ENGLISH SUMMARY

Introduction
Amongst adults aged 55 years and older, depression is common. Its prevalence is estimated to be 11-25% and in 30-80% of the cases, depression is a chronic health condition. When depression occurs together with other chronic health conditions like diabetes mellitus type 2 (DM2) or coronary heart disease (CHD), this is associated with higher burden of disease, lower health related quality of life, adverse health outcomes, more health care use and higher health care related costs. Unfortunately, patients with DM2 and/or CHD seem to have a higher risk to become depressed compared to people without these conditions.

Given the high prevalence and chronicity rates of depression in older adults with chronic medical conditions, it is key to prevent the onset of major depressive disorder in this population. Other studies show that this can be done by offering stepped depression care to patients who are already experiencing depressive symptoms, but do not yet fulfill all criteria for a major depressive disorder. In this stepped care approach, minimally invasive depression care will be offered to a patient, only increasing the intensity of the treatment when depressive symptoms remain present. To be able to successfully use this approach in older adults with DM2 and/or CHD, it is needed to answer the following questions and use the answers to optimize preventive depression care in this population:

1) Which course do depressive symptoms usually take within an older population with a high rate of medical illnesses? And furthermore, can we predict the course of depression based on patient characteristics?

2) How can depression and depressive symptoms best be measured in patients with diabetes mellitus type 2 (DM2) and/or coronary heart disease (CHD)?

3) Is a stepped care program that is specially developed to be used for patients with comorbid chronic health conditions (the Step-Dep program) (cost-)effective as compared to usual care in preventing the onset of depression in patients with DM2 and/or CHD?

This thesis is aimed to answer these three main questions.

Part 1: The course of depression in an older primary care population
In Chapter 2, three distinct trajectories of depression were identified in a population of older primary care patients with subthreshold depression and a high prevalence of chronic medical illnesses. Most patients showed predominantly persistent subthreshold depression. Two relatively small groups showed a more adverse pattern: one trajectory followed an intermittent course of depressive symptoms over
time, the other trajectory was characterized by initially severe depression improving over time, but never reaching total remission. In all three identified trajectories, subthreshold depression remained present during the whole three-year follow-up period. Other studies mainly found the same distinct courses of depression in older adults.

The strongest predictor of a more adverse depression trajectory was severity of baseline depression. Living without a spouse and not feeling in control of the situation were predictive for an intermittent depression trajectory. Other studies found comparable predictors for adverse depression trajectories, and also showed that the prognosis is worst for older depressed adults who also experience problems in other domains, for example the social domain. Also, evidence suggests that having a chronic medical illnesses increases the risk for a chronic course of depression in older depressed adults, underlining the poor prognosis of patients who also experience problems in other domains.

Part 2) Measurement properties and diagnostic accuracy of self-reported depression questionnaires in patients with DM2 and/or CHD

In Chapter 3, the reliability and validity of depression questionnaires in patients with DM2 was described. To do so, the results of a systematic review of the literature were reported. Overall, it was recommended to use the CES-D, with strong evidence for a positive internal consistency, structural validity, and construct validity, moderate evidence for a positive criterion validity and limited evidence for positive cross-cultural validity. The WHO-5 and the PHQ-9 also showed strong measurement properties to assess depression in patients with diabetes. However, the WHO-5 was originally developed as a general questionnaire to measure health related quality of life and evidence for the structural validity of the PHQ-9 was contradictory. Thus, users should be cautious when using the WHO-5 or the PHQ-9. For all other questionnaires, evidence was too limited to give any recommendations.

In Chapter 4 the diagnostic accuracy of a specific questionnaire (the PHQ-9) was assessed. The performance of the PHQ-9 was satisfactory when using the sum score. To identify major depression, a cut-off score of 10 was most appropriate. Subthreshold depression could best be identified using a cut-off score of 8. It was not recommended to use the pre-specified algorithm to diagnose major or subthreshold depression in the current population. However, recommended cut-off scores for subthreshold depression differ greatly between studies and the recommended cut-off scores for subthreshold depression and major depression are very close to each other. Therefore it is questionable whether the PHQ-9 can be used reliably in daily practice.
Part 3) Effectiveness and cost-effectiveness of stepped care to prevent major depressive disorder in primary care patients with DM2 and/or CHD and comorbid subthreshold depression

In Chapter 5, the design of a cluster-randomized controlled trial (RCT) to assess the effectiveness and cost-effectiveness of Step-Dep was described. Step-Dep is the first stepped care program designed to prevent major depression in primary care patients with DM2 and/or CHD who experience subthreshold depression. It consists of four subsequent evidence-based treatment steps with increasing intensity based on the level of depressive symptoms experienced by the patient. Step-Dep was compared to usual care.

Chapter 6 and 7 showed that Step-Dep was neither effective nor cost-effective in comparison with usual care to prevent major depressive disorder in primary care patients with DM2 and/or CHD who screen positive for subthreshold depression. No significant effect on secondary outcomes such as severity of depression, severity of anxiety, perceived recovery and health related quality of life was found either.

DISCUSSION

Based on current findings it is not recommended to implement the Step-Dep protocol as studied into primary care. However, it is not yet possible to draw definite conclusions about the effectiveness and the cost-effectiveness of stepped care to prevent major depressive disorder in this population.

Two major considerations apply. First, it is possible that screening patients with DM2 and or CHD for depressive symptoms did not result in finding the patients who were in need of preventive depression care. This might also explain the relatively low uptake of the Step-Dep intervention by the participating patients. Evidence from Part 2 of this thesis strengthens this hypothesis, demonstrating high false positive rates using the PHQ-9 with a cut-off of 6 to screen for clinically relevant symptoms of depression. When this is the main reason for Step-Dep to be ineffective, another case finding strategy targeting patients who really are at risk for major depression may be helpful.

Second, it is possible that Step-Dep was not effective because patients with depressive symptoms do get better by themselves in this population. Also, usual care is already relatively enhanced in the Netherlands, possibly reducing the contrast between treatment groups. When one (or both) of these possibilities apply, patients do not need an extra care program to prevent depression. When this is the main reason for the found results, it is not feasible to further research or use the Step-Dep intervention in primary care patients with DM2 and/or CHD.
When considering all evidence, it seems that the key to improving the results of stepped care to prevent depression in patients with subthreshold depression and CHD and/or DM2 is to identify the patients who are at highest risk of developing major depression and experience a need for preventive depression care. The main remaining question is whether these patients exist and can be found using a different case finding strategy.