eHealth in cardiovascular risk management to prevent cognitive decline
Jongstra, S.

Citation for published version (APA):
Jongstra, S. (2017). eHealth in cardiovascular risk management to prevent cognitive decline

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
Chapter 8

SUMMARY
In chapter one we introduced the rationale and background of this thesis. This thesis is divided in two parts: (1) eHealth in cardiovascular risk management and (2) Cognitive functioning – assessment, dementia risk prediction and prevention. All chapters have a connection with at least two of the four following themes: eHealth, older adults, management of cardiovascular risk factors (prevention) and cognition.

The Netherlands is one of the frontrunners in internet use. High internet penetration across all age groups and educational levels creates an opportunity to deliver (preventive) healthcare at home via the internet. This is what we call eHealth nowadays. Other countries, especially in Europe, follow rapidly in spreading internet access and this gives us the opportunity to develop and validate internet interventions to improve and prevent major health problems like cardiovascular disease and dementia.

**PART I EHEALTH IN CARDIOVASCULAR RISK MANAGEMENT**

In chapter two of this thesis we describe the extensive, profound and time-consuming process of developing an internet platform for the prevention of cardiovascular disease in older adults. A clear overview and guideline divided into five phases from the first thoughts to the final end product is provided. Phase one is about the conceptual framework, and this explains that the beginning of this process (building a platform) cannot start without a fundamental basis substantiated by literature. We describe that a blended approach to motivate people for a better lifestyle seems to work best, combining automated digital contact with actual human support. Phase two describes the platform concept and functional design. In this phase we brought the three most important parties together to fulfil the needs and possibilities of the platform (end users, health care researchers and software developers). It is crucial to understand the end users: what do they expect, what motivates them and what are they capable of in terms of computer use. The software developers provide the required technology and the researchers design the study to test the actual effectiveness of the platform. Phase three describes the building of the platform and its content; the latter based on the most recent literature and international health guidelines. Phase four shows the results of the international pilot study (N=41) in the testing and evaluating stage. Phase five is about the end product of the platform, ready to test in a randomised controlled trial (which is described in chapter three).
In **chapter three** we present the rationale and design of the HATICE trial (Healthy Ageing Through Internet Counselling in the Elderly). The HATICE trial is a pragmatic, multinational, multicentre, investigator initiated, prospective, randomised, open-label blinded end point (PROBE) trial with 18 months intervention and follow-up. In this study, researchers from three different European study groups collaborate based on their shared experience with large clinical dementia prevention trials (preDIVA, FINGER and MAPT). This previous experience was translated into the development of the interactive internet platform as described in chapter 2 to be tested in this RCT. This platform is aimed at optimising self-management of cardiovascular risk factors in older individuals. The aim of the HATICE trial is to investigate whether this coach-supported interactive internet platform can improve the cardiovascular risk profile and reduce the risk of cardiovascular disease and cognitive decline. Recruitment of 2725 participants aged 65 years and older with at least two cardiovascular risk factors or manifest cardiovascular disease (primary and secondary prevention) took place in three European countries (The Netherlands, Finland and France). The older population as target group for cardiovascular prevention through the internet is chosen with care, since this is a population that is usually overlooked in such trials, but can profit from cardiovascular prevention. The primary outcome is a composite score based on the difference between baseline and 18 months follow-up values of systolic blood pressure, low-density-lipoprotein and body mass index, which are measurable risk factors not amenable to reporting bias. In addition to clinical outcomes including cardiovascular disease and cognitive decline, cost-effectiveness is an important secondary outcome, which is pivotal in the rapidly developing world of eHealth.
PART II COGNITIVE FUNCTIONING – ASSESSMENT, DEMENTIA RISK PREDICTION AND PREVENTION

In chapter four, we present the results of the cognitive testing part in the iVitality study. We show that it is technically feasible to perform repeated cognitive tests on a smartphone and that adherence of older people with an increased risk of developing dementia, because they have a family history of dementia, is reasonable. We used several cognitive tests, which are based on existing paper and pencil cognitive tests. It is a challenge to make a smartphone-based cognitive test that measures exactly the same cognitive domain and is comparable to the validated conventional test. The relative validity of some of the tests compared to the conventional neuropsychological tests was only moderate. However, performance of the participants improved with repeated measures and this improved the relative validity as well. The performance improvement was mostly due to technical difficulties at the start of the study rather than an actual learning effect. We conclude that smartphone-based cognitive testing seems very promising for modern, future, large-scale data-collection in population studies.

In chapter five we present the added predictive value of a neuropsychological test of visual memory (Visual Association Test, VAT) over and above a cognitive screening instrument (Mini Mental State Examination, MMSE) based on data from the preDIVA trial (Prevention of Dementia by Intensive Vascular Care). PreDIVA is a large randomised controlled trial performed in the primary care setting to assess whether intensive vascular care can prevent or postpone dementia in community-dwelling older adults (>70 years old). For the study described in this chapter, we considered the study as a cohort (N=2690). We assessed whether the score on the VAT could improve prediction of who will develop dementia in the next 4-6 years of those who have a decrease of their score on the MMSE after two years of follow-up. In total, dementia developed in 157/2690 (5.8%) participants and a decline of two or more points in total MMSE score over two years was associated with an odds ratio of 3.55 (95% confidence interval 2.5-5.0) for developing future dementia. Strikingly, participants with a decline of two or more points on their MMSE score and an additional imperfect VAT score (5 points or less) had an odds ratio of 9.55 (95% CI 5.9-15.4) for developing future dementia. Whereas those with a decline on the MMSE score and a maximum score on their VAT had an odds ratio of 3.61 (95% CI 2.1-6.3) for developing future dementia. It seemed that such a short, simple test as the VAT has substantial incremental value for distinguishing older individuals that are at increased risk of developing dementia.
High blood pressure (hypertension) is one of the most important risk factors for developing cardiovascular diseases, but also dementia. Some fear that blood pressure reduction may lead to cerebral hypoperfusion and as such actually will increase the risk of dementia, which is supported by observational data showing an increased risk of dementia in those with a low blood pressure. To test the hypothesis that a low blood pressure by antihypertensive medications might be harmful for cognitive performance, in chapter 6 we systematically reviewed the literature regarding the effects of complete withdrawal of at least one antihypertensive medication on the incidence of dementia and cognitive decline. Unfortunately, high quality research in this topic is scarce and only two studies could be included in this Cochrane review. Neither of these two studies investigated incident dementia, so no conclusions about the effect of developing dementia could therefore be drawn. Cognition was measured in both studies in a very different way, precluding meta-analysis, but withdrawal of antihypertensive medications did not show a significant effect on cognition in either study.

In chapter 7 we present and discuss the main findings of this thesis in context of the latest literature and potential clinical implications for future research.