidelijk dat vroegdiagnostiek verschillende betekenissen kreeg, afhankelijk van de actoren en de contexten die ik als onderzoeker bezocht. Ook de benadering van de ziekte van Alzheimer was heel verschillend.

De verschillende betekenissen van vroegdiagnostiek voor de ziekte van Alzheimer zijn daardoor het centrale onderwerp van dit proefschrift geworden.

Dit proefschrift geeft antwoord op de volgende onderzoeksvragen:

1. Wat zijn de betekenissen van vroegdiagnostiek van de ziekte van Alzheimer in verschillende omgevingen?
2. Brengt dit onderzoek naar betekenissen van vroegdiagnostiek evaluaties van vroegdiagnostiek aan het licht en als dat zo is, hoe wordt vroegdiagnostiek dan geëvalueerd?
3. Wat leren we met deze studie naar de betekenissen van vroegdiagnostiek van de ziekte van Alzheimer over maatschappelijk verantwoord innoveren?

## SETTING THE STAGE

### **Hoofdstuk 2 Denken over vroegdiagnostiek van de ziekte van Alzheimer: geschiedenis, diagnose en ziekteconcept.**

Dit hoofdstuk bestaat uit een verzameling van literatuur over het denken over vroegdiagnostiek van de ziekte van Alzheimer, de ziekte van Alzheimer en het denken over diagnose en ziekte in het algemeen.

Een historische reconstructie van het concept 'de ziekte van Alzheimer' laat zien dat de het begrip van deze aandoening flink veranderd is in de loop van de tijd, onder invloed van wetenschappelijke, technologische en sociale ontwikkelingen. De huidige discussies over vroegdiagnostiek van de ziekte van Alzheimer zijn geworteld in een lange traditie van vergelijkbare discussies.

In medische literatuur wordt het vroeg signaleren van biomarkers van de ziekte van Alzheimer gezien als de sleutel naar een doorbraak in onderzoek naar de ziektemechanismen en naar het versnellen van de ontwikkeling van een geneesmiddel. Deze beloftes zijn niet onbetwist. Er zijn terugkerende discussies onder medici over het ziektemodel waarop de beloften van vroegdiagnostiek gebaseerd zijn.

In klinische literatuur is de belangrijkste vraag rondom vroegdiagnostiek of het een wenselijke interventie is voor patiënten en op welk moment deze interventie wenselijk zou zijn. Psychosociale studies onderzoeken de implicaties voor patiënten van het krijgen van een (vroeg) diagnose.

De sociologie van diagnostiek beschouwt een diagnose als een sociale overeenkomst dat een bepaalde staat een diagnostisch label behoeft. Zo'n diagnostisch label werkt als een ordenend element in veel verschillende domeinen.

De sectie over denken over dementie en ziekte in het algemeen laat zien dat dementie op meerdere manieren begrepen kan worden: als een onderdeel van normale veroudering, als een medische conditie, als een (bio)psychosociaal proces, vanuit sociaal gerontologisch

perspectief en er zijn spirituele verklaringen voor dementie. Als laatste presenteert het hoofdstuk een model om over ziekte in het algemeen te denken en een benadering van hoe ziekten in praktijk 'gedaan' worden.

### **Hoofdstuk 3 Verlegenheden rondom verantwoord innoveren**

Verantwoord innoveren is een concept dat het afgelopen decennium in zwang is geraakt onder beleidsmakers, bedrijven en onderzoekers. Aan het begin van deze studie liepen we aan tegen een aantal basale vragen over de ambities en aannames die het concept verantwoord innoveren met zich meebrengt. Deze hebben we verlegenheden ('quandaries') genoemd: problematische, moeilijke en ambigue situaties die om fundamentele of praktische beslissingen vragen. We identificeerden zes verlegenheden: (1) Waar te beginnen – een technocentrische of een multi-actor gezichtspunt op innovatie? (2) Waar te eindigen – een enkele of meerdere toekomst? (3) Met wie – ontwikkelaars of belanghebbenden? (4) Wat is het doel – proces of uitkomst? (5) Wat te betwijfelen – speculatie of aannemelijkheid? (6) Voor wie – verantwoordelijkheid voor de toekomst of voor het heden? Overwegingen met betrekking tot deze quandaries hebben bijgedragen de specifieke benadering van verantwoord innoveren in dit proefschrift.

### **Hoofdstuk 4 Aanpak van het onderzoek: bestuderen van de betekenissen van vroegdiagnostiek.**

Geïnspireerd door literatuur over discourse analyse, modes of ordering en framing, is gekozen voor een discursieve aanpak om de betekenissen van vroegdiagnostiek te analyseren. Deze betekenissen worden opgespoord en geanalyseerd in vier verschillende omgevingen: in publieke media, in een health technology assessment, in Alzheimer Cafés en tijdens de ontwikkeling van het Deltaplan Dementie (onderdeel van een nationale dementiestrategie). In de publieke media, de health technology assessment en de Alzheimer Cafés lag de focus op de meervoudigheid van betekenissen en was de analyse meer een momentopname. Bij het Deltaplan Dementie werd ook de dynamiek van het gelijktijdig bestaan van meerdere betekenissen over de tijd geanalyseerd.

### **STAGING THE SETTING**

De empirische hoofdstukken (hoofdstuk 5, 6 en 7) beantwoorden de eerste onderzoeksvraag: *Wat zijn de betekenissen van vroegdiagnostiek van de ziekte van Alzheimer in verschillende omgevingen?* Elke omgeving biedt een venster op het culturele repertoire van vroegdiagnostiek van de ziekte van Alzheimer. Het uiteenzetten van de veelvoudige betekenissen onthult de reikwijdte van de implicaties van vroegdiagnostiek voor de ziekte van Alzheimer. Wanneer de betekenissen in verschillende omgevingen met elkaar vergeleken wordt zichtbaar dat er overlappen en verschillen zijn wat betreft welke betekenissen geconstrueerd worden en ook hoe deze betekenissen naast elkaar bestaan.

**Hoofdstuk 5** geeft de analyse van de constructie van betekenissen van vroegdiagnostiek voor de ziekte van Alzheimer in krantenartikelen, gepubliceerd tussen 1995 en 2010. Krantenartikelen zijn geanalyseerd als een indicator van het culturele repertoire rondom vroegdiagnostiek. In kranten worden interpretatieve pakketjes - clusters van gerelateerde elementen – geanalyseerd, waardoor betekenissen van vroegdiagnostiek worden gevormd. Uit de analyse komen schetsen van negen interpretatieve pakketjes, negen betekenissen van vroegdiagnostiek van de ziekte van Alzheimer:

- *Apocalyptische demografie*: Vroegdiagnostiek is een stap naar een oplossing van de maatschappelijke uitdaging die dementie vormt, door het verbeteren van gezondheidszorg en het verlagen van de kosten van de gezondheidszorg.
- *Wetenschappelijke vooruitgang*: Vroegdiagnostiek zorgt voor het verleggen van de grenzen van de hersenwetenschappen en neurowetenschappen, voor het vergroten van kennis van de ziekte van Alzheimer, en voor vorderingen richting een medische oplossing voor de ziekte van Alzheimer.
- *Wetenschappelijke complexe puzzel*: Vroegdiagnostiek helpt bij het vinden van stukjes van de complexe puzzel die de ziekte van Alzheimer is, waarbij Alzheimer beschouwd wordt als de uitkomst van opeenhopen van biologische, persoonlijke en sociale mechanismen.
- *Technologische vooruitgang*: Vroegdiagnostiek is een stap richting het veranderen van gezondheidszorg naar voorspellende geneeskunde, en ontwikkeling van testen om de ontwikkeling van Alzheimer in een individu te voorspellen.
- *Economische concurrentiepositie*: Vroegdiagnostiek is een innovatief product voor een enorme markt.
- *Zorgverlening*: Vroegdiagnostiek maakt het mogelijk een tijdige start te maken van goed georganiseerde en gepaste zorg en ondersteuning voor patiënten en hun familie.
- *Succesvol ouder worden*: Vroegdiagnostiek levert meer kennis over risicofactoren van dementie en maakt maatregelen om de ziekte van Alzheimer te voorkomen mogelijk.
- *Angst en zorgen*: Vroegdiagnostiek zorgt voor duidelijkheid voor patiënten, wat een opluchting kan zijn of een doemscenario dat waarheid wordt.
- *Goed leven en goede dood*: Vroegdiagnostiek is een vonnis dat een zelf verkozen dood mogelijk maakt.

De analyse van krantenartikelen bevestigt de diversiteit en ambiguïteit van de betekenissen van vroegdiagnostiek van de ziekte van Alzheimer. De betekenissen beperkten zich niet tot een medisch begrip van Alzheimer. Vroegdiagnostiek kreeg telkens betekenis in relatie tot een groter probleem of een hoger doel. Het omgaan met de maatschappelijke uitdagingen van dementie, het vinden van een geneesmiddel voor dementie, wetenschappelijke of technologische vooruitgang, een sterke economie, een goed gezondheidszorgsysteem, of het behoud van autonomie.

**Hoofdstuk 6** vergelijkt de betekenissen van vroegdiagnostiek van de ziekte van Alzheimer in twee omgevingen: in een health technology assessment (HTA) en in Alzheimer cafés. De HTA werd uitgevoerd om de klinische en economische waarde van vroegdiagnostische tests ontwikkeld in het LeARN consortium in te schatten. Zes interpretatieve pakketjes konden daarin onderscheiden worden:

- *Vroegdiagnostiek als waar voor je geld.* De gezondheidszorg is duur en wordt steeds duurder. Nieuwe technologieën zouden potentieel de gezondheidszorg en de kwaliteit van leven van patiënten en mantelzorgers kunnen verbeteren, maar kunnen ook bijdragen aan nog hogere zorgkosten. Daarom moet de afweging gemaakt worden hoeveel meerwaarde een technologie heeft ten opzichte van wat hij kost. Voor vroegdiagnostiek is dit nog niet duidelijk.
- *Vroegdiagnostiek heeft onzekere gevolgen voor toekomstige gezondheidszorgpraktijken.* Consequenties van nieuwe gezondheidszorgtechnologieën zijn moeilijk in te schatten. Je moet weten hoe deze de mogelijkheden van diagnostische en klinische praktijken veranderen, wat de gevolgen daarvan zijn voor patiënten en mantelzorgers, en het effect op de totale kosten van gezondheidszorg.
- *Vroegdiagnostiek als innovatietrajecten.* Vooruitgang in gezondheidszorg is mogelijk met innovatie. Vroegdiagnostiek is een paraplueterm voor verschillende technologische ontwikkelingen, uit verschillende expertisegebieden. Deze technologieën hebben hun eigen trajecten en ze concurreren met elkaar.
- *Vroegdiagnostiek verandert de definitie van de ziekte van Alzheimer.* Een diagnose van de ziekte van Alzheimer werd gedaan op basis van symptomen en de exclusie van andere aandoeningen. Met vroegdiagnostiek kunnen juist de sporen van de ziekte in de hersenen aangetoond worden. Hierdoor verandert de basis van de diagnose van symptomen naar pathologie en dit maakt het mogelijk om de ziekte van Alzheimer in een vroeg stadium te diagnosticeren. Met vroegdiagnostiek op basis van pathologie ontstaan er betere definities voor onderzoek, medicijnontwikkeling en het monitoren van patiënten. Dit verandert ook de notie van wat het betekent om als patiënt gediagnosticeerd te worden met de ziekte van Alzheimer.
- *Vroegdiagnostiek als eens stap richting medicatie.* Vroegdiagnostiek zou moeten leiden tot betere medicatie. Wanneer patiënten meer nauwkeurig gediagnosticeerd worden, kunnen patiënten en medicijnen beter gekoppeld worden. Bovendien maakt vroegdiagnostiek een behandeling mogelijk in een eerder stadium van het ziekteproces, waarop de behandeling waarschijnlijk effectiever is. Hoewel er nu nog geen behandeling mogelijk is, is het belangrijk om te anticiperen op de toekomstige beschikbaarheid ervan.
- *Vroegdiagnostiek als onderdeel van vroege zorgmanagement.* De kwaliteit van nieuwe technologieën in de gezondheidszorg wordt bepaald door de baat die patiënten erbij hebben. Omdat er geen geneesmiddelen beschikbaar zijn voor de ziekte van Alzheimer, biedt vroegdiagnostiek geen baat in termen van geneesmiddelen. Vroegdiagnostiek zou daarom deel uit moeten maken van de management van de ziekte in de vroege stadia.

Alzheimer Cafés zijn ontstaan om mensen met dementie informatie en steun te verlenen om beter om te gaan met hun situatie. Vijf interpretatieve pakketjes konden onderscheiden worden in de Alzheimer Cafés:

- *Vroegdiagnostiek als het identificeren van een biomedische aandoening.* Bezoek een arts bij zorgen over vergeetachtigheid. Met de ontwikkeling van nieuwe diagnostische tests kan een diagnose steeds eerder gesteld worden. Vergeetachtigheid is een belangrijk symptoom van de ziekte van Alzheimer, maar dat kan ook andere oorzaken hebben. Het is dus belangrijk om te weten wat de oorzaak is van de vergeetachtigheid.
- *Vroegdiagnostiek als vroege zorgmanagement.* Het is belangrijk dat patiënten en mantelzorgers vroege signalen van dementie herkennen en hun leven aanpassen aan de nieuwe situatie en vooruitzichten. Een officiële diagnose helpt bij het begrijpen wat er aan de hand is en biedt toegang tot zorg en ondersteuning. Het allerbelangrijkst bij de ziekte van Alzheimer is hoe patiënten en mantelzorgers ermee omgaan.
- *Vroegdiagnostiek als het labelen van personen.* Nu de ziekte van Alzheimer in een steeds eerder stadium gediagnosticeerd kan worden, is er een groeiende mismatch tussen de publieke perceptie van dementie en het functioneren van mensen die gediagnosticeerd worden met de ziekte van Alzheimer. Een diagnose plakt een label op mensen en dit heeft diepgaande sociale consequenties.
- *Vroegdiagnostiek als een existentiële gebeurtenis.* Gediagnosticeerd worden met de ziekte van Alzheimer verandert je leven. Het roept een herziening op van het verleden en toekomst van een persoon. Wil je dit aangaan en in welke fase van de aandoening wil je dit aangaan?
- *Vroegdiagnostiek als het reduceren van gezondheidszorgkosten.* In een vergrijzende samenleving zijn mensen met de ziekte van Alzheimer een grote belasting op het gezondheidszorgsysteem. Door de demografische trend lopen we tegen financiële grenzen aan en tegen grenzen in de beschikbaarheid van zorgpersoneel. Een tijdige diagnose kan de kosten van gezondheidszorg reduceren omdat het ervoor kan zorgen dat mensen langer thuis blijven wonen.

Zowel in de omgeving van de HTA als de Alzheimer Cafés zien we meerdere betekenissen van vroegdiagnostiek naast elkaar bestaan. In gesprekken en documenten komen meerdere interpretatieve pakketjes tegelijk voor en wordt tussen pakketjes geschakeld. Elk interpretatief pakketje zou je kunnen zien als een 'kraal' en elk verhaal of elk gesprek als een unieke 'ketting'.

Een vergelijking tussen de HTA en de Alzheimer Cafés laat verschillen en gelijkenissen zien. Door ze naast elkaar te zetten wordt een gevoeligheid gecreëerd voor de politiek in elke specifieke omgeving, in gesprekken en discussies, en het maakt het mogelijk om in een individuele situatie te identificeren wat zichtbaar gemaakt wordt en wat naar de achtergrond verdwijnt.

**Hoofdstuk 7** analyseert de framing van dementie en de betekenissen van vroegdiagnostiek in als onderdeel van het Deltaplan dementie, dat een onderdeel uitmaakt van een Nederlandse nationale dementie-strategie. Wereldwijd worden dergelijke strategieën om om te gaan met dementie in de samenleving ontwikkeld. Binnen deze omgeving zien we dat de poging om collectief de uitdagingen rondom dementie aan te pakken een veelvoud aan framings van dementie naar voren kwam. Dit ontketende een strijd over wie uiteindelijk definieerde wat een dementiestrategie in zou moeten houden. Verschillende modellen van dementie bestonden tegelijkertijd en werden oftewel gezien als onderdelen van een geheel, als tegengestelde posities, of als dat zij in verschillende richtingen bewegen. Ik betoog dat het belangrijk is om te reflecteren op welk model het meest geschikt is in welke situatie.

De analyse van betekenissen van vroegdiagnostiek laat wederom een veelvoud aan betekenissen zien, maar ook de dynamiek die hiermee gecreëerd wordt. De volgende vier dynamieken waren zichtbaar. (1) Een veelvoud aan betekenissen geeft een overtuigend argument waarom vroegdiagnostiek een betekenisvolle ontwikkeling is en waar het allemaal goed voor zou kunnen zijn. (2) Tegelijkertijd roept het ook vragen op in wiens belang het nou eigenlijk ontwikkeld wordt en wie er nou eigenlijk baat bij gaat hebben, bv. patiënten, onderzoek, of industrie? (3) De meervoudige betekenissen leiden ook tot het trekken van grenzen wat betreft verantwoordelijkheden en beloften. Bijvoorbeeld, door het creëren van allerlei subcategorieën en in uitspraken als 'dit is interessant voor onderzoek en uiteindelijk misschien ook voor de klinische praktijk' (4) En we zien dat de ontwikkeling zich niet houdt aan de grenzen die de actoren strekken. Dit zien we bijvoorbeeld in de behoefte aan vroegdiagnostiek, niet voor het tijdig organiseren van zorg en ondersteuning, maar voor het organiseren van euthanasie, en in de kritiek op vroegdiagnostiek als het medicaliseren van verouderingsprocessen.

## DISCUSSIE EN CONCLUSIE

Hoe draagt een empirische studie van meervoudige betekenissen bij aan verantwoord innoveren? De aannames waarmee dit proefschrift gestart is voor verantwoord innoveren is dat dit een technology assessment 'in het wild' mogelijk maakt, zonder gebruik van specifieke technology assessment instrumenten, en dat de gevolgen van opkomende technologieën in het heden bestudeerd kunnen worden.

### **Wat zijn de betekenissen van vroegdiagnostiek van de ziekte van Alzheimer in verschillende omgevingen?**

Elke omgeving liet meervoudige betekenissen zien van vroegdiagnostiek van de ziekte van Alzheimer, met overlap en verschil tussen de omgevingen (zie de samenvatting van hoofdstuk 5 tot 7). Het analyseren van betekenissen in de verschillende omgevingen vormt een gevoeligheid voor de specificiteit van elke situatie, en een bewustzijn van wat op de voorgrond geplaatst wordt en wat naar de achtergrond verdwijnt.

## **Brengt dit onderzoek naar betekenissen van vroegdiagnostiek evaluaties van vroegdiagnostiek aan het licht en als dat zo is, hoe wordt vroegdiagnostiek dan geëvalueerd?**

Ja, evaluaties van vroegdiagnostiek werden zichtbaar.

De meerdere betekenissen die in de vier omgevingen naar voren kwamen spannen het bereik op van de implicaties van vroegdiagnostiek voor de ziekte van Alzheimer. Elk pakketje bevat in zichzelf een beperkte technology assessment, doordat ze assessment criteria bevatten over de waarde van vroegdiagnostiek.

Binnen de verschillende omgevingen werd zichtbaar dat hoe betekenissen aan elkaar gerelateerd werden, samenhang met wat er op het spel stond in die specifieke omgeving en daarmee ook langs welke lat vroegdiagnostiek geëvalueerd werd. In elke omgeving werd er daardoor ook een ander soort evaluatie uitgevoerd. In elke omgeving verhielden de interpretatieve pakketjes zich op verschillende manieren tot elkaar: gefragmenteerd, middels in/exclusie, als hulpmiddelen die ingezet kunnen worden als dat gepast is, of als met elkaar concurrerend. De manier waarop betekenissen zich tot elkaar verhielden was afhankelijk van wat er op het spel stond in die specifieke omgeving: de maatschappelijke relevantie, het verzamelen van bewijs voor het bepalen van de waarde voor de patiënt ten opzichte van de financiële kosten, het beter om gaan met dementie in het dagelijks leven, of het op de maatschappelijke agenda krijgen ban bepaalde oplossingsrichtingen.

Als laatste, waren tussen de verschillende omgevingen patronen zichtbaar van hoe verschillende betekenissen zich tot elkaar verhielden, in de vorm van terugkerende verhalen of discussies. Deze terugkerende verhalen zijn dus niet specifiek voor een omgeving en zijn onderdeel van een breder cultureel repertoire. Verschillende dynamieken kwamen naar voren: een controverse, een scheiding tussen toekomstige beloftes en ontwikkelingen in het heden, een gelukkig huwelijk, twee kanten van dezelfde medaille, lastige verwickelingen, en polarisatie. Deze kleine verhalen en discussies laten zien dat de implicaties van vroegdiagnostiek van de ziekte van Alzheimer meerdere routes volgen. Deze patronen zijn het soort standaard discussies, of standaardverhalen die te verwachten zijn rondom vroegdiagnostiek.

## **Wat leren we met deze studie naar de betekenissen van vroegdiagnostiek van de ziekte van Alzheimer over maatschappelijk verantwoord innoveren?**

Het lappenkleed aan betekenissen en implicaties van vroegdiagnostiek voor de ziekte van Alzheimer zoals voortgekomen uit dit onderzoek leidt tot een benadering van verantwoord innoveren die ik samenvat als 'het voordeel van de twijfel'. Het is een aansporing tot gevoeligheid voor de samenhang van de sociale werkelijkheid, een bewustzijn van de rafelrandjes die vaak afgeknipt worden in representaties daarvan en wat daarin op de voorgrond of achtergrond geplaatst wordt, een erkenning dat problemen rondom dementie er veelal zijn om mee te leren omgaan (in plaats van ze op te kunnen lossen) en dat we niet ontkomen aan het gezamenlijk zoeken naar een gepast en tijdelijk evenwicht. 'Het voordeel

van de twijfel' vraagt om bescheidenheid in het aangezicht van dramatische ziektes, luide oplossingen en een duizelingwekkende veelvoud van betekenissen.



# Dankwoord

En dan nu het belangrijkste onderdeel van het proefschrift – het dankwoord.

Allereerst hartelijk dank aan diegenen die hebben meegewerkt aan het onderzoek: De onderzoekers van LeARN, de vrijwilligers en bezoekers van de Alzheimer Cafés in Nijmegen, de leden van het valorisatiepanel, de betrokkenen bij het Deltaplan Dementie die hebben meegewerkt aan de interviews, de Posten in Enschede voor het meelopen op de psychogeriatrische afdelingen, van de geheugenpolikliniek van het Radboud en het ziekenhuis in Tilburg, de medewerkers van Alzheimer Nederland, en alle andere mensen die hebben meegewerkt aan het onderzoek. Ook wil ik NWO bedanken voor het financieren van het onderzoek.

Dit onderzoek was onderdeel van een breder project. Ons onderzoeksteam bestond uit Marianne, Ellen, Harro, Anna Laura en ik. Graag ik wil Harro en Ellen bedanken voor de begeleiding. Het is een hele reis geweest zo samen en ik ben dankbaar voor het vertrouwen dat jullie me geschonken hebben tot het punt waar we nu zijn. Ellen, dank voor je oog voor detail en je nadruk op consistentie. Harro dank voor het blijven vasthouden van de grote lijnen en vooral ook voor je vriendschap. Marianne, je was altijd bereid om mee te denken en hebt me door onze gesprekken door te tijd weer goed vooruit geholpen. Anna Laura, mijn collega-aio, ik heb genoten van de tijd die we samen hebben opgetrokken. Ik heb bewondering voor je passie en het werk dat je gedaan hebt en de kwaliteiten die je daarin liet zien. Ik ben dan ook heel blij dat je mijn paranimf wilt zijn nu, zodat we samen over een eindstreep gaan.

Er zijn een aantal collega's met wie ik lief en leed heb gedeeld die vijf jaar dat ik in Utrecht rondgelopen heb en ik hier graag persoonlijk wil bedanken. Joyce: superbedankt voor al het contact dat we gehad hebben, de gesprekken in de trein en op het werk over wat ons ook maar bezig hield, of het nu inhoudelijk, persoonlijk, werkgerelateerd, of wat dan ook was. Marlous was een altijd optimistische, constructieve factor, die de waarde van quality-time hoog in het vaandel had. Vooral de mini-uitstapjes naar de koffiebar tegenover het gebouw voor een goed gesprek met verwennerij herinner ik me nog goed. Nadat ik verhuisd was van kamer voor een plekje bij het raam, heb ik lief en leed gedeeld met Colette – ook jij bent zo'n no-nonsense, positieve, constructieve en ook heel grappige collega, met wie het fijn is om proefschriftperikelen, maar ook alle andere perikelen des levens mee te delen om vervolgens weer wat beter beslagen verder te gaan. Gaston, jou wil ik ook heel hartelijk danken voor je vriendschap, alle gesprekken over het leven in breedste zin en steun gedurende de hele periode in Utrecht.

I would like to thank Annette Leibing who hosted my stay in Montreal. It was a good period for me to work on the theoretical chapter and discuss the thesis as a whole. More importantly for me today, my visit in Montreal turned out to be a sabbatical. Particularly the housemates with whom I was staying, stoked up the fire that was already simmering in my heart. This time in Montreal has encouraged me to really take my passion for nature seriously. I have

now managed to devote all my time to stimulate innovation that works along with and strengthens ecological processes.

Het is een heel traject geweest tot het punt waar we nu zijn en dat is zeker niet zonder slag of stoot gegaan. Er zijn veel mensen die mij persoonlijk hebben geholpen onderweg om het promotietraject af te ronden. In de tijd dat het proefschrift echt niet meer wilde vorderen en het voelde of ik aan een dood paard aan het trekken was, zijn er een aantal mensen geweest die een eindje naast mij zijn gaan meelopen om me er doorheen te coachen en te zorgen dat ik stappen bleef zetten. Voor nu wil ik vooral Threse en Mauk graag bedanken. Threse, dankjewel voor de hulp door op vaste tijden af te spreken en de volgende stap te bespreken. Dat was heel fijn en gaf me telkens weer een klein zetje. Mauk, jou ben ik vooral heel dankbaar in deze voor je stevige coaching en betrokkenheid. Er was een enorme hoeveelheid vasthoudendheid en (zelf)discipline nodig was om er telkens weer aan gaan zitten, en alles aan te kijken wat ik daarin tegen kwam. Dat had ik niet gered zonder jou. Ik ben blij dat het nu klaar is en ik kan terugkijken op een afgerond proefschrift en het vertrouwen dat ik een groot project tot een eind kan brengen op de één of andere manier, als ik er maar bij blijf. Ik denk dat het belangrijk is om te weten dat ik dat kan, voor alles wat ik in de toekomst nog oppak. Wat ik nu merk in mijn nieuwe werkzaamheden is dat ik grote projecten die ik niet goed kan overzien durf aan te gaan, door het doel voor ogen te houden en telkens de volgende stap te zetten. Ik merk dat ik vertrouwen heb dat als ik dat doe, dat het zich dan verder zal uitkristalliseren.

En dan als laatste Tijs. Je hebt me de afgelopen jaren onvoorwaardelijk gesteund en me gestimuleerd om te doen wat ik te doen heb. Dat was enerzijds het afronden van het proefschrift en anderzijds een zoektocht naar 'wat een Yvonne zou moeten doen'. Dat heeft me de ruimte (of de leegte) gegeven om mezelf opnieuw uit te vinden. Zo maken we heel wat mee samen. Hoewel het soms ook niet meer samen ging, ben ik heel gelukkig dat we telkens weer besluiten dat het leven mooier is *met* elkaar. En dan is het nu nog mooier met Ram! Ram, ik ben jou ook ontzettend dankbaar, gewoon omdat je bestaat!

Har Hare Hari – Wahe Guru

# Curriculum Vitae

Yvonne Cuijpers holds a MSc degree in Philosophy of Science Technology and Society with a technological background in chemical engineering. After obtaining her MSc degree, she worked as a researcher in projects to stimulate system innovation in animal husbandry and to stimulate the use of alternatives for animal testing in medical research. During the PhD she also supervised BSc students on their thesis, was PhD representative in the WTMC graduate school and was involved in teaching activities. In addition to research activities, she worked as a nature guide and followed trainings for nature guides and in permaculture. Currently she works as a researcher and entrepreneur on a nature-inclusive society, by stimulating and developing innovations that work along with natural processes.