

Summary

Depression and comorbidity. General practice-based studies on occurrence and health care consequences.

Introduction (chapter 1)

Depression often co-occurs with other mental and somatic disorders in one patient. This comorbidity is associated with increased personal and societal burden. Depression comorbid with another mental disorder is more severe and has a poorer prognosis than depression alone. The course of depression also tends to be more protracted in the context of somatic illness. The other way around, there is ample evidence that depression negatively affects the course and outcome of chronic somatic disorders. From a societal viewpoint, comorbidity involving depression is important given its association with increased use of health care services and increased absence from work.

Although its relevance is clear, substantial knowledge gaps about comorbidity involving depression remain. In this thesis two sets of research questions were examined to extend knowledge about: (a) the occurrence of comorbidity involving depression; and (b) the health care consequences of comorbidity involving depression, specifically consequences for quality of care and health care utilization. The studies are mainly based on general practice data collected within the framework of the second Dutch National Survey of General Practice (DNSGP-2) and the National Information Network of General Practice (LINH).

Part A. Studies on occurrence

Knowledge on somatic *cluster* comorbidity, i.e. somatic illness that occurs at a higher rate than expected by chance, among depressive patients in the general population is limited. Dutch general practice provides a good opportunity to study the pattern of somatic cluster comorbidity in a largely unselected sample of depressed persons. *Chapter 2* reports on a cross-sectional study that

used medical records of general practitioners (GPs) to address the following research question:

What are the patterns of somatic and psychiatric cluster comorbidity in depression, stroke, multiple sclerosis, Parkinson's disease/ parkinsonism, dementia, migraine and epilepsy?

Of the 30 categories of somatic illness studied, a broad and diverse set of 21 categories were identified as possible or highly probable instances of somatic cluster comorbidity in a large group of general practice patients with a lifetime GP diagnosis of depression.* This finding indicates that patients who have (had) depression are generally more likely to have a somatic illness than those who never had a depression. Noteworthy, when analyses were restricted to the subgroup of patients with a current GP diagnosis of depression, 12 of the 21 somatic disease categories were no longer identified as (possible or highly probable) cluster comorbidity. This was interpreted to reflect reduced statistical power due to the smaller size of this subgroup.

Part A continued with a case-control study that examined the association between cerebrovascular risk factors (CVRFs) and the subsequent development of depression in later life. There is little research on this relationship. Demonstrating the existence of such a link would lend support for the vascular depression hypothesis of late-life depression, which postulates that cerebrovascular disease may cause or exacerbate depression with late onset in life. The following research question was addressed in *chapter 3*:

Is there a relationship between CVRFs and the subsequent development of depression in older general practice patients?

In this study, CVRFs included diagnoses of hypertension, diabetes mellitus, and cardiovascular disease. None of the CVRF variables examined (i.e. any CVRF, individual CVRF, number of CVRFs, and exposure duration to CVRFs) was found to be significantly associated with the subsequent onset of depression in a sample of older general practice patients. However, several of the CVRF variables under study were associated with a significantly increased odds of developing depression with onset between ages 50 and 69 years. It was suggested that these findings could indicate that CVRFs play a relevant role in the development of depression with onset between ages 50 and 69 years, but

* Being of most interest to this thesis, summary of findings is limited to those concerning somatic cluster comorbidity in depression.

that no evidence was found that CVRFs contribute to the occurrence of depression with onset at age 70 years or later. These results should be considered preliminary given the possibility of bias inherent in using morbidity data recorded by GPs.

Part A finished with a systematic review. The various cross-sectional studies performed to date that have examined the relationship between severity of Alzheimer's disease (AD) and prevalence of comorbid depressive symptoms or depression have yielded inconsistent results. *Chapter 4* describes a systematic review of these cross-sectional studies to address the following research question:

Is there a relationship between severity of AD and prevalence of comorbid depressive symptoms and depression?

A search strategy identified twenty-four studies that fulfilled pre-defined inclusion criteria. Of these, 19 reported findings on the relationship between severity of AD and prevalence of depressive symptoms and seven on the association of AD severity with frequency of diagnosed depression. Four of the 19 studies on the former association were rated as being of high quality, and three of these found no significant association. Three of the seven studies on the latter relationship were rated as being of high quality, and none of these reported a significant result. It was concluded that no evidence exists for a relationship between severity of AD and prevalence of comorbid depressive symptoms or depression.

Part B. Studies on health care consequences

Consequences for quality of care

The focus was laid on the influence of comorbidity on the care for depression in general practice in the Netherlands, as Dutch GPs play a central role both in the diagnosis and management of depression.

Given that previous studies have suggested opposite effects of psychiatric and somatic comorbidity on underdiagnosis of depression by GPs, the study described in *chapter 5* set out to answer the following research question:

Is there an interaction effect between psychiatric and chronic somatic

comorbidity on GPs' diagnosis of depression?

It was shown that approximately half of a group of patients with major depression and/or dysthymic disorder established according to a structured diagnostic interview had either comorbid psychiatric (as indicated by the interview) or comorbid chronic somatic disease (as indicated by GP records). Almost a quarter of them had both types of comorbidity. About 65% of the patients with psychiatric comorbidity were not diagnosed as being depressed by their GP, as reflected by having no GP record of a diagnosis of depression or depressive feelings. The rate of underdiagnosis of depression was somewhat higher among those with comorbid chronic somatic illness (74%). Multivariate analysis demonstrated an interaction effect between somatic and psychiatric comorbidity on GPs' diagnosis of depression. Further analysis showed that - among the patients without chronic somatic comorbidity - a lower educational level, less severe depression, and fewer GP contacts all were independently associated with a decreased likelihood of being diagnosed as depressed. Among the chronic somatically ill patients only having no comorbid psychiatric disorder was associated with a decreased likelihood of receiving a depression diagnosis. It was concluded that the factors associated with underdiagnosis of depression by GPs differ depending on whether or not depressed patients have a chronic somatic illness.

There is limited information on whether having a specific chronic somatic condition influences the care for depression in general practice. *Chapter 6* presents a prospective study in which two research questions were addressed:

What is the influence of specific chronic somatic conditions on the initiation of any depression care in patients newly diagnosed with depression by their GP?; and

Among those being prescribed antidepressants by their GP, what is the influence of these conditions on prescription of continuous antidepressant treatment?

Any depression care was initiated in 86% of the patients with chronic somatic illness. A comparable percentage was observed among the non-chronically ill patients (88%). Rate of initiation of any depression care varied by type of condition, ranging from 59% in patients with cardiac arrhythmia to 93% among those with a thyroid condition. Multivariate analysis showed that patients with pre-existing ischaemic heart disease or cardiac arrhythmia had a significantly

lower likelihood of having any depression care being initiated after being newly diagnosed with depression by their GP than patients without chronic somatic illness. None of the other 12 chronic somatic conditions under study was found to significantly impact the initiation of any depression care. The proportion of patients with continuous prescription after initiating antidepressant therapy was comparable among the groups with and without chronic somatic illness (resp. 37% and 39%). The rate of continuous prescription differed according to the type of the comorbid condition. Patients with cardiac arrhythmia showed the highest rate (50%), while the lowest rate was observed among those with a thyroid condition (23%). Multivariate analysis demonstrated that none of the chronic somatic conditions significantly influenced the prescription of continuous antidepressant treatment. These findings were interpreted as pointing to the relevance of supporting GPs in the management of comorbid depression in patients with heart disease to reduce its negative impact.

Consequences for health care utilization

Although a number of studies have addressed the impact of depression on use of health care services by patients who suffered a stroke, none of them has specifically focussed on the influence of already existing depression. Part B finished with a prospective study that attempted to answer the following research question (*chapter 7*):

What is the impact of having pre-existing depression at hospital admission for stroke on the length of acute hospital stay and discharge destination?

It was found that having pre-existing depression at the time of hospital admission for a new or recurrent stroke did not significantly affect length of acute hospital stay. It was further shown that among the survivors of hospitalization for acute stroke, the patients who were already depressed at admission had a significantly greater likelihood of being discharged to an institution instead of their home than those without any pre-existing mental health condition. Having a pre-existing mental health condition other than depression did neither influence length of acute hospital stay nor discharge destination. These findings were interpreted as indicating that having pre-existing depression is a possibly important factor in determining discharge to institutional care after hospitalization for acute stroke.

General discussion (chapter 8)

Strengths and limitations of using general practice records

The studies showed that using data from general practice records for studying the occurrence of comorbidity involving depression and its health care consequences has its strengths and limitations.

Strengths include:

- Data represent a largely unselected population, at least in countries where GPs act as a gatekeeper to other health care facilities;
- Data on a large number of persons are available;
- Morbidity data reflect doctor-defined health problems rather than being based on self-report;
- Morbidity information is relatively comprehensive given that GPs come across a broad spectrum of somatic and mental health problems;
- Data are continuously collected, which allows prospective or retrospective research to be conducted that spans long periods of time;
- Opportunities exist to link datasets from general practice networks with data from patient based registers from other care settings;
- In various countries GPs play a important role in the diagnosis and management of persons with depression and in their referral to other health care professionals.

Potential limitations include:

- Reliance on GP-diagnosed depression including its inherent variability;
- Suboptimal recording of morbidity in terms of completeness and accuracy;
- Variation between GPs and practices regarding quality of recording;
- Low specificity of diagnoses recorded, by which no information is available on the type and severity of depression and other health problems;
- No or restricted information is available about important potential confounders or effect modifiers, such as psychological and social risk factors for depression.

Directions for future research

Research on occurrence

Based on the findings in Part A, it was concluded that there exists a need for well-designed longitudinal research to better describe the occurrence of comorbidity between depression and other health conditions and to better understand its underlying mechanisms. Three more specific research objectives were suggested regarding comorbidity between depression and somatic illness:

- Gain more insight into the specificity of cluster comorbidity between depression and somatic illness;
- Gain more insight into the interplay between having a chronic health condition and other risk factors in the onset of depression;
- Gain more insight into the course of depression in the context of a chronic health condition and its determinants.

Research on health care consequences

Three objectives for future research were proposed based on the findings in Part B:

- Gain more insight into the mechanisms that underlie suboptimal diagnosis and management of depression in the context of somatic illness;
- Gain more insight into the mechanisms underlying the association between comorbid depression and increased health care utilization among persons with somatic illness;
- Gain more insight into the (cost-)effectiveness of interventions for depression comorbid with somatic illness.

Relevance and implications for Dutch general practice

Study findings indicate that the diagnosis and management of comorbid depression in patients with chronic somatic illness is less-than-optimal in general practice in the Netherlands. This finding is of concern given the commonness of comorbidity between depression and chronic somatic illness and the evidence that depression negatively affects the course and outcome of somatic illnesses, and vice versa. Some suggestions are given to improve care for chronic somatically ill patients with comorbid depression in general

practice, such as regular screening for depression, stepped-care treatment, the availability of a care manager and supervision by a mental health specialist.

Summary