## Onset and recurrence of depressive disorders

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## SUMMARY

People with depressive disorders frequently come to see their general practitioner (GP) as these conditions are highly prevalent. In the Netherlands, 19% of the general population experiences a major depressive disorder during their life. Besides, depressive disorders are a leading cause of disability, affecting many aspects of life, and are associated with substantial societal costs due to associated healthcare utilization and productivity losses. The high disease burden of depressive disorders partly stems from its recurrent course: recurrence rates of 27% are reported in primary care in the Netherlands. Each additional depressive episode increases the risk of recurrence by 18%.

Interventions aimed at the prevention of relapse or recurrence could greatly reduce the disease burden of depressive disorders. Knowledge of predictors of the onset and course of depressive disorders is important in order to match limited treatment resources to the needs of patients and may result in more effective prevention and treatment of depressive disorders. Several important predictors of depressive disorders have been identified, such as subclinical depressive symptoms and number of previous depressive episodes, but further study is needed to clarify determinants. For instance, mostly cross-sectional studies have suggested that financial strain and somatization are related to mental health problems but the associations with the onset and course of depressive disorders are not yet fully understood.

A commonly used strategy for preventing relapse or recurrence is continuation of using antidepressant medication but many patients find long-term use of antidepressants unattractive and non-adherence is high. Psychological interventions offered after recovery have proven to be effective in reducing the risk of relapse and recurrence of depressive disorders. Most psychological interventions take place in secondary care, drawing on scarce resources in terms of therapists' time and at high costs. A minimally supported psychological intervention for prevention of relapse and recurrence would help overcome this problem. The effectiveness of a supported self-help intervention in primary care for preventing relapse or recurrence has not yet been studied. Besides, it is not yet known to whom preventive self-help interventions can be successfully applied.

Given this background, this thesis aimed to answer the following research questions:

- Are somatization and financial strain associated with the onset, presence and recurrence of depressive and anxiety disorders? (part I)

- What is the evidence on measurement properties of self-report questionnaires measuring somatization in primary care? (part II)
- Is a supported self-help intervention (S-PCT) effective in preventing relapse and recurrence of depressive disorders, compared to treatment as usual, in remitted, recurrently depressed patients? (part III)
- In which subgroups of patients is a supported self-help intervention (S-PCT) aimed at preventing relapse and recurrence of depressive disorders particularly (cost)effective? (part III)

## PART I Onset and recurrence of depressive disorders: contributing factors

For the studies described in the first part of this thesis, we used longitudinal data from the Netherlands Study on Depression and Anxiety (NESDA), a prospective cohort study which included nearly 3000 persons in various psychopathological stages and from various settings. In chapter 2, we found that financial strain was associated with the presence of depressive and anxiety disorders and that this association was independent of income level. However, financial strain and income were not related to onset/recurrence of depressive and anxiety disorders during the four-year follow-up period. In chapter 3, we showed that somatization was related to the onset of depressive and anxiety disorders in persons without a history of a depressive or anxiety disorder: having a higher somatization score at baseline increased the risk of becoming depressed during the four-year follow-up period. When subclinical depressive symptoms at baseline were taken into account, the association between somatization and onset of depressive and anxiety disorders attenuated but remained statistically significant.
Besides, the results in chapter 4 indicated that somatization increased the risk of recurrence of depressive and anxiety disorders over a four-year period, independent of the effect of residual depressive and anxiety symptoms. When residual depressive and anxiety symptoms were measured by questionnaires that only focus on mood and cognitive aspects of depressive and anxiety disorders (i.e. the IDS mood-cognition scale and the BAI subjective scale), these results did not change substantially.

To conclude: persons experiencing financial strain are more likely to have a depressive or anxiety disorder and persons with elevated somatization scores have a higher risk of onset and recurrence of depressive and anxiety disorders. In general practice, therefore, one should be alert to the presence of depressive and anxiety symptoms in patients showing elevated levels of financial strain or

somatization. Besides, our findings indicate that depressive and anxiety disorders may frequently be a reaction to somatization and suggest that somatization, depression and anxiety are overlapping but distinctive concepts.

## PART II Measurement of somatization

In the studies reported in chapter 3 and 4, we used the Four-Dimensional Symptom Questionnaire (4DSQ) somatization scale to measure somatization and operationalized somatization as a high frequency and severity of physical symptoms. In chapter 5, we evaluated the evidence on measurement properties of self-report questionnaires measuring somatization in primary care patients, such as the 4DSQ. Twenty-four articles on nine questionnaires were included in the review. For the Patient Health Questionnaire-15 (PHQ-15) and the 4DSQ somatization scale, the broadest range of measurement properties were studied. These questionnaires turned out to have good internal consistency, test-retest reliability, structural validity, construct validity (PHQ-15), and cross-cultural validity (4-DSQ). The Bodily Distress Syndrome (BDS) checklist had good internal consistency and structural validity. Some evidence was found for good construct validity and criterion validity of the Physical Symptom Checklist (PSC-51) and good construct validity of the Symptom Check-List (SCL-90-R) somatization subscale. However, these three questionnaires were studied in only a few studies in primary care. So for now, we recommend using the PHQ-15 or 4DSQ for measuring somatization in primary care patients.

## PART III Prevention of recurrent depression

In the third part of this thesis I focused on the (cost)effectiveness of supported self-help Preventive Cognitive Therapy (S-PCT), a minimal psychological intervention to prevent relapse and recurrence in primary care. We conducted a randomized controlled trial among 248 patients with recurrent depression, who were in remission or recovered at the start of the intervention. Participants were randomized to treatment as usual (TAU) plus S-PCT or TAU only. S-PCT consisted of a self-help book with assignments and was supported by weekly telephone guidance by a trained mental health nurse of psychologist. The primary outcome was the incidence of relapse or recurrence during 12 months and was assessed by the Structural Clinical Interview for DSM-IV axis 1 disorders (SCID-I). Secondary outcomes were depressive symptoms, quality of life, co-morbid symptoms of anxiety, somatization and distress, and self-efficacy during the 12 months follow-up.

In chapter 6 we showed that, compared to TAU, S-PCT is effective in preventing relapse and recurrence over a one-year period. Besides, S-PCT significantly reduced depressive symptoms and improved quality of life, compared to TAU. No effect of S-PCT was found on anxiety, somatization, distress, and self-efficacy. In chapter 7 we assessed the moderating effects of subclinical residual symptoms, number of previous depressive episodes, age of onset, somatization, self-efficacy, antidepressant medication use, age, gender and education level. We found that S-PCT was not more effective in any of the subgroups. This suggests that S-PCT can be offered to a broad range of patients to prevent relapse and recurrence. However, the number of previous depressive episodes was a moderator of total costs during follow-up. Costs were statistically significantly higher in the S-PCT group compared to the TAU group for participants with four of more previous episodes. Total costs were not significantly different in the S-PCT group compared to the TAU group for participants with two or three previous episodes. Lastly, the cost-effectiveness acceptability curves indicated that S-PCT was likely to be cost-effective in persons with two or three previous depressive episodes but not in persons with four or more episodes and thus at higher risk of recurrence.

## General discussion

In chapter 8, I discussed the main findings of this thesis and the methodological considerations. Thereafter, I elaborated on the clinical implications of these findings and gave recommendations for future research:

### *Clinical implications*

- In general practice, actively asking about and monitoring of depressive and anxiety symptoms in people with elevated levels of financial strain and somatization is advised.
- The findings of our review implicate that the PHQ-15 or 4DSQ should be used to measure somatization in primary care.
- Our findings implicate that a supported self-help intervention may be an effective alternative or addition to conventional psychological interventions to prevent relapse or recurrence of depressive disorders.
- S-PCT can be offered to a broad range of patients. However, one should keep in mind that S-PCT is not likely to be cost-effective in persons with four or more previous depressive episodes.
- I suggested that the use of preventive interventions for relapse and recurrence of depressive disorders should be tailored according to the risk profile of relapse and recurrence.

***Future research***

- Regarding the operationalization and measurement of somatization, future research should focus on psychological and behavioral aspects of somatization and on evaluating the measurement properties of promising questionnaires in primary care.
- The (cost)effectiveness of S-PCT should be studied in trials with longer follow-up periods and by assessing time to relapse or recurrence.
- Future studies should focus on which type of interventions and delivery modus are most suitable for whom.