Cardiovascular risk self-management in older people: Development and evaluation of an eHealth platform
Beishuizen, C.R.L.

Citation for published version (APA):

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.

UvA-DARE is a service provided by the library of the University of Amsterdam (http://dare.uva.nl)

Download date: 06 Dec 2018
Chapter 7

General discussion

Chapter 7

General discussion
This thesis focuses on how cardiovascular risk management (CVRM) can be provided to older people using eHealth. In part 1, we describe the development of the internet-platform for cardiovascular risk self-management in older people for the HATICE-study. In part 2, we aim to gain better understanding on engagement of older people in eHealth and nurse-led CVRM. This chapter summarises the main findings of this thesis and discusses these in the context of current literature. Furthermore, some methodological considerations, directions for future research and clinical implications are provided.

### PART 1: DEVELOPMENT OF AN INTERNET-PLATFORM FOR CARDIOVASCULAR RISK SELF-MANAGEMENT IN OLDER PEOPLE

**Reviewing the literature**

In order to provide an evidence based foundation for the HATICE internet-platform, we first performed a systematic review and meta-analysis to answer the question whether internet-interventions for CVRM in older people are effective in reducing cardiovascular risk and disease (chapter 2). Although 57 RCTs could be included, only seven RCTs contained participants that were all above 50 years of age. Therefore, we concluded that internet-platforms specifically designed for older people are still scarce. Thus, the conclusions of our the meta-analysis apply to both middle-aged and older people with elevated cardiovascular risk. We found that internet-platforms lead to improvement of the individual cardiovascular risk factors systolic and diastolic blood pressure, LDL-cholesterol, HbA1c, weight, physical activity levels. These findings affirmed conclusions of other meta-analyses in younger adult populations. The reductions found in systolic blood pressure (mean difference –2.66 mmHg (95% CI –3.81 to –1.52)) and LDL-cholesterol (mean difference –2.18 mg/dL (95% CI –3.96 to –0.41)) were modest but could potentially translate into clinically relevant reductions of CV mortality or disease on a population level, if reductions were maintained over a longer period of time. CVRM is most effective when the complete CV risk profile is targeted. We could assess this with a meta-analysis of nine studies and found that internet-interventions also improved cardiovascular composite scores. We did not find an effect of the internet-interventions studied on cardiovascular event rates, but this was only reported in six studies with an average duration of 13 months. This finding was in contrast with the meta-analysis by Widmer et al, who did report a significant reduction in CVD outcomes by digital health interventions compared to usual care. However, these analyses cannot be directly compared to ours, because the latter also included mobile health and telecare devices and the CVD outcomes were more broadly defined, also including hospitalisations and all-cause mortality. We further...
evaluated the general effect of internet-platforms on cardiovascular risk factors, by pooling the standardised primary outcomes of all included studies that had defined a primary outcome (37 studies, n=11,021). We found a standardised mean difference of –0.24 (95% CI –0.31 to –0.16) in favour of the intervention. This effect-size can be interpreted as a small effect. In a further meta-regression, to assess the association between effect size and study-duration, we found that the beneficial effects on risk factor reduction declined over time. We hypothesised that declining effects over time could be associated with decreasing adherence. This was consistent with crumbling adherence rates reported in several of the included studies. Also in literature, difficulty to induce long-term adoption of internet-platforms is frequently reported and better adherence rates have been associated with positive outcomes. Lastly, from sub-group analyses, we could conclude that internet-platforms combined with human support (ranging from online communication to face-to-face meetings) are more effective than stand-alone digital interventions. This finding was consistent with research on interventions for diabetes self-management and strengthened our decision to include support by health coaches in the HATICE platform.

Consulting end-users
The importance of adding human support to an internet-platform was confirmed by the results described in chapter 3. Here we performed an international focus group study with seven Dutch and six Finnish primary care nurses, to learn from their experiences and practices with behaviour change support for CVRM and to discuss how to integrate their practices in a coach-supported internet-platform. We found that Finnish and Dutch primary care nurses with experience in CVRM had similar experiences in supporting health behaviour change in their patients. Both groups emphasised three preconditions needed for optimal behaviour change support: establishment of a relationship of trust, attention for awareness and expectation-management, and appropriate timing of support (matching the stage of change). These findings are in line with the preferences of older people for support in CVRM. However, small differences existed between the countries in the clinical practices the nurses used to meet these preconditions. The Finnish nurses for example had frequent consultations by phone, which was practical due to the large distances their patients needed to travel to their clinic. The Dutch nurses relied mostly on face-to-face contact. When discussing how health behaviour change support could be optimally provided online, both groups emphasised the importance of human support and integration with regular primary care. The Dutch nurses, however, were convinced that an internet-platform supported by a coach could never create the same strength of relationship they had built with their patients, and therefore they kept a slightly more reserved approach.

Consulting end-users
The importance of adding human support to an internet-platform was confirmed by the results described in chapter 3. Here we performed an international focus group study with seven Dutch and six Finnish primary care nurses, to learn from their experiences and practices with behaviour change support for CVRM and to discuss how to integrate their practices in a coach-supported internet-platform. We found that Finnish and Dutch primary care nurses with experience in CVRM had similar experiences in supporting health behaviour change in their patients. Both groups emphasised three preconditions needed for optimal behaviour change support: establishment of a relationship of trust, attention for awareness and expectation-management, and appropriate timing of support (matching the stage of change). These findings are in line with the preferences of older people for support in CVRM. However, small differences existed between the countries in the clinical practices the nurses used to meet these preconditions. The Finnish nurses for example had frequent consultations by phone, which was practical due to the large distances their patients needed to travel to their clinic. The Dutch nurses relied mostly on face-to-face contact. When discussing how health behaviour change support could be optimally provided online, both groups emphasised the importance of human support and integration with regular primary care. The Dutch nurses, however, were convinced that an internet-platform supported by a coach could never create the same strength of relationship they had built with their patients, and therefore they kept a slightly more reserved approach.
Synthesis of the platform

In chapter 4, we described the full development of the interactive HATICE internet-platform. Apart from the literature review (chapter 2) and focus groups with nurses (chapter 3), the developmental process also involved focus groups with the target population (manuscript currently in preparation), extensive brainstorm sessions with the software developers of the company involved, consultations of experts in CVRM and communication with older patients and representatives of patients organisations and its evaluation in an international pilot study.

The final HATICE internet-intervention is a personalised, secured, interactive internet-platform for self-management of the lifestyle aspects of seven modifiable cardiovascular risk factors with support from a health coach. The developmental process and pilot resulted in a number of adaptations made to meet the specific needs of the target population (summarised in table 1). The support of the health coach included: initial face-to-face meetings for assessment of the cardiovascular risk profile, explanation of the platform and initial goal setting, continuous online support of health behaviour change in an empathic, positive and counselling fashion following the principles of Motivational Interviewing, referral to their general practitioner if cardiovascular risks required medical evaluation and, at 12 months, a follow-up telephone call to boost motivation.

attitude towards online support. Moreover, they only regarded the platform suitable for support of lifestyle changes. They argued that care of medical issues should remain in the general practice domain. In contrast, the Finnish nurses saw no limitations of a digital approach. They argued that a relationship of trust could just as well be induced through internet, provided that the platform would be combined with human support and incorporated in regular care. Furthermore, they had no objections to supporting both lifestyle aspects and medical aspects of CVRM in this fashion. We attributed the differences found to local differences in culture, health care structure and geography. The attitudes we found were consistent with descriptions of attitudes towards self-management and enhancing patient autonomy of Finnish and Dutch health care professionals in other studies. Self-management requires health care professionals to adopt a different attitude towards the patient. Perhaps the Finnish nurses are further ahead in adopting this attitude than the Dutch nurses.

The attitudes we found were consistent with descriptions of attitudes towards self-management and enhancing patient autonomy of Finnish and Dutch health care professionals in other studies. Self-management requires health care professionals to adopt a different attitude towards the patient. Perhaps the Finnish nurses are further ahead in adopting this attitude than the Dutch nurses.
Table 1: Age-related problems and solutions in the HATICE intervention platform

<table>
<thead>
<tr>
<th>Age-related problems</th>
<th>Platform solutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual impairments</td>
<td>• Large font size&lt;br&gt;• Simple layout&lt;br&gt;• High contrast colour scheme</td>
</tr>
<tr>
<td>Motor impairments</td>
<td>• Large buttons&lt;br&gt;• No use of mouse hover-over</td>
</tr>
<tr>
<td>Cognitive ageing</td>
<td>• Content written in concise and easy-to-understand language&lt;br&gt;• Interactive content to stimulate capturing information&lt;br&gt;• Information offered in text, interactive audio format and in videos</td>
</tr>
<tr>
<td>Limited navigation skills</td>
<td>• Concise site-map, limited to max. 3 levels of navigation&lt;br&gt;• Static main menu that remains visible on every page</td>
</tr>
<tr>
<td>Drowning in information</td>
<td>• Only showing information relevant for health priorities&lt;br&gt;• Concise information&lt;br&gt;• No linking to information outside the platform</td>
</tr>
<tr>
<td>Login difficulties</td>
<td>• Help-assistance through email and phone&lt;br&gt;• Simple passwords</td>
</tr>
<tr>
<td>Feeling insecure about internet skills</td>
<td>• Introduction video explaining how to use the platform&lt;br&gt;• Help-buttons on every page&lt;br&gt;• Help-assistance through email and phone&lt;br&gt;• Paper instruction manual</td>
</tr>
<tr>
<td>Focus on health instead of disease</td>
<td>• Positive tone of voice: e.g., health factors instead of risk factors&lt;br&gt;• Positive and empathic attitude of health coach</td>
</tr>
<tr>
<td>Reliability concerns</td>
<td>• Study being recommended by own general practitioner&lt;br&gt;• Face-to-face meeting with health coach&lt;br&gt;• Explanation that information is based on clinical guidelines&lt;br&gt;• Picture of the health coach</td>
</tr>
</tbody>
</table>

Self-management was facilitated in the following way: insight in personal risk profile, educational modules, ability to choose risk factors as priorities and create lifestyle goals, self-monitoring tools and online communication with the coach. The available functionalities corresponded with the different stages of change that participants could be in (table 2).
The platform was developed to function independently of regular primary care but to be easily implementable in existing care structures if proven effective. The platform intervention focussed on the lifestyle aspects of CVRM. Still, interactions with regular primary care were foreseen in case new cardiovascular risks were detected that required medical treatment. In that case, the health coach advised people to see their general practitioner.

The pilot (41 older participants from the Netherlands, Finland and France, 8 weeks) detected various teething problems such as the login procedure being regarded too complicated and the platform not working optimally in older internet browsers. The evaluation sessions revealed that participants had difficulty in creating lifestyle goals by themselves, but succeeded together with the coach. The self-monitoring tool was frequently used for measuring of blood pressure, weight and exercise level, but not at all for smoking and diabetes. The participants positively valued the coach support. In conclusion, the pilot showed that an interactive internet-platform is acceptable and feasible for use by older people with basic computer skills. Continuous interaction between researchers, software developers and end-users (both patients and health care professionals) was necessary to generate solutions for the detected problems that worked for all parties involved. Figures 1-3 provide an impression of the final platform.
General discussion

Figure 1 Final version of platform – homepage

Figure 2 Final version of platform – Goal setting page
Currently, there is still a dearth of scientifically tested internet-platforms for CV risk self-management that specifically target older people. Internet-platforms targeting people of middle-age and older can induce modest improvements of individual CV risk factors and the CV risk profile, but effects decline over time. Studies on effects of internet-interventions on incident CVD are limited in number and follow-up time, therefore there is currently insufficient evidence on effects on this pivotal outcome. Blended interventions (combining the internet-platform with human support) are more effective than stand-alone interventions. Primary care nurses from Finland and the Netherlands also emphasise the importance of human support when CVRM is integrated in an online setting. Human support is essential for the establishment of a relationship of trust, to manage people’s expectations and for appropriate timing of support (matching the stage of change). When carefully designed with consultation of current literature and experts, continuous involvement of the end-users and pilot testing, it is possible to develop an internet-platform that is acceptable and feasible for use by European older people with basic computer skills and increased cardiovascular risk. We showed that older people start to actively use such a platform and use the different features. Based on the extensive developmental process, we propose several solutions for age-related problems associated with internet-platform use (table 1).
PART 2: ENGAGEMENT OF OLDER PEOPLE IN EHEALTH OR NURSE-LED CVRM

In part 2 of this thesis, we studied engagement of older people with CVRM, by performing a qualitative evaluation study of the HATICE internet-platform (chapter 5) and a quantitative assessment of engagement with the intensive vascular nurse-support intervention from the preDIVA trial (chapter 6).

Engagement to the HATICE-platform

In chapter 5, we performed 17 interviews with 20 Dutch participants of the HATICE trial to evaluate their initial and long-term engagement with the platform. Regarding initial engagement (initial use of the platform and familiarising oneself with the platform), we identified as influential factors for use: perceived computer literacy, senior user-friendliness of the platform, acceptability and perceived appropriateness of the intervention and initial interaction with the health coach. In sustained engagement (using the platform for a longer period for self-management purposes), we found that establishment of a relationship with the coach was the most important factor, followed by the use of regular automatic and personal reminders, having clear expectations of the platform, incorporating the use of the platform into daily routine, getting social support and having a loyal and persistent attitude. Some of the factors identified have been described in literature before, such as platform user-friendliness, perceived benefits and expectations of the platform and incorporation into personal life.27 A novel finding was that coach support was identified as an important factor for both initial and sustained engagement, suggesting that one of the strengths of adding human support to an internet-platform may lie in inducing sustained engagement with the platform. With regard to the regular automatic and personal reminders from the platform, we found that participants preferred to use the platform in a ‘reactive’ way rather than in an ‘active’ way, i.e., to respond to reminders rather than to use the platform on one’s own initiative. This seems to resemble the way people use smartphone applications such as Facebook and Whatsapp. Electronic reminders have been proven an effective tool to increase adherence to medication and reduce cardiovascular risk,18,19 but if they are used too frequently, ‘alert fatique’ can arise.20 Besides engagement we also discussed with the participants whether a platform like HATICE should be implemented in regular primary care. Participants were positive about this. In fact, they experienced it as a barrier that the HATICE-platform was offered independently from regular care. In their view, the alignment of the internet-platform to regular CVRM visits with the practice nurse would optimise continuity of care. This may improve engagement with the intervention, as has been suggested in literature on optimal diabetes management.21

Engagement to the HATICE-platform

In chapter 5, we performed 17 interviews with 20 Dutch participants of the HATICE trial to evaluate their initial and long-term engagement with the platform. Regarding initial engagement (initial use of the platform and familiarising oneself with the platform), we identified as influential factors for use: perceived computer literacy, senior user-friendliness of the platform, acceptability and perceived appropriateness of the intervention and initial interaction with the health coach. In sustained engagement (using the platform for a longer period for self-management purposes), we found that establishment of a relationship with the coach was the most important factor, followed by the use of regular automatic and personal reminders, having clear expectations of the platform, incorporating the use of the platform into daily routine, getting social support and having a loyal and persistent attitude. Some of the factors identified have been described in literature before, such as platform user-friendliness, perceived benefits and expectations of the platform and incorporation into personal life.27 A novel finding was that coach support was identified as an important factor for both initial and sustained engagement, suggesting that one of the strengths of adding human support to an internet-platform may lie in inducing sustained engagement with the platform. With regard to the regular automatic and personal reminders from the platform, we found that participants preferred to use the platform in a ‘reactive’ way rather than in an ‘active’ way, i.e., to respond to reminders rather than to use the platform on one’s own initiative. This seems to resemble the way people use smartphone applications such as Facebook and Whatsapp. Electronic reminders have been proven an effective tool to increase adherence to medication and reduce cardiovascular risk,18,19 but if they are used too frequently, ‘alert fatique’ can arise.20 Besides engagement we also discussed with the participants whether a platform like HATICE should be implemented in regular primary care. Participants were positive about this. In fact, they experienced it as a barrier that the HATICE-platform was offered independently from regular care. In their view, the alignment of the internet-platform to regular CVRM visits with the practice nurse would optimise continuity of care. This may improve engagement with the intervention, as has been suggested in literature on optimal diabetes management.21
Engagement to intensive nurse-led CVRM

We also evaluated engagement of older people with a non-digital CVRM intervention, by studying dropout from and adherence to intervention tested in the preDIVA trial (chapter 6). The preDIVA intervention consisted of 4-monthly consultations with the regular practice nurse at the general practice for intensive vascular care. This included assessment of the complete cardiovascular risk, provision of tailored lifestyle advice and optimization of medical treatment. In an exploratory analysis, we examined sociodemographic, clinical, and neuropsychiatric determinants of dropout and nonadherence. The clinical determinants included cardiovascular risk factors. In the analysis on dropout we focussed on dropout that could potentially be prevented and therefore, we excluded dropout due to death or dementia. Along study follow-up time, the dropout rate remained stable. The preventable dropout rate was stable along study follow-up. However, the non-adherence rate increased with a longer follow-up duration. We found that participants with, at baseline, a higher age, a lower level of cognition, more symptoms of depression or disability had the highest risk to drop out. Higher age and lower level of cognition were already known factors to be consistently associated with dropout.23 Symptoms of depression and disability have also been previously assessed but results on associations were inconsistent.25–26 Our findings provide additional evidence that symptoms of depression and disability are important determinants of dropout in older people. We also found that there was more dropout of people with symptoms of depression or lower cognition allocated to the control condition than to the intervention condition. In clinical practice, it may merit to give these people extra attention, since the findings of differential dropout could also suggest that the extra nurse contact stimulated these people to continue participation. The latter finding also seems important for other dementia trials. Selective loss of people in the control condition that are more prone to cognitive decline can lead to an underestimation of intervention-effects if the primary outcome is a cognitive screening measure. Solutions to reduce this risk of bias are taking a major clinical endpoint as primary outcome, such as diagnosis of dementia, and putting effort in dropout-retrieval. Next to dropout, we also assessed determinants of non-adherence to the intervention. The same factors were assessed but different associations were found. The factors associated with dropout did not emerge in the analysis on non-adherence, although in other studies associations between non-adherence to cardiac rehabilitation programs high age and symptoms of depression have been reported.27

Instead, being overweight was a risk factor for non-adherence, and elevated blood pressure and physical inactivity were associated with adherence. These findings are novel and need to be reproduced. Although the preDIVA intervention was offered in the context of an RCT, we think that the external validity of our findings is high, since the preDIVA population closely resembles a normal unselected population of older people. The preDIVA intervention consisted of 4-monthly consultations with the regular practice nurse at the general practice for intensive vascular care. This included assessment of the complete cardiovascular risk, provision of tailored lifestyle advice and optimization of medical treatment. In an exploratory analysis, we examined sociodemographic, clinical, and neuropsychiatric determinants of dropout and nonadherence. The clinical determinants included cardiovascular risk factors. In the analysis on dropout we focussed on dropout that could potentially be prevented and therefore, we excluded dropout due to death or dementia. Along study follow-up time, the dropout rate remained stable. The preventable dropout rate was stable along study follow-up. However, the non-adherence rate increased with a longer follow-up duration. We found that participants with, at baseline, a higher age, a lower level of cognition, more symptoms of depression or disability had the highest risk to drop out. Higher age and lower level of cognition were already known factors to be consistently associated with dropout.23 Symptoms of depression and disability have also been previously assessed but results on associations were inconsistent.25–26 Our findings provide additional evidence that symptoms of depression and disability are important determinants of dropout in older people. We also found that there was more dropout of people with symptoms of depression or lower cognition allocated to the control condition than to the intervention condition. In clinical practice, it may merit to give these people extra attention, since the findings of differential dropout could also suggest that the extra nurse contact stimulated these people to continue participation. The latter finding also seems important for other dementia trials. Selective loss of people in the control condition that are more prone to cognitive decline can lead to an underestimation of intervention-effects if the primary outcome is a cognitive screening measure. Solutions to reduce this risk of bias are taking a major clinical endpoint as primary outcome, such as diagnosis of dementia, and putting effort in dropout-retrieval. Next to dropout, we also assessed determinants of non-adherence to the intervention. The same factors were assessed but different associations were found. The factors associated with dropout did not emerge in the analysis on non-adherence, although in other studies associations between non-adherence to cardiac rehabilitation programs high age and symptoms of depression have been reported.27

Instead, being overweight was a risk factor for non-adherence, and elevated blood pressure and physical inactivity were associated with adherence. These findings are novel and need to be reproduced. Although the preDIVA intervention was offered in the context of an RCT, we think that the external validity of our findings is high, since the preDIVA population closely resembles a normal unselected population of older people. The preDIVA intervention consisted of 4-monthly consultations with the regular practice nurse at the general practice for intensive vascular care. This included assessment of the complete cardiovascular risk, provision of tailored lifestyle advice and optimization of medical treatment. In an exploratory analysis, we examined sociodemographic, clinical, and neuropsychiatric determinants of dropout and nonadherence. The clinical determinants included cardiovascular risk factors. In the analysis on dropout we focussed on dropout that could potentially be prevented and therefore, we excluded dropout due to death or dementia. Along study follow-up time, the dropout rate remained stable. The preventable dropout rate was stable along study follow-up. However, the non-adherence rate increased with a longer follow-up duration. We found that participants with, at baseline, a higher age, a lower level of cognition, more symptoms of depression or disability had the highest risk to drop out. Higher age and lower level of cognition were already known factors to be consistently associated with dropout.23 Symptoms of depression and disability have also been previously assessed but results on associations were inconsistent.25–26 Our findings provide additional evidence that symptoms of depression and disability are important determinants of dropout in older people. We also found that there was more dropout of people with symptoms of depression or lower cognition allocated to the control condition than to the intervention condition. In clinical practice, it may merit to give these people extra attention, since the findings of differential dropout could also suggest that the extra nurse contact stimulated these people to continue participation. The latter finding also seems important for other dementia trials. Selective loss of people in the control condition that are more prone to cognitive decline can lead to an underestimation of intervention-effects if the primary outcome is a cognitive screening measure. Solutions to reduce this risk of bias are taking a major clinical endpoint as primary outcome, such as diagnosis of dementia, and putting effort in dropout-retrieval. Next to dropout, we also assessed determinants of non-adherence to the intervention. The same factors were assessed but different associations were found. The factors associated with dropout did not emerge in the analysis on non-adherence, although in other studies associations between non-adherence to cardiac rehabilitation programs high age and symptoms of depression have been reported.27

Instead, being overweight was a risk factor for non-adherence, and elevated blood pressure and physical inactivity were associated with adherence. These findings are novel and need to be reproduced. Although the preDIVA intervention was offered in the context of an RCT, we think that the external validity of our findings is high, since the preDIVA population closely resembles a normal unselected population of older people. The preDIVA intervention consisted of 4-monthly consultations with the regular practice nurse at the general practice for intensive vascular care. This included assessment of the complete cardiovascular risk, provision of tailored lifestyle advice and optimization of medical treatment. In an exploratory analysis, we examined sociodemographic, clinical, and neuropsychiatric determinants of dropout and nonadherence. The clinical determinants included cardiovascular risk factors. In the analysis on dropout we focussed on dropout that could potentially be prevented and therefore, we excluded dropout due to death or dementia. Along study follow-up time, the dropout rate remained stable. The preventable dropout rate was stable along study follow-up. However, the non-adherence rate increased with a longer follow-up duration. We found that participants with, at baseline, a higher age, a lower level of cognition, more symptoms of depression or disability had the highest risk to drop out. Higher age and lower level of cognition were already known factors to be consistently associated with dropout.23 Symptoms of depression and disability have also been previously assessed but results on associations were inconsistent.25–26 Our findings provide additional evidence that symptoms of depression and disability are important determinants of dropout in older people. We also found that there was more dropout of people with symptoms of depression or lower cognition allocated to the control condition than to the intervention condition. In clinical practice, it may merit to give these people extra attention, since the findings of differential dropout could also suggest that the extra nurse contact stimulated these people to continue participation. The latter finding also seems important for other dementia trials. Selective loss of people in the control condition that are more prone to cognitive decline can lead to an underestimation of intervention-effects if the primary outcome is a cognitive screening measure. Solutions to reduce this risk of bias are taking a major clinical endpoint as primary outcome, such as diagnosis of dementia, and putting effort in dropout-retrieval. Next to dropout, we also assessed determinants of non-adherence to the intervention. The same factors were assessed but different associations were found. The factors associated with dropout did not emerge in the analysis on non-adherence, although in other studies associations between non-adherence to cardiac rehabilitation programs high age and symptoms of depression have been reported.27

Instead, being overweight was a risk factor for non-adherence, and elevated blood pressure and physical inactivity were associated with adherence. These findings are novel and need to be reproduced. Although the preDIVA intervention was offered in the context of an RCT, we think that the external validity of our findings is high, since the preDIVA population closely resembles a normal unselected population of older people.
community dwelling older people, and the intervention was integrated in regular primary care.

Conclusions of part 2
Qualitative research with participants of the HATICE trial showed that interaction with a health coach was regarded an important factor to stimulate engagement with the HATICE platform, both for initial and long-term engagement. Other important factors were senior user-friendliness of the platform, perceived appropriateness of the intervention, use of automatic and personal reminders, motivational status and incorporation of platform use into daily routine. Quantitative analysis of dropout and non-adherence to the preDIVA intervention showed that people at advanced age, with lower levels of cognition, with symptoms of depression or functional disabilities are more prone to dropout from nurse-led CVRM. Differential dropout rates were found for symptoms of depression and lower levels of cognition, where controls with these characteristics dropped out more often than intervention participants. These findings need to be taken into account in the design of future dementia trials when choosing cognitive outcomes. In clinical practice, it may merit to give patients with these characteristics extra attention to keep them allied, since the findings might indicate that the extra nurse contact stimulated them to keep participating.

METHODOLOGICAL CONSIDERATIONS

Meta-analysis: limits and possibilities of the pooled standardised effects analysis
In the meta-analysis, one method we used to evaluate the general effect of internet-platforms on cardiovascular risk factors, was pooling the standardised primary outcomes of all included studies. This original approach may initially look like a comparison of apples and oranges. However, when inferences based on this analysis are limited to the intention of the analysis, being to estimate the overall effect of internet-platforms on cardiovascular risk factors, and one keeps in mind that the analysis only tells us what the direction of the effect is and what order of effect size can potentially be expected on a cardiovascular risk factor in general, we regard the analysis not only valid, but also informative. In addition, this method provided further opportunities for sufficiently powered analyses on heterogeneity and risk of bias. The heterogeneity analyses provided insights on declining effects with increasing study duration and convincing evidence that blended interventions induced larger effects than internet-only interventions. Bias assessment in systematic review and meta-analysis can be undertaken in several ways. Sometimes scales are used and summary

community dwelling older people, and the intervention was integrated in regular primary care.

Conclusions of part 2
Qualitative research with participants of the HATICE trial showed that interaction with a health coach was regarded an important factor to stimulate engagement with the HATICE platform, both for initial and long-term engagement. Other important factors were senior user-friendliness of the platform, perceived appropriateness of the intervention, use of automatic and personal reminders, motivational status and incorporation of platform use into daily routine. Quantitative analysis of dropout and non-adherence to the preDIVA intervention showed that people at advanced age, with lower levels of cognition, with symptoms of depression or functional disabilities are more prone to dropout from nurse-led CVRM. Differential dropout rates were found for symptoms of depression and lower levels of cognition, where controls with these characteristics dropped out more often than intervention participants. These findings need to be taken into account in the design of future dementia trials when choosing cognitive outcomes. In clinical practice, it may merit to give patients with these characteristics extra attention to keep them allied, since the findings might indicate that the extra nurse contact stimulated them to keep participating.

METHODOLOGICAL CONSIDERATIONS

Meta-analysis: limits and possibilities of the pooled standardised effects analysis
In the meta-analysis, one method we used to evaluate the general effect of internet-platforms on cardiovascular risk factors, was pooling the standardised primary outcomes of all included studies. This original approach may initially look like a comparison of apples and oranges. However, when inferences based on this analysis are limited to the intention of the analysis, being to estimate the overall effect of internet-platforms on cardiovascular risk factors, and one keeps in mind that the analysis only tells us what the direction of the effect is and what order of effect size can potentially be expected on a cardiovascular risk factor in general, we regard the analysis not only valid, but also informative. In addition, this method provided further opportunities for sufficiently powered analyses on heterogeneity and risk of bias. The heterogeneity analyses provided insights on declining effects with increasing study duration and convincing evidence that blended interventions induced larger effects than internet-only interventions. Bias assessment in systematic review and meta-analysis can be undertaken in several ways. Sometimes scales are used and summary
scores are calculated. The Cochrane Collaboration discourages this practice because it is not transparent and its validity is low.\textsuperscript{20, 31} Frequently used is the Cochrane Risk of Bias assessment tool to uniformly assess the risk of bias in seven domains (selection bias, performance bias, detection bias, attrition bias, reporting bias and other biases) in RCTs.\textsuperscript{32} Recommendations are provided to summarise the domain assessments within studies or across studies using the well-known distinctions ‘low risk of bias’, ‘unclear risk of bias’ and ‘high risk of bias’. The way bias is judged and summarised is a subjective process, depending on the interpretation of the assessor. The Cochrane Collaboration therefore recommends that this is performed blindly. The Cochrane Collaboration recommends to judge a study to be overall low risk of bias if all key domains are judged to be of low risk of bias. Studies have an unclear risk of bias if one or more domains are judged unclear. And studies have a high risk of bias if one or more key domains have a high risk of bias. In meta-analyses, a common procedure is to exclude all studies that are overall evaluated as having an unclear or high risk of bias. Next, sensitivity analyses can be performed to assess quantitatively how the low quality studies influence the outcome. Limitations of this method are that it is not possible to take into account that studies may have very different bias profiles. We therefore chose another approach by looking at each domain of bias separately. We performed sensitivity analyses assessing differences in pooled standardised effect size for each domain of bias that we regarded key for our research question. In our opinion, this enables a nuanced, transparent and more objective bias assessment. This method may be useful for other meta-analyses if risk of bias is very much spread over different domains in the included studies.

**Qualitative research in an international setting**

We performed a qualitative study in an international setting. This imposes an extra challenge to distinguish ‘real’ differences between the nurses’ practices and recommendations from differences in language and culture. We therefore took much time to comprehend each other’s primary care systems and the direct context in which the nurses work. We also put effort in translating all the relevant documents to English and had extensive meetings with the research teams. We did not include French nurses in our sample, although the HATICE platform is also being tested in France, since no nurses are currently engaged in CVRM care.

**Optimal development of internet-platforms**

During the development of the HATICE-platform, we realised how difficult it is to robustly develop and scientifically test an internet-platform in the fast changing world of digital development. At the time the HATICE-trial will be completed, part
of the lay-out and functionalities will appear out-dated. One option to allow for more flexibility is the use of adaptive trial designs. This may enable more rigorous software updates during the ongoing trial. In this way the functionalities will be kept up-to-date while the principle content of the intervention will not change. This approach also has adverse effects, because most older people with limited computer skills may become confused by small lay-out changes and thus, this approach could induce extra disengagement.

Mixed methods
In this thesis, different research designs were used to develop the internet-platform and to study engagement with different forms of CVRM. This can be regarded as a mixed methods approach. The most important conclusions from this thesis were drawn from both quantitative and qualitative research and were further explored with qualitative research. We therefore provide an example of the synergy effect of combining quantitative and qualitative methods. This is especially appropriate for novel research fields involving health behaviour.

DIRECTIONS FOR FUTURE RESEARCH

Recommendations for the development of future internet-platforms for older people
Based on the developmental process of the HATICE-platform we offer a set of solutions for age-specific problems in using eHealth applications (table 1). An internet-platform for older people can be further personalised if the platform is adapted to the specific age related problems, for example adjusted to level of visual acuity, digital literacy or cognitive performance.

To prevent reinventing the wheel, the development of medical internet-platforms for older people may benefit from more cross-pollinations with other fields that develop eHealth applications. To stimulate engagement, best practices from application designers and online marketing might also be useful for medical applications. The application development industry has become very successful in developing applications, such as Facebook, Whatsapp, WeChat, Pinterest and Wordfeud, that are even considered addictive. An important mechanism that is used by these apps is habit-forming. Potentially, health applications can adopt these strategies, since internet-platforms for self-management may be most effective if they induce habit-forming as well.

Another suggestion to stimulate engagement with internet-platforms for CVRM is to facilitate ‘reactive’ use. One way to do this is to offer the functionalities of the platform of the lay-out and functionalities will appear out-dated. One option to allow for more flexibility is the use of adaptive trial designs. This may enable more rigorous software updates during the ongoing trial. In this way the functionalities will be kept up-to-date while the principle content of the intervention will not change. This approach also has adverse effects, because most older people with limited computer skills may become confused by small lay-out changes and thus, this approach could induce extra disengagement.

Mixed methods
In this thesis, different research designs were used to develop the internet-platform and to study engagement with different forms of CVRM. This can be regarded as a mixed methods approach. The most important conclusions from this thesis were drawn from both quantitative and qualitative research and were further explored with qualitative research. We therefore provide an example of the synergy effect of combining quantitative and qualitative methods. This is especially appropriate for novel research fields involving health behaviour.

DIRECTIONS FOR FUTURE RESEARCH

Recommendations for the development of future internet-platforms for older people
Based on the developmental process of the HATICE-platform we offer a set of solutions for age-specific problems in using eHealth applications (table 1). An internet-platform for older people can be further personalised if the platform is adapted to the specific age related problems, for example adjusted to level of visual acuity, digital literacy or cognitive performance.

To prevent reinventing the wheel, the development of medical internet-platforms for older people may benefit from more cross-pollinations with other fields that develop eHealth applications. To stimulate engagement, best practices from application designers and online marketing might also be useful for medical applications. The application development industry has become very successful in developing applications, such as Facebook, Whatsapp, WeChat, Pinterest and Wordfeud, that are even considered addictive. An important mechanism that is used by these apps is habit-forming. Potentially, health applications can adopt these strategies, since internet-platforms for self-management may be most effective if they induce habit-forming as well.

Another suggestion to stimulate engagement with internet-platforms for CVRM is to facilitate ‘reactive’ use. One way to do this is to offer the functionalities of the platform
in a more sequential form, adapting what is offered to the stage of change that the participant is in (table 2) and reducing the number of functionalities the participant can choose from. This was in fact already suggested by Albert Bandura in the practical elaboration of his social-cognitive theory for self-management and behavioural change.44,45 In combination with the use of electronic reminders, the patient is guided through the intervention, instead of having to explore everything him/herself. One may argue if stimulating ‘reactive’ use is still compatible with self-management as originally defined.36,37 Medical ethics philosopher Maartje Schermer makes a distinction between concordant self-management and compliant self-management.38 Concordant self-management matches the original definition of self-management (as described in the introduction of this thesis), aiming to empower patients to become well-informed problem solvers of their conditions and lives, supported by their health care providers. In compliant self-management, the educational and empowering aspects of self-management are less self-evident and the patient self-monitors his/her symptoms following suggestions from his/her health care provider. The health care provider reacts on the data provided and adjusts the therapy if needed, but the patient only executes the management but does not necessarily learn from it. This type of self-management may be stimulated with the ongoing development of technologies for monitoring that becomes more and more automated. This may impress as eHealth development taking the wrong turn. However, we do not think that facilitating ‘reactive’ use of our internet-platform will hamper ‘concordant’ self-management. The whole internet-intervention is centered around the motivational status of the user, and the user him/herself decides on what goals to set and how to monitor them. Furthermore, the use of motivational interviewing techniques by the health coach is specifically aimed to stimulate concordant self-management as well. Furthermore, it is also possible that ‘concordant’ self-management more easily leads to lack of commitment than ‘compliant’ self-management, especially in people with only minor elevated cardiovascular risk. This was mentioned by the interviewed participants in chapter 5, they preferred reactive use, because they found it difficult to self-initiate everything. Possibly, different combinations of ‘concordant’ and ‘compliant’ self-management are optimal for different patients, as was also suggested by one of the nurses interviewed in chapter 3:

“I think 2 or 3 types of platform users will arise: people who really get the concept of self-management (and start coaching themselves), people who need the coach (and give the coach access to their complete profile) and a group in between, alerting the coach if a goal has not been met.” (Dutch nurse 2)
Recommendations for future trials testing internet-platforms for older people

Based on our systematic review we recommend that future trials testing internet-platforms for older people specifically include older populations. Sustainability of effectiveness of the interventions can be better assessed by including prolonged follow-up intervals. Moreover, this would allow for measuring major clinical outcomes such as cardiovascular disease. Individual changes in levels of cardiovascular risk factors (blood pressure, cholesterol levels, weight) over time should be analysed in relation to adherence rates. More standardised descriptions of interventions and standardised evaluation methods will facilitate comparisons of interventions.

The HATICE RCT was designed with the aim to evaluate the clinical effectiveness of the HATICE internet-platform. The multi-component intervention was considered a ‘black box’. First, its effectiveness on improving the cardiovascular risk profile needs to be assessed and, hopefully, established. Next, it can be assessed which components of the intervention make it successful. However, if the RCT fails to demonstrate effectiveness, questions will rise regarding its implementation and it will be attempted to analyse the components of the intervention more in depth. We hope that this thesis has provided some starting points for further fine-tuning of the intervention. Internet-platforms for CVRM in older people may benefit from implementation research, “to understand what, why, and how interventions work in “real world” settings and to test approaches to improve them.” (Peters DH et al. BMJ 2013).89

It is difficult to test an intervention for improvement of CVRM in a context of care were CVRM is already quite good and still being intensified, as is the case in the Netherlands, Finland and France. A strategy can be to target high-risk populations in countries with less developed CVRM programs, because these people have the largest window of opportunity. Furthermore, health care systems in these countries may profit most from the incorporation of eHealth applications.40 Because of these reasons, the AMC study group, together with the HATICE consortium initiated Prevention of Dementia using Mobile phone Applications (PRODEMOS). In this large scale project, the implementation of an mHealth dementia prevention intervention for people aged 55 years and older at increased risk for dementia will be tested in deprived area’s in the UK and in China. The mHealth dementia prevention intervention will build on the HATICE intervention adapted to a smart phone, and adapted to be socio-culturally appropriate in these different settings.
CLINICAL CONSIDERATIONS – HOW TO SHAPE ONLINE SELF-MANAGEMENT OF CVRM FOR OLDER PEOPLE IN PRIMARY CARE?

We found compelling evidence that internet-platforms for CVRM work better if combined with human support. Furthermore, both the interviewed nurses and HATICE participants recommended to incorporate the internet-platform into the regular primary care setting. We first need to await the results of HATICE on the clinical effectiveness of the intervention, but one can already discuss potential benefits and drawbacks of the incorporation into regular care. An important benefit of incorporating the platform into regular care was formulated by the HATICE participants interviewed in chapter 5:

“I already visit the practice nurse, but there is a lot of time in between [visits] and then yes… Of course together we assess the results, look at it and discuss it. But when I’m gone, it [the support] is also gone. […] And this is, the continuity that you’re always working on it, that is good.” [P2]

Thus, combining periodic face-to-face nurse visits with in-between use of the platform could augment the perceived continuity of support in self-management. By enhancing patients’ commitment with the goals set, this may potentially also stimulate long term engagement with health behaviour change. Other benefits are that it provides a safe context for the internet-platform to target both the lifestyle and medical aspects of CVRM, rather than the lifestyle aspects only, as is the case in the current HATICE-platform. One could hypothesise that online self-management interventions that also target medical aspects of CVRM are more powerful but may induce more adverse events. In the systematic review and meta-analysis (chapter 2), most of the included internet-interventions targeted both lifestyle and medical aspects of CVRM but some interventions only targeted lifestyle aspects of CVRM. Unfortunately, no subgroup analysis was performed to compare their effectiveness on CV risk reduction. In line with this issue, one could consider whether the person supporting the internet-platform should have a medical background or not. If an internet-platform is incorporated into regular primary care, it seems most obvious to attribute the support to a primary care nurse that is already dealing with CVRM. The interviewed Dutch and Finnish primary care nurses also suggested such an approach (chapter 3). In countries where primary care is organised differently, like in France, this role might fit other health care providers better. However, the interviewed HATICE participants (chapter 5) were very positive about the support provided by the HATICE health coaches who did not have a medical background. Possibly, a non-medical context of the platform...
contributes to a focus on health instead of disease, and a positive tone of voice. The preference for this positive attitude was one of the findings from the focus groups we performed with older Dutch, Finnish and French people in the developmental process of the HATICE-platform (briefly mentioned in chapter 4, manuscript currently under preparation). Further, people preferred a coaching attitude to a patronising attitude when it concerned lifestyle advice. This was also emphasised in a qualitative study with preDIVA participants evaluating the preDIVA intervention: lifestyle was regarded as something personal and should be discussed in dialogue. Last, people feared that internet-interventions would completely substitute face-to-face care. This fear is not unfounded considering the foreseen large rises in people in need of CVRM in the near future. However, the conclusions from this thesis indicate that human support is an essential element to increase the efficacy of eHealth applications. Perhaps, based on the level of cardiovascular risk (primary or secondary prevention), interventions could have different intensities, saving more intensive programs with more periodic face-to-face meetings for people with the highest risk.
REFERENCES


15. Krijgsman J, Peeters J, Burghouts A, et al. Between the spark and the flame: 2015 eHealth...


