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The interplay between depression, anxiety and physical health

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2014

document version

Publisher's PDF, also known as Version of record

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citation for published version (APA)

Gerrits, M. J. G. (2014). *The interplay between depression, anxiety and physical health*. [PhD-Thesis - Research and graduation internal, Vrije Universiteit Amsterdam].

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SUMMARY

INTRODUCTION

Pain and chronic somatic diseases often accompany depressive and anxiety disorders in the general population. Co-morbidity of physical and mental ill health often leads to a high burden at a personal level due to problems with treatment adherence, decreased treatment response, and social and occupational disability, and also to a huge societal burden due to loss in work days and high health care costs. There is ample evidence that depressive disorders, and to a lesser extent anxiety disorders, exert a negative effect on the course and outcome of pain and several chronic somatic diseases. By contrast, the effect of pain symptoms and chronic somatic diseases on depressive and anxiety disorders over time is not well studied. This thesis focused on the longitudinal associations between pain (by location, duration, severity as assessed by self-report during an interview) and depressive and anxiety disorders, and also on the longitudinal associations between self-reported chronic somatic diseases (such as cardiovascular, pulmonary or rheumatic disease) and depressive and anxiety disorders. Data were derived from the Netherlands Study of Depression and Anxiety (NESDA) examining 2981 participants aged between 18 and 65 selected to study the long-term course of depressive and anxiety disorders. By answering the following questions we hoped to provide a more in-depth insight into the role of physical health problems – pain and specific chronic somatic diseases - on depression and anxiety over time in order to guide future prevention and treatment strategies and consequently reduce this public health burden. Are (particular) physical health problems associated with recognition of depressive and anxiety disorders by general practitioners? Are pain symptoms and (particular) chronic somatic diseases associated with the onset, presence and prognosis of depressive and anxiety disorders? And how do changes in depressive and anxiety disorder course affect changes in pain over time?

GENERAL PRACTITIONER (GP) RECOGNITION OF DEPRESSION AND ANXIETY

The associations between physical health problems and the GP recognition of depression and anxiety were described in *Chapter 2*. Physical health problems were defined as the report of the experience of pain symptoms or of specific chronic diseases. By using the Electronic Medical Records (EMR) from the GPs, we found that the GPs recognized 60% of patients as depressed or anxious when compared to the 'gold standard', the NESDA diagnostic interview data. GPs tended to recognize depression and anxiety better in patients who reported pain symptoms (particularly

chest pain and greater severity of pain), partly due to more severe psychiatric symptoms among those with pain. Both the reporting of pain symptoms and the signalling of affective symptoms could thus have led to the GP recognition of depression and anxiety. It is reassuring that GPs tend to recognize depressive and anxiety disorders better in these patients since patients with pain are at higher risk of onset and worse course of depression and anxiety (as discussed in *Chapters 4, 5, 7* and below). None of the particular chronic somatic diseases were either positively or negatively associated with GP recognition. It is, however, important to note that some associations between specific chronic somatic diseases and GP recognition may have gone undetected due to the low power of infrequently reported diseases.

COMORBIDITY OF PHYSICAL HEALTH PROBLEMS AND DEPRESSIVE AND ANXIETY DISORDERS

Pain, migraine and depressive and anxiety disorders

We were interested in whether associations between pain and depressive and anxiety disorders depend on the location of pain. Therefore, we investigated whether there was a specific relationship between migraine and depressive or anxiety disorder or whether other locations of pain were also consistently associated with depression and anxiety. In addition, we tested whether there was a consistent association between migraine and other types of pain when taking into account depression and anxiety comorbidity.

In *Chapter 3* we showed that depressive and anxiety disorders were consistently associated with pain in all measured locations, which were neck, back, orofacial area, chest, abdomen, joints and also headache (non-migrainous, probable and strict migraine). These findings were stronger for patients with both a depressive and anxiety disorder compared to only depression, only anxiety or a history of depression or anxiety. Also, we found a synchrony of change between pain and depression and anxiety. When the number of pain locations changed over the course of two years, depressive and anxiety symptomatology changed in a similar direction.

Migraine was associated with pain in all other anatomical sites, but these associations weakened substantially after correction for the severity of depression and anxiety. This suggests that a considerable part of the comorbidity between migraine and other types of pain may be explained by the presence of depression and anxiety. We would therefore suggest that when studies focus on the comorbidity of multiple pain symptoms, measures on depressive and anxiety disorders should be included. In daily practice, physicians should actively enquire after depression and anxiety when patients (frequently) visit for multiple pain complaints.

Pain, and onset and course of depressive and anxiety disorders

Since pain and depressive and anxiety disorders are so often comorbid, we wanted to examine whether pain is associated with the onset and course of depressive and anxiety disorders. In addition, we wanted to examine whether pain is directly associated with depressive and anxiety disorders or (also) indirectly by being associated with the severity of (subthreshold) depressive and anxiety symptoms.

In *Chapter 4*, we demonstrated that pain, particularly when more widespread and of higher severity, was associated with onset of depressive and anxiety disorders. By contrast, there was no association with duration of pain symptoms - which traditionally is regarded as the key aspect of chronic pain - and depression and anxiety onset. When also considering the severity of subthreshold depressive and anxiety symptoms, we found that only joint pain and increasing number of pain locations were still significantly associated with depression and anxiety onset.

In *Chapter 5*, we found that next to being a risk indicator for onset of depressive and anxiety disorders, pain was also associated with worse course of depression and anxiety. Again, a higher number of pain locations and increasing severity of pain were associated with a worse course. Also, the daily use of pain medication was associated with a worse course. Even over and beyond the severity of depressive and anxiety symptoms, joint pain was associated with a worse depressive and anxiety course.

Because depressive and anxiety disorders are so often remitting and recurring, we wanted to examine whether physical health problems are related to recurrence of depression and anxiety. In *Chapter 7*, we examined whether pain was significantly associated with recurrence of depression and anxiety. We found that several pain locations, increasing number of locations and increasing pain severity were associated with depression recurrence. However, when considering the severity of subthreshold depressive symptoms, these symptoms accounted for a considerable part of the associations. None of the pain variables was associated with anxiety recurrence. We adjusted for having chronic somatic diseases in the above mentioned chapters, which did not change these associations.

In summary, when assessing the longitudinal associations between pain, and depression and anxiety we found that pain was associated with a higher likelihood of onset and worse course of depression and anxiety, partly through being associated with the severity of depressive and anxiety symptoms. This may support the idea of a vicious cycle in which pain, depression and anxiety are reinforcing each other.

Clinicians should be aware that when patients report pain in multiple locations (particularly also affecting joints), they are at increased risk of first onset, recurrence and worse course of depressive and anxiety disorders, even when they do not display depressive and anxiety symptomatology (yet). In patients with a previous history of depressive and anxiety disorder, pain symptoms do not seem to have an significant impact on recurrence of these disorders over and

beyond such subthreshold depressive and anxiety symptoms. However, since pain is the main reason for consulting clinicians, pain symptoms may be important clues to further examine risks of depressive and anxiety disorder recurrence.

Chronic somatic diseases and course of depressive and anxiety disorders

Since chronic somatic diseases (i.e. migraine, diabetes or COPD) and depressive and anxiety disorders are so often comorbid, we wanted to examine whether specific chronic diseases were associated with the onset and course of depressive and anxiety disorders. The participants of the NESDA study are all adults between 18 and 65 years, were rather healthy and did not have many chronic diseases. Also, we did not include measures of chronic somatic disease severity. Therefore, we could not study the associations between specific chronic diseases and onset of depression and anxiety. Similarly, the results that are presented here regarding the associations between specific chronic diseases and course of depression and anxiety are based on rather small numbers.

In *Chapter 6*, we found that musculoskeletal diseases, particularly osteoarthritis, were associated with a worse 2-year course of depressive and anxiety disorders. Individuals with diabetes were at increased risk of a recurrent or chronic course of depression and anxiety over a period of two years.

In *Chapter 7*, we found that none of the chronic somatic diseases was associated with a recurrent course of depression and anxiety over a four-year period.

These findings suggest that having a specific chronic somatic disease does not seem to have a major impact on the course of depression and anxiety, except for musculoskeletal diseases and diabetes in adults. Findings could be different for children and the elderly, and particularly for individuals with more severe diseases. Future studies would benefit from including severity of disease measures (such as pain or disability caused by the disease). It could be that the findings for musculoskeletal diseases and diabetes (with peripheral neuropathy as complication) were in part driven by pain caused by these diseases.

Depressive and anxiety course as prognostic indicator of pain over time

We focused on the longitudinal associations between changes in depressive and anxiety symptomatology and disorders, and changes in pain over the course of four years. We concentrated on whether pain course is different in chronic or temporary states of depression and anxiety versus healthy controls.

In *Chapter 8*, at depressive and anxiety symptom level we found a synchrony of change between change in depressive and anxiety symptoms and change in pain, which concurs with our findings in *Chapter 3*. Next, we found that depressive and anxiety disorders - whether incident, remitting or chronic- were associated with worse pain severity and higher number of pain locations over

time compared to being mentally healthy. Chronically depressed and anxious individuals showed the highest pain ratings and even if individuals recovered from the depressive or anxiety disorder their pain ratings were still significantly higher than of mentally healthy individuals. These findings add to the idea that experiencing pain, and depression and anxiety may lead to a vicious cycle of increasing symptomatology. Surprisingly, when individuals developed a depressive or anxiety disorder over time, pain levels were already high before depression or anxiety onset and pain ratings did not significantly increase over time. This last finding may support our finding from *Chapter 4* that pain is a risk indicator of depression and anxiety onset.

DISCUSSION

This thesis ends with a general discussion (*Chapter 9*), in which the findings of *Chapters 2 through 8* were reported and discussed. To conclude, poor physical health does not have a major impact on the recognition of depressive and anxiety disorders by general practitioners. Our findings suggest that there is a bidirectional relationship between pain and depressive and anxiety disorders. First, we found strong cross-sectional associations between pain, regardless of its location, and depressive and anxiety disorders. Second, we found that pain is a risk indicator of onset, recurrent and chronic course of depression and anxiety. Last, having a depression and anxiety negatively affects pain symptomatology over time. These findings seem to point to a vicious cycle in which pain and depression and anxiety reinforce each other. In addition, musculoskeletal disease and diabetes were associated with worse prognosis of depressive and anxiety disorders, whereas no other specific chronic somatic disease exerted a negative impact on depression and anxiety course. Clinicians should be alert to signals of pain, when caring for patients with depression and anxiety. Also, when physical health problems, with pain problems and diabetes in particular, occur in depressed and anxious individuals specific attention should be paid to integrated treatment options.