Suffering in silence: studies on screening for major depressive disorder in primary care
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Summary
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This thesis is about major depressive disorder (MDD) as it occurs in a general practice population in the Netherlands. At a rough estimate 5.2% of the adult Dutch population suffers from MDD (12-month prevalence, Nemesis-2 study). In 2010, 3.5% of primary care population consulted their general practitioner (GP) with MDD and 0.1% of primary care population was referred to specialized mental health care for MDD treatment (Nivel).

The recognition and diagnosis of MDD in primary care is sometimes difficult. Eighty percent of patients with MDD consult their GP with non-specific physical complaints without spontaneously mentioning the existence of psychological problems. International studies indicate that up to 50% of patients with MDD are not recognised by (GPs).

Screening is often proposed to improve the recognition by GPs. However, former studies on the effectiveness of screening for MDD in primary care have failed to demonstrate a positive effect because of two aspects. First, screening for MDD in the unselected primary care population seems not efficient because of the relatively low prevalence of MDD, leading to low positive predictive value of an MDD screening test, despite acceptable sensitivity and specificity. Screening a pre-selected high-risk population with a corresponding higher positive predictive value of the screener as a logical consequence, could lead to improved screening efficiency.

Secondly, although screening increases the detection rate of MDD in primary care, screening has not led to improved patient outcomes until now. As with every screening program, it has to be combined with effective diagnosis and treatment. Embedding screening into a disease management program including diagnosis and treatment for MDD has been suggested to improve patient outcomes.

These recommendations were used for the development of our screening study. We (1) increased the pre-test prevalence of MDD by selecting a population at high-risk for MDD; and (2) we combined the screening study with a treatment trial. Unfortunately the number of patients that wanted to start treatment after screening was too low to expect any effect of the program on patient outcomes. Therefore we decided to split both studies and for this thesis we focussed on the feasibility of screening and the diagnostic process for MDD and comorbid psychiatric disorders. The study on treatment for MDD is described elsewhere.
To study the feasibility of screening for MDD we used the Wilson and Jungner criteria as described in the introduction of this thesis. These criteria were developed already 4 decades ago to ensure a positive net effect of screening programs. Ever since, these criteria have been used to evaluate screening programs. Considering screening for MDD, we focused on three of the ten Wilson and Jungner criteria that needed more study: (1) the validity of the screening instrument; (2) the effectiveness of screening and (3) the acceptability of screening for the target population.

As was stated in the introduction in chapter 1, this thesis consists of three parts:

I. Part I: the psychiatric morbidity of the selected high-risk population for screening;

II. Part II: the validity of three modules of the screening instrument, the Patient Health Questionnaire (mood, somatoform and panic module);

III. Part III: the effectiveness of the screening program and the acceptability to the target population.

Part I
 High-risk population

Chapter 2 describes the characteristics and psychiatric morbidity of the selected high-risk population. The high-risk population consists of three overlapping patients groups selected from primary care practices: (1) patients that frequently attend their general practitioner; (2) patients who consult with psycho-social problems; and (3) patients with somatically unexplained physical complaints. These patients were screened with four modules of the Patient Health Questionnaire (PHQ): MDD, panic disorder (PD), other anxiety disorder (OAD) and undifferentiated somatoform disorder (USD). The PHQ is a self-report questionnaire aimed at diagnoses of mental disorders commonly encountered in primary care.

Diagnoses were defined according to the strict criteria of the DSM-IV, the Diagnostic and Statistical Manual of mental disorders. The main finding was that one-fourth (26.1%) of these high-risk patients suffered from any of these four psychiatric disorders. MDD was present in 12.6% of all patients, PD in 5.7%, OAD in 11.1% and USD in 8.0% of all patients. These figures confirm that we succeeded in selecting patients at high-risk for psychiatric disorders. Because of the high prevalence of psychiatric disorders in these 3 groups of patients we advise general practitioners to attentively explore the possibility of the presence of one or more of these disorders in these patients.
Part II
Screening instrument: Patient Health Questionnaire

Chapter 3 describes a systematic review and meta-analysis of the diagnostic accuracy of the mood module of the Patient Health Questionnaire (PHQ-9). Diagnostic accuracy studies that compared the PHQ-9 to a DSM-IV based reference standard were selected. All data of primary care studies that were aimed at the diagnostic accuracy of the PHQ-9 were combined to calculate summary sensitivity and specificity of the PHQ-9. The summary sensitivity was 0.77 and the summary specificity was 0.94. When used in selected subgroups of patients with MDD prevalence above 30% the PHQ-9 is a valid tool for diagnosing MDD, at the cost of missing an MDD with a probability of about 10%. However, in primary care populations with lower prevalence additional diagnostic interviewing is necessary to prevent overdiagnosis.

Chapter 4 describes the accuracy of the PHQ-9 in (1) screening for MDD, (2) diagnosing MDD and (3) measuring severity of MDD in our high-risk study-population. The PHQ-9 results can be scored in two ways. The summary score of all 9 items of the PHQ-9 is used for screening purposes. The algorithmic score (similar to the DSM-IV criteria for MDD) is used for diagnosis of MDD (see for details supplement 1). The different scores of the PHQ-9 were compared to a DSM-IV based reference standard, the Structured Clinical Interview for DSM-IV axis I Disorders (SCID-I) for the diagnosis of MDD and to the Hamilton Depression Rating Scale for severity measurement. The test characteristics for the summary score were sensitivity 0.93 and specificity 0.85; those for the algorithm were sensitivity 0.68 and specificity 0.95. For severity measurement the Pearson correlation coefficient of the PHQ-9 to the HDRS-17 was $r = 0.52$.

The main conclusions were that the PHQ-9 performs well as a screening instrument, but in diagnosing depressive disorder a formal diagnostic process following the PHQ-9 remains imperative, as we also found in chapter 3. In addition, the PHQ-9 does not seem adequate for measuring severity. Remarkably, the developers of the PHQ-9 claim that the instrument could be used for screening as well as diagnosing and severity measurement of MDD. Our results only support the screening ability of the PHQ-9.

Chapter 5 describes the validity of the panic module of the PHQ (PHQ-PD) in detecting panic disorder (PD) in the high-risk population in primary care. The original scoring algorithm (see supplement 1) as well as three modified algorithms were compared to the reference standard, the SCID-I. Since a high detection rate is the first objective for screening instruments, we tested whether modified (less strict) algorithms would increase the sensitivity for diagnosing panic disorder. In
addition, the influence of psychiatric comorbidity on the test characteristics of the PHQ-PD was studied. According to the SCID-I, 4.8% of the study population suffered from PD. The main conclusion was that for screening on PD, using only the first question of the PHQ-PD (‘In the last 4 weeks, have you had an anxiety attack - suddenly feeling fear or panic?’) generated the best psychometric properties (sensitivity 0.71, specificity 0.81). Patients with psychiatric comorbidity scored relatively higher on the PHQ-PD compared to patients without psychiatric comorbidity. This increased sensitivity while decreasing specificity of the PHQ-PD.

Chapter 6 describes the validity of the somatoform disorder module of the PHQ (PHQ-15) in screening for undifferentiated somatoform disorder in the high-risk population. The PHQ-15 was again compared to the reference standard, the SCID-I. An undifferentiated somatoform disorder was diagnosed when at least one somatic symptom that is present during at least 6 months (1) could not be fully explained by a general medical condition (confirmed by the general practitioner), another mental disorder, or the effects of a substance; and (2) caused serious impairment in social, occupational, or other functioning.

The prevalence of undifferentiated somatoform disorder according to the SCID-I in this population was 8.6%. The results showed that when patients were severely bothered by 3 or more somatic symptoms during the past 4 weeks, sensitivity of the PHQ-15 was 78% and specificity 71%. These results showed that the PHQ-15 is able to detect patients at risk for somatoform disorders. However this study is hampered by difficulties in diagnosing an undifferentiated somatoform disorder by the SCID-I, because the SCID-I does not include extensive somatic diagnostic tests. The fact that the reference standard of this study is not perfect regarding the presence of somatic illnesses, implicates that the results of this study have to be interpreted with caution. More research is needed to validate the diagnostic procedure of an undifferentiated somatoform disorder.
Chapter 7 describes the results of screening for major depressive disorder (MDD) in high-risk groups in primary care. Before the screening, GPs excluded all patients that were already diagnosed with MDD (7.3% of 2005 high-risk patients) and patients that were unable to participate for other reasons (8.6%). Remaining high-risk patients were screened with the PHQ-9 and diagnosed with the SCID-I. Of the 1687 invitees, 780 patients participated and 71 patients suffered from MDD. Of these 71 patients 36 (50.7%) received treatment for psychological problems, possibly other than MDD, 14 (19.7%) refused treatment and 4 individuals did not show up for an appointment. As a final result of the screening, 17 individuals (1% of 1687) started treatment for major depressive disorder. The number needed to invite to treat 1 additional MDD is 99 (17/1687), the number needed to be actually screened is 46 (17/780) and the number needed to identify for screening to treat 1 not yet diagnosed major depressive disorder was 118 (17/2005).

Considering that a considerable number of patients will recover within 3 months and that the number needed to treat to cure one additional patient is between 6 and 10 in primary care, we conclude that the possible health gain that could have been achieved by the treatment of the 17 participants is probably limited compared to treatment as usual. Screening for depression in high-risk populations does not seem to be effective, mainly because of the low rates of treatment initiation, even if treatment is freely and easily accessible.

Chapter 8 describes the view of depressed patients on screening for MDD in primary care. We performed a qualitative study on patients who participated and were screened and diagnosed with MDD in the above screening study. After the screening and diagnosis of MDD, patients were asked to participate to this qualitative study. All patients that were asked participated in semi-structured in-depth interviews (n=17).

We concluded that screening for MDD detects a group of patients that appreciate the active approach of the GP and the fact that they receive attention for their problems, but who also show resistance to being diagnosed as having MDD. Three reasons for this resistance were found: (1) patients experienced their symptoms as a normal and transitory reaction to adversity; (2) MDD was experienced as a severe psychiatric disorder and patients expressed fear of stigmatization; and (3) patients had doubts about the necessity and effectiveness of treatment.

We conclude that one important criterion for the viability of screening programs, the complete screening program (test, diagnostic procedures and treatment/
intervention) is clinically, socially and ethically acceptable to the target population, is hard to comply with in screening programs for MDD.

In chapter 9 the findings of the previous chapters are discussed. In conclusion data of this thesis suggest one cannot recommend implementing MDD screening in high-risk groups in primary care. Although we succeeded in selecting a population at high-risk for MDD, and the test-characteristics of the PHQ were acceptable, screening for MDD in primary care seems to be not feasible. Considering the three Wilson and Jungner criteria that were mentioned in the introduction, we can conclude that only the first criterion is met; the validity of the screening instrument seemed acceptable. The second and third criteria are not met; the effectiveness and acceptability of screening to the target population was too low.

However, more than a quarter of patients (26.1%) from the high-risk population suffered from a psychiatric disorder (major depressive disorder, panic disorder, other anxiety disorder or somatoform disorder). In addition, participants expressed their appreciation for being actively approached by their GP for exploration of emotional distress. Therefore, a more active approach of these high-risk group patients with explicit attention by their GP to psychological wellbeing may be recommended. GPs are probably aware of the possibility of underlying psychiatric morbidity in these groups, but an active approach should be advocated.

More research is needed on how to implement this active approach by GPs (or practice nurses) in daily practice. In this context, we recommend that the patients’ view about a psychiatric diagnosis like MDD should be elicited before diagnosing and offering treatment for a psychiatric problem, especially MDD. Aversion to being labeled as being depressed can have a deterrent effect on the willingness of patients to accept help, even though they might benefit from care for their depressive symptoms.