Functional limitations associated with mental disorders
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Chapter 7

**Summary and general discussion**
In this thesis, the functional limitations associated with mental disorders were examined using general population samples. Results regarding the six research questions formulated in the introduction will be summarized and discussed in this chapter. Additionally, implications of the findings for further research and for clinical practice will be portrayed.

7.1   Psychometric properties of the ESEMeD WHODAS

7.1.1   Summary of the findings

In ESEMeD the WHODAS-II was simplified by using filter questions and reducing the number of questions to make it more time-efficient. In the so-called ESEMeD WHODAS, like in the original WHODAS-II, a single unidimensional global disability latent variable was found. This Global Disability variable was an accurate summary of six distinct subscales: Role Functioning, Cognition, Mobility, Self-care, Social Interaction, and Participation, which is in accordance with the WHODAS-II. Each subscale consists of 4-7 items that measure frequency and severity of the disability. Excluding the frequency items of Cognition, Mobility, Self-care, and Social Interaction from the questionnaire improved the questionnaire, as indicated by a better overall fit of the model. The model in which items load on a specific subscale, which subsequently load on the General Disability factor was the same in Mediterranean and non-Mediterranean countries, except for Embarrassment.

Preliminary analysis suggests that the validity of the ESEMeD WHODAS is acceptable, because there was a clear distinction in functioning between (1) individuals without any lifetime mental disorder, (2) individuals with a lifetime, but no 12-month mental disorder, (3) individuals with a 12-month mental disorder that was (a) not severely or (b) severely interfering with their work, social life, or their personal relationships. The analysis was repeated for individuals with physical disorders who reported 1) no, 2) moderate, or 3) severe interference of their physical disorders with work, social life, or their personal relationships. Those who reported no interference functioned better than those with moderate interference on all domains, while those with moderate interference functioned better than those with severe interference on all domains of the ESEMeD WHODAS, which also suggest validity of the questionnaire.

7.1.2   Discussion

The current study suggests that the ESEMeD WHODAS may well be a valuable shortened version of the WHODAS-II to measure functional limitations, but several issues need to be addressed. First, the embarrassment item (FD20) showed country non-invariance, i.e. individuals from Mediterranean countries...
Summary and general discussion

seem to interpret this item in a different manner than those from non-Mediterranean countries. Any comparison based on this item should, therefore, be interpreted with caution.

Second, for all domains except Role Functioning, filter questions were used. The low prevalence of functional limitations in some domains suggest that the filter questions may have been too stringent. Too stringent filter questions reduce the ability of the ESEMeD WHODAS to differentiate individuals with relatively mild limitations from those without limitations. A related, potentially problematic issue regarding the very skewed data is that most statistical procedures assume a normal distribution. Solutions to this problem may be to (a) use statistical procedures that do not rely on a normal distribution, but can handle very skewed and even zero-inflated data, (b) categorize functional limitations in ‘zero’ ‘some’, and ‘many’, or (c) dichotomize at the 90th percentile of the population scores. The most profitable strategy depends on the purpose of the analyses.

Third, there are two issues regarding Role Functioning. First, the General Disability factor explains little variance in Role Functioning. This may have been caused by the nature of the questions in Role Functioning, i.e. Role Functioning includes only frequency items and no severity items which is different from the other domains. Second, Role Functioning and Participation regard functioning at a general level which is different from the other domains that all entail specific functional domains. Possibly, a hierarchy among the domains of the ESEMeD WHODAS is present, i.e. disfunctioning in one domain will occur before functioning in another domain is impaired. Further support for a hierarchy is the considerable variation in the percentage of individuals who scored zero on each subscale.

Fourth, the psychometric properties of the ESEMeD WHODAS were examined in a cross-sectional study. Some important psychometric properties, such as responsiveness to change and test-retest reliability, could, therefore, not be measured. This issue needs to be addressed in future longitudinal studies.

7.2 Which domains of functioning are affected by mental disorders?

7.2.1 Summary of the findings

Results presented in Chapter 3 suggest that mood, anxiety and alcohol disorders are related to significant limitations in all domains of functioning measured with the ESEMeD WHODAS. Anxiety disorders were associated with more functional limitations than mood disorders, which were in turn related to more functional limitations than alcohol abuse and dependence. This general trend did not hold for the domain of Cognition, which measures mostly concentration and
attention. Individuals with a mood disorder functioned worse than those with an anxiety disorder on this domain.

It was hypothesized that problems in Cognition would be associated with mental disorders and not with physical disorders. Within the ESEMeD WHODAS, domains of functioning are mapped onto 0-100 scales in which a higher score indicates greater disability in the past 30 days. It was found that individuals with mental disorders scored 2.5-6.7 (sd 8.7 and 13.2, respectively) on Cognition. This is 8.3-22.3 times higher than those without mental disorders who scored 0.3 (sd: 2.8) on the same scale and 1.8-5.2 times higher than those with arthritis or heart disease who scored 1.4 (sd: 6.7) and 1.3 (sd: 7.3) respectively. Thus, Cognition was indeed stronger associated with mental disorders than with physical disorders, as was hypothesized, but individuals with physical disorders had problems with Cognition as well, which was not in line with our hypothesis.

The opposite was hypothesized for Mobility, i.e. an association with physical disorders, but not with mental disorders. Individuals with arthritis or heart disease scored 13.3 (sd: 25.5) and 18.9 (sd: 31.2), respectively. Individuals with mental disorders scored 3.1-12.4 (sd 8.5 and 23.1, respectively) on Mobility, which is 1.1-1.6 times less than those with physical disorders. Compared to those without disorders, Mobility was strongly associated with physical disorders, which is in line with the hypothesis, but mood and anxiety disorders were also significantly associated with Mobility problems, which again was not in line with the hypothesis.

Overall, the mental disorders examined in this chapter were associated with more functional limitations than physical disorders, except for mobility problems. Since the prevalence of these mental disorders in the general population is substantial, the total effect of mental disorders addressed in this Chapter on society as a whole is considerable as well.

7.2.2 Discussion

The finding that mental disorders are related to significant functional limitations supports the notion that mental disorders, by definition, must result in either distress or functional disability. An average score of less than ten on a 0-100 scale does not seem a major issue at first glance. However, the thresholds of the filter questions used in the ESEMeD WHODAS are probably too stringent. As a consequence, the ESEMeD WHODAS is not very accurate in differentiating individuals without limitations from those with mild limitations. Therefore, a score that is one standard deviation above the score of individuals without any mental and physical disorders, should be considered severe functional
limitations. The finding that alcohol disorders are related to fewer functional limitations than mood and anxiety disorders can be explained in other ways than pointing to the stringent filter questions: a) alcohol abuse may not indicate a pathological condition (de Graaf et al., 2003; de Graaf et al., 2002), and b) excessive alcohol use is widely tolerated in European societies.

The functional limitations associated with mental disorders reported in Chapter 3 are probably an overestimation of the effect of each pure disorder, because we did not control for mental comorbidity. Patients with mood disorders often show comorbid anxiety disorders and alcohol disorders (Kessler et al., 2005; Kessler et al., 1994; The ESEMeD/MHEDEA 2000 investigators, 2004a). This comorbidity is associated with greater symptom severity (Andrade et al., 1994; Roy-byrne et al., 2000) and persistence (Kessler et al., 1994; Roy-byrne et al., 2000), more severe role impairment (Bijl and Ravelli, 2000; Hecht et al., 1990; Roy-byrne et al., 2000), increased help-seeking behavior (Bijl and Ravelli, 2000; Kessler et al., 1994), and higher risk of suicide (Kessler et al., 1999). Although we probably overestimated the functional limitations associated with pure mental disorders, this Chapter did demonstrate the functional limitations associated with mental disorders as they occur in the general population.

In this study, functional limitations associated with mental disorders were, in general, at least comparable to that of physical disorders, which has been established in previous studies as well (e.g. (Hays et al., 1995; The ESEMeD/MHEDEA 2000 investigators, 2004b)). In general, mental disorders were related to more limitations in Cognition, Embarrassment and Discrimination. Physical disorders were associated with more Mobility problems. This finding is in line with the ESEMeD investigators (2004) who state that functional limitations associated with mental and physical disorders are likely to differ (Alonso et al., 2004). They suggest that physical disorders may be associated with limitations in physical capacities, such as mobility, vision, aerobic capacity, lower and upper body strength, manual dexterity, and incontinence, whereas mental disorders may be associated with limitations in cognitive and motivational capacities, affect regulation, social perception, and a tendency to amplify physical symptoms such as fatigue and pain.

7.3 What are the unique and shared effects of physical and mental disorders on absence from work?

7.3.1 Summary of the findings
In Chapter 4, the unique and shared associations of mental and physical disorders with work loss and the prevalence of physical-mental comorbidity were described. We found that all mental disorders were associated with
significant work loss. Individuals with a mood disorder were almost 29 days more absent from work in the past 12 months than those with the same gender, age, and educational attainment, but without a mood disorder. Individuals with anxiety disorders were 17.6 and those with a substance use disorder 7.6 days more absent from work compared to individuals with the same age, gender and educational attainment, but no disorder. Also, mood disorders were more often associated with being totally unable to work than anxiety and alcohol disorders. Compared to physical disorders, mental disorders were associated with more (sinus infection, hypertension, asthma, and migraine), comparable (rheumatism, disease of the digestive system, and accidental injury), or less (chronic back trouble) work loss days.

In general, individuals with a physical disorder were more likely to have a mental disorder than those without (OR ranges from 1.4 to 2.6 for anxiety and mood disorders) except accidental injury was not associated with any mental disorders. Vice versa, individuals with a mood or anxiety disorder were more likely to have a physical disorder. Substance use disorders were only significantly associated with five out of eight physical disorders. In conclusion, physical-mental comorbidity is common, but not extremely common, and not for every combination of mental and physical disorders. In addition, physical-mental comorbidity was associated with more work loss days than pure mental and pure physical disorders, even after controlling for number of disorders. The effect of physical-mental comorbidity was additive, except for chronic back pain and hypertension which showed synergistic effects.

7.3.2 Discussion
The finding that both mental and physical disorders are related to work loss days has been previously reported (e.g. (Kessler et al., 2001; Kessler and Frank, 1997)). Three findings reported in Chapter 4 need to be elaborated on. First, accidental injury was not associated with mental disorders. Although repeated injuries may be associated with mental disorders, single injuries were not related to mental disorders in previous studies either (Visser et al., 2007). Second, pure chronic back pain leads to more work loss than mental disorders. This may be due to avoidance of work-related pain. Third, synergistic effects for chronic back pain and hypertension on work loss were found while additive effects were found for all other physical disorders. A possible explanation for this finding in chronic back pain may be that emotional stress may increase pain sensation, and in addition cause a motivational deficit that keeps people at home longer than pure back pain or a pure mental disorder. An explanation of the synergistic effect of hypertension is that there may be low prevalent, unmeasured comorbid
physical disorders that cause additional work loss. A more detailed examination of these synergistic effects is needed, but this was beyond the scope of this thesis.

The results reported in Chapter 4 should be interpreted in light of the following limitations. First, only prevalent disorders were assessed. Unmeasured disorders, for example eating disorders, schizophrenia, or heart failure, could have caused work loss as well and if these disorders are not randomly distributed, which is not unlikely (Neeleman et al., 2001), the findings in Chapter 4 are influenced in an unpredictable way. For example, if eating disorders are associated with a large number of work loss days and frequently co-occur with depression we would have overestimated the work loss associated with mental disorders. If, on the other hand, eating disorders frequently co-occur with disease of the digestive system, the work loss associated with physical disorders would have been overestimated. Although prevalence of a single disorder is low, overestimation of work loss might not be minor if there are many low prevalent, unmeasured disorders that cluster together.

Second, there are two issues related to the work loss questions that need to be addressed. First, we asked respondents the number of days they were totally unable to work in a given year. The number of days a person was present at work, but had to cut down on quantity or quality of work was not taken into account. The focus on days completely absent from work probably leads to an overall underestimation of the costs related to productivity loss. However, the underestimation probably affects mental disorders more than physical disorders. Dewa et al. (2000) found that mental disorders affect productivity more subtly than physical disorders, e.g. a person with depression may be present at work, but be less productive than normal, while a person with a broken leg is completely absent from work (Dewa and Lin, 2000). The use of a more objective and refined measurement of work impairment would be a major advancement in assessing full and partial work days missed. An example of such a questionnaire is the World Health Organization’s Health and Work Performance Questionnaire (Kessler et al., 2003a). Second, we added the number of work loss days respondents attributed to mental disorders to work loss attributed to physical disorders. In case of physical-mental comorbidity, it is not clear whether respondents were able to attribute the correct number of work loss days to each disorder. We did find, however, that only 16 (0.2%) of the total sample reported more work loss days than there are days in a year after adding the mental and the physical work loss days. Furthermore, the additive effects are in line with results from the National Comorbidity Survey (Kessler et al., 2003b).
7.4 Is the effect of Major Depressive Episode (MDE) on participation restriction mediated by activity limitations? Which limitations mediate most of the effect?

7.4.1 Summary of the findings
In Chapter 5, the pathway from major depressive episode to reduced role functioning at home or in paid employment, i.e. participation restriction was described. The difference between the direct effect before (0.43) and after (0.17) adding activity limitations to the model, suggests that about half of the total effect is mediated by activity limitations. Of the activity limitations, only Cognition, i.e. concentration and attention problems, and Embarrassment were significant mediators.

To test the robustness of the mediation model, we fitted it in four subgroups: a) persons without any other disorder than MDE; b) persons with one or more non-MDE mental disorder, but not a physical disorder; c) persons with physical disorders, but not a mental disorder other than MDE, and d) persons with both non-MDE mental disorders and physical disorders. The strength of the significant paths from the final model could not be constrained to be equal across the four subgroups without significant loss of fit. However, the final model had a good overall fit if the strength of these paths was allowed to differ. In conclusion, the final mediation model was considered robust, because its fit was independent of whether or not MDE was comorbid with other mental or physical disorders.

7.4.2 Discussion
Results presented in Chapter 5 show that Cognition and Embarrassment were mediators in the association between MDE and participation restriction, which has, to our knowledge, not been addressed previously. Interventions aimed at improving cognition and reducing embarrassment may relieve personal suffering associated with MDE and could also positively influence the societal costs of MDE by reducing participation restrictions. In addition, treatment of cognition and embarrassment may also improve effectiveness of antidepressant therapy and cognitive behavior therapy. In previous studies, problems in cognition, defined as neuropsychological impairments, predicted unfavorable outcome of antidepressant therapy (Kampf-Sherf et al., 2004) and cognitive behavior therapy (Crews and Harrison, 1995). Embarrassment is closely linked to self-stigmatization, which in the context of MDE is associated with greater unmet mental health care needs (Roeloffs et al., 2003), and predicts
antidepressant drug noncompliance (Sirey et al., 2001a) and treatment discontinuation (Sirey et al., 2001b).

The major limitation of this study is the cross-sectional design. In order to assess mediating effects, the following requirements have to be met: a) the mediating variables must precede participation restriction (outcome), but follow the onset of the MDE (determinant), and b) when limitations are modelled as mediators, the direct associations between MDE and the participation restriction weakens or disappears. Cross-sectional design prohibits firm conclusions about time order and causality, although the time order that we assumed between MDE, limitations, and participation restrictions can easily be made plausible. Another limitation is that our current approach allowed the activity limitations to correlate and did not specify restrictive causal relationships among them. The activity limitations, however, might be causally related in a highly specific way. For instance, cognition problems, caused by MDE might precede and influence Social Interaction which itself may not be causally affected by MDE. While we do not think that different causal structures will yield much different mediation effects, some dependency on how the activity limitations influence one another cannot be ruled out. It is firmly recommended that the findings will be replicated using longitudinal data. NEMESIS was longitudinal of design, but activity limitations were not addressed in accordance with the ICF and data regarding work loss was not complete in the final wave of the study. Therefore, this model could not be fitted in the NEMESIS population.

7.5 Does functioning return to (a) premorbid and (b) normal population levels after recovery from a major depressive episode? Can complete recovery be predicted?

7.5.1 Summary of the findings
In Chapter 6, we used longitudinal data to follow initially non-depressed individuals through a major depressive episode and remission. Initially, these individuals functioned significantly worse than their non-depressed counterparts. During the MDE, functioning worsened and after recovery from the MDE, functioning returned to premorbid levels. On average, postmorbid levels of functioning were, however, lower than in the non-depressed individuals. Although mean levels of functioning returned to premorbid levels or above, functioning of some individuals was worse after recovery of the MDE than before onset. After controlling for initial SF-36 score, low mastery before the MDE, comorbid anxiety disorder, comorbid substance use disorder, low social support (all measured during the episode), and post episode physical disorders were the best predictors of worsened functioning after the depressive episode.
7.5.2 Discussion

In this study no support was found for the scar hypothesis that states that depression permanently changes a person in such a way that subsequent depressive episodes are more likely to occur. It was, however, found that respondents who will go through a depressive episode, already functioned worse than their non-depressed counterparts before onset of the depressive episode. One possible explanation of the lower level of functioning is that depressive symptoms are already present before onset of a full-blown depressive episode or that anxiety or substance use symptoms were present. This is in line with Judd et al. (2000) and Ormel et al. (2004). Judd et al. (2000) found a return to normal levels only in patients who were asymptomatic at the time of measurement. Ormel et al. (2004) obtained similar results and concluded that there was evidence for a trait effect, i.e. functioning before the depressive episode is lower in the to-be depressed group compared to the non-depressed group and a state effect, i.e. deterioration during the MDE, but not a scar effect, i.e. return to premorbid levels.

7.6 Discussion of methodological issues

Data used in this thesis are all derived from population-based samples which typically include mostly untreated and less severely affected individuals than clinical samples. This thesis, in line with other research, has demonstrated that mental disorders are associated with serious and long-lasting functional limitations that affect individuals and the society as a whole. The findings should be interpreted in light of the following methodological issues.

7.6.1 General population samples

The two samples used in this thesis were population-based, whereas other studies often used specific groups such as primary care attendees, patients with diagnosed depression, etc. The main advantage of using a population-based sample is that the findings can be generalized to other individuals in the population. There are some minor drawbacks of a general population sample as well. First, some disorders are rare in the general population and can therefore not be properly studied. These disorders may, however, alter the association of common mental disorders with functional limitations. Second, in a large sample even trivial differences between two groups may become statistically significant. Third, certain groups such as prisoners, long-term admitted individuals, homeless individuals, persons who are unable to speak the language in which they were being assessed are excluded from the study sample. The prevalence of mental disorders is probably higher in the excluded groups and thus, functional
limitations associated with mental disorders reported in this thesis might actually be an underestimation.

Overall, the generalizability of general population samples is a benefit far outweighing the drawbacks and, thus, the use of data from large general population samples in this thesis can be considered a major strength.

### 7.6.2 Cross-sectional and longitudinal design

Most of the chapters in this thesis draw on cross-sectional data. Since functioning and disorder are measured at the same point in time it is not possible to distinguish whether functional limitations preceded or followed the disorder. Time invariant individual differences can be excluded in a longitudinal design (Costa and McCrae, 1982), and it is possible to observe the temporal order of events. Longitudinal data can aid the interpretation of cross-sectional findings. However, risk factors are still difficult to determine in longitudinal studies, because manipulation of variables is not carried out.

An additional challenge in longitudinal design is selective attrition. To illustrate, if males selectively drop out of a longitudinal study, researchers might conclude that individuals turn more feminine with increasing age. This is a silly example, because gender is a fixed trade, but it does illustrate the difficulties in interpreting results when the nature of factors is not well understood. In addition, selective attrition is a potential threat for generalizability of the results. If attrition is selective, researchers could be drawing conclusion about individuals high in study compliance rather than individuals representative of the general population. In NEMESIS attrition was associated with younger age, low educational attainment, urban environment, not cohabiting with a steady partner, and born outside the Netherlands. Overall, attrition was only slightly higher among respondents with one or more mental disorders (OR: 1.20, 95% CI: 1.04-1.38) (de Graaf et al., 2000). Although attrition was not completely random in NEMESIS, effects of the mentioned variables was low to modest at best.

In conclusion, longitudinal design is superior to cross-sectional design in addressing many research questions. However, we cannot simply ignore what can potentially be learned from time and cost efficient cross-sectional studies, particularly since such cross-sectional studies may be the basis of conceptualizing and designing the necessary longitudinal studies. Likewise, results from longitudinal studies may lead the way to designing appropriate random control trials.

### 7.6.3 Self-report

In both NEMESIS and ESEMeD, all data, including mental symptoms, physical disorders, and functional limitations, are collected using self-report
questionnaires. Three issues of concern about the accuracy of self-report questionnaires will be described. First, respondents may not understand the question being asked. Belson (1981) found that more than 70% of respondents interpreted some questions differently from the researcher, leading Belson to conclude that subtle misinterpretations are pervasive in survey situations (Belson, 1981). Second, respondents may not be able to answer correctly. As time passes, our ability to distinguish those parts of our memory that were directly derived from an experience from those added through second-hand reports or imagination, diminishes. Third, respondents may not be motivated to answer correctly or are unwilling to report stigmatizing or embarrassing symptoms, disorders, or events. Special concern is warranted when a mental disorder is present. Some types of mental disorders lead to distorted and pessimistic perceptions (e.g. (Coyne and Gotlib, 1983)) which may partly explain the excess functional limitations reported by individuals with mental disorders. However, an interview situation is fundamentally different from usual personal encounters and individuals may tell an interviewer things they may be reluctant to share with friends or legal authorities. Some of these issues have been addressed in the new version of the CIDI, which incorporates simpler questions and a more straightforward order in which the questions were asked (Kessler and Ustun, 2004).

Despite the abovementioned limitations, collecting objective data is often too difficult and costly, and self-report is the only alternative. In addition, the major advantage of self-report over more objective measures is that self-reported symptoms, disorders, and functional limitations are associated with personal suffering and mental health care use and thus relevant to individuals, professionals, researchers and policy makers.

7.6.4 Measurement of physical disorders

In both studies used in this thesis a checklist of 19 (ESEMeD) and 31 (NEMESIS) physical disorders was included. The respondents were asked whether a disorder was present in the previous 12 months. If the answer was affirmative, respondents were asked whether they received medical treatment for the disorder and received medication. In this thesis only treated and/or medicated disorders were used, because we assume that these disorders are more likely to meet full diagnostic criteria than a simple ‘yes’-response to the question if a disorder is present. A disadvantage of addressing physical disorders in this manner is that it greatly depends on respondents’ understanding of the nature of the disorder and willingness to report stigmatizing disorders. For example, highly neurotic individuals may overreport physical disorders while individuals with a sexually transmitted disease may be reluctant to disclose such
information. A better assessment of physical disorders would be to use disorder specific procedures, for example blood examination to establish diabetes. This information is often present in medical files which are generally considered a better way to assess the presence of physical disorders than measures that rely on self-report. However, not all disorders are reported in medical files. Skinner et al. (2005) found that symptom-based conditions such as low-back pain or osteoarthritis are underestimated using data from medical records and patients appear to be a useful source of information (Skinner et al., 2005). Additionally, disorders like a common cold, flu, or occasional back pain may be treated by over the counter medication. These disorders are unlikely to appear in medical files too. Additionally, silent disorders are missed in both self-report questionnaires and medical files, but may still influence functional limitations.

An argument in favour of assessing presence of physical disorders using self-report checklists is that these physical disorders are strong predictors of future outpatient service use, hospitalization, and mortality (Fan et al., 2002). Thus, assessing physical disorders by means of such a checklist that was used in NEMESIS and ESEMeD may not be perfect, it does provide an useful impression about the prevalence of physical disorders in the general population and the functional limitations associated with these disorders.

### 7.6.5 Assessment of functional limitations

In this thesis, the SF-36 (NEMESIS) and the ESEMeD WHODAS (ESEMeD) were used to assess functional limitations in the past month. In addition to the problem related to self-report, two additional issues need to be addressed: (1) the timeframe of the questionnaires and (2) the skewness of the data derived from these questionnaires. First, functional limitations were assessed in the past month while presence of mental and physical disorders was assessed in the past 12 months. The association between disorders and functional limitations may be underestimated if the individuals did not meet the diagnostic criteria anymore when the timeframe of the ESEMeD WHODAS was reached. This problem is more obvious for mental disorders than for physical disorders, because mental disorders often have a cyclic nature, while physical disorders run a more chronic course. For example, most episodes of major depression last approximately 3 months (Spijker et al., 2002) in the general population and limitations tend to wax and wane with the onset and remission of depression (Buist-Bouwman et al., 2004; Judd et al., 2000; Ormel et al., 2004). In the ESEMeD sample, approximately 65% of the individuals did not meet the diagnostic criteria for MDE anymore when the timeframe of the ESEMeD WHODAS was reached. Thus, an underestimation of the functional limitations associated with mental disorders is likely. On the other hand, when using a relatively short timeframe, individuals are more accurate about reporting functional limitations.
The second issue related to the assessment of functional limitations is the skewness of the data derived from these questionnaires. Although low prevalence of functional limitations is a natural consequence of using a general population sample, it is potentially problematic because most statistical procedures assume a normal distribution. Solutions to this problem are not readily available. One way is to log-transform the data, but this has only minor effects on our data, because so many people report perfect functioning. Another solution that we have tried is transform the data into categories, or even dichotomize variables. Data can be statistically analysed in this manner at the cost of loss of information. A final solution that we tried is using a statistical technique that does not assume normal distribution such as the Mann-Whitney test.

7.7 Suggestions for future research

The findings presented in this thesis show that functioning is an important concept, but also that many questions remain unanswered. A major strength of this thesis is the use of general population samples which enables the examination of functioning without assuming a direct link to mental or physical disorders. The longitudinal design of NEMESIS is also a major strength and further understanding of functioning could well be established using a longitudinal study like NEMESIS.

A disadvantage of general population samples is that functioning is generally good, which could be overcome by oversampling individuals who are more prone to functional limitations, for example children of psychiatric patients or individuals from underprivileged areas. In NEMESIS and ESEMeD factors that potentially affect functioning, i.e. mental and physical symptoms and disorders, personality and environmental characteristics are included, but should be expanded in the future. More detailed information about environmental characteristics such as social structures, social support, health care system, climate among other things and personality, such as extraversion, agreeableness, coping, neuroticism, openness to experience, etc. should be included as well in future studies. In addition, functioning should be established in a standard environment, which enables us to assess capacity of an individual in addition to performance, i.e. functioning in the usual environment.

More insight in the factors that increase susceptibility to functional limitations could lead to accurate allocation of treatment resources and, consequently, a reduction of societal costs and personal suffering associated with mental disorders.
7.8 Implications for clinical practice

Although functioning is often associated with mental disorders, individual differences in functioning are large. While many individuals with relatively severe mental disorders go through life functioning quite well, others are unable to function with seemingly mild disorders. In clinical practice, functioning should be used as (a) a diagnostic criteria and (b) a determinant of treatment success. DSM-IV incorporates the criterion that symptoms should cause clinically significant distress or impairment in social, occupational, or other important areas of functioning before a mental disorder can be diagnosed. Additionally, if treatment leads to minimal reduction in number and severity of symptoms, but positively influences the way an individuals and his/her environment handles the symptoms, it may still be considered a success.

7.9 Conclusion

Taken the cautionary remarks into account, data presented in this thesis support four conclusions:

1) The limitations associated with mental disorders are different, but often equally or more severe, than those associated with physical disorders;

2) The functional limitations associated with substance use disorders are generally less severe than those associated with anxiety and mood disorders;

3) Depression and functional limitations show a synchrony of change;

4) The association between depression and participation restrictions seems mediated by cognition and embarrassment;

Taken together, the findings underline the importance of functional limitations associated with mental disorders. A better understanding of the mechanisms that positively and negatively influence functioning is essential in alleviating the economic burden and personal suffering associated with mental disorders.