Summary and Discussion
The aim of this PhD thesis was to investigate the association between depression on the one hand, and role functioning and disability on the other hand. During adolescence, we focused on the existence, strength and direction of the association between depressive problems and functioning at school and in the social domain. During adulthood, we focused on explaining heterogeneity in disability of patients with MDD.

This final chapter summarises the findings and implications of our research, and places the results in the context of the two theoretical frameworks that were used throughout this thesis. To recapitulate, the ICF model provides a framework that describes why depression may impair functioning and cause disability.\(^1\) This model asserts that disability is influenced both by health conditions (i.e., illness characteristics and comorbid disorders) and contextual characteristics (i.e., personal and environmental characteristics). The competency-based model of depression describes why impairment in role functioning may increase the risk of depressive problems in adolescents. This model asserts that adolescents’ poor functioning leads to negative feedback from others, which triggers a negative self-perception of the adolescent that subsequently can increase risk of depression.\(^2\)

**Depressive problems and role functioning in adolescents**

Psychopathology during adolescence is associated with several adverse outcomes such as poor functioning at school and social problems.\(^3\)\(^6\) Among the most important types of psychopathology are depressive problems. Other dimensions of psychopathology in adolescents include anxiety problems, attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), and conduct disorder problems (CD). Although previous studies reported on the association between psychopathology and functioning during adolescence, a number of important issues needed further exploration. Consequently, we conducted two studies based on the TRAILS data to investigate two of these issues: (1) the informant-specific association between problems in five dimensions of psychopathology and three domains of school functioning, while considering differences in gender and developmental time-frame, and (2) the bidirectional and longitudinal effects of depressive problems and role functioning during adolescence.

Four measures of adolescents’ functioning were used: (1) academic performance, (2) social well-being, (3) social preference, and (4) social problems. Academic performance was based on items on work pace, effort, and achievement. Social well-being of the adolescent at school represented a self-reported measure that contains items on how the adolescent perceives how he/she is regarded by classmates (e.g., “my classmates like having me around”).\(^6\) Social preference was derived from the peer nominations that were collected in a subsample of TRAILS. All children in the classroom could nominate their classmates as liked or disliked.\(^7\) Social preference was constructed by subtracting the standardized number of dislike nominations from the standardized number of like nominations. The Social Problem
scale contains items on problems with regard to social relations with others (peers, adults) and motor difficulties that are associated with poor social functioning (e.g., being clumsy, speech problems).

Our first TRAILS study was described in Chapter 2. We showed that depressive problems were significantly associated with poor academic performance, and reduced social well-being and social preference, over and above other symptoms of psychopathology. These unique associations between depressive problems and functioning were tested by adjusting for symptoms of anxiety, ADHD, ODD, and CD. Moreover, there were significant gender interactions and differences between primary and secondary school: academic performance was particularly affected by depressive problems in girls and at primary school.

Taking into account the association between depressive problems and functioning, in Chapter 3 we extended this finding by investigating whether depressive problems lead to poor functioning, poor functioning leads to depressive problems, or whether the relation is bidirectional. In addition, we investigated whether this relation differed between boys and girls. Our analyses yielded four important findings. First, there was sizable stability in depressive and functional problems over time and there were clear within-wave correlations between depressive problems and functioning. Second, the relationship between depressive problems and social problems was bidirectional: depressive problems predicted later social problems and social problems predicted later depressive problems. Third, poor social well-being preceded depressive problems but not the other way around. Finally, depressive problems and academic performance were bidirectionally related to each other, but only in girls. In boys, there was no prospective association between depressive problems and academic performance.

Taking both studies together, we found that depressive problems particularly affect social functioning (i.e., social well-being, social preference, and social problems). The path that we found from depressive problems to more social problems and poor social well-being is in line with the ICF model. In addition, more social problems in adolescents with depressive problems may be due to the decline in social activity of these adolescents. Adolescents with depressive problems are on average less involved in organised activities compared to healthy adolescents, which may negatively influence their social skills and their social status. The engagement in more excessive and negative feedback seeking of adolescents with depressive problems may explain why depressive problems are associated with poor social perceived well-being in both boys and girls. The finding of a prospective association between social problems and increased depressive problems is in line with the competency-based model of depression. Another explanation for the path from social problems to depressive problems may lie in the motor difficulties that are taken into account in the social problems measure. Motor difficulties, such as clumsiness, were previously shown to increase proneness to victimisation in adolescence. In addition, children with poor motoric skills are likely to receive less positive and social feedback and recognition from peers as
compared to children with normal motoric abilities.\textsuperscript{10} Both proneness to victimisation and negative social feedback can trigger depressive problems. In contrast to the competency-based model of depression, we did not find support for the hypothesis stating that social well-being affects depressive problems. However, previous studies also reported mixed results regarding this relation.\textsuperscript{11,12}

The association between depressive problems and academic performance was less robust than the association with functioning in the social domain and not consistent across gender. In boys, poor academic performance seemed to be affected more by externalising than internalising problems. Thus, different types of psychopathology (internalising versus externalising problem behaviour) are associated with poor academic performance in boys and girls. The finding that depressive problems are associated with poor academic performance in girls is in line with both the ICF model and the competency-based model of depression. However, the path from depressive problems to academic performance is not entirely in accordance with previous studies.\textsuperscript{13,14} Nonetheless, higher levels of school absence, more days with impairments, less active participation, and distraction by depressive thoughts in depressed versus non-depressed adolescents are plausible explanations for this relationship.\textsuperscript{4,8,14,15}

Explaining heterogeneity in disability associated with major depressive disorders in adults

In previous studies among adults, severity of depressive symptoms and disability showed synchrony of change during the course of the illness. However, the association between MDD and disability did not hold for every patient: some functioned quite well despite their depression, whereas others functioned poorly.\textsuperscript{16-18} This a-synchrony of change suggests that, above and beyond the strong effect of MDD symptom severity, there may be certain contextual factors (i.e., personal and environmental characteristics) that hamper or enhance the effect of a decrease in MDD symptom severity on disability. Explaining heterogeneity in disability among persons with a current episode of MDD is an important step forward in disentangling the complex relationship between the two.

Departing from the ICF model, we conducted three studies to investigate which factors may be responsible for the heterogeneity in disability among these patients, using data from NESDA. In Chapter 4, we studied to what extent measures of MDD symptom severity, other illness characteristics of MDD, and comorbid mental disorders could account for the heterogeneity in disability of MDD patients. Extending this study, in Chapter 5 we investigated whether the residual variance in disability that could not be explained by illness characteristics and comorbidity, could be explained by contextual factors. In Chapter 6, we attempted to explain heterogeneity in disability associated with MDD by assessing potential moderators of the synchrony of change between decreasing MDD symptom severity and disability.
To assess disability in adults, three measures were used: (1) WHODAS disability, (2) days out of role, and (3) absence from paid work. WHODAS disability refers to the World Health Organization Disability Assessment Schedule and is a broad and subjective measure of disability that measures to what extent someone had difficulties with functioning in several domains. WHODAS domains include communication, getting around, self-care, getting along, household activities, work activities, and community participation. In contrast, days out of role and absence from paid work are objective and specific measures that determine the actual number of days or weeks the participant was out of function or experienced functional decline in certain activities. As the measures differ in specificity and subjectivity, their possible association with illness, personal and environmental characteristics may vary.

Analysing illness characteristics (Chapter 4) revealed that the MDD symptom severity is the most important characteristic in explaining disability with a current MDD. This finding is in line with other studies. An onset of MDD at an older age was associated with more work absence, as well as with limitations in getting around and self-care. This may be due to adaptation in coping with depression of persons that have an onset of MDD early in their lives. Of the assessed comorbid mental disorders, agoraphobia was significantly associated with more WHODAS disability, when controlling for MDD symptom severity and other characteristics. A diagnosis of alcohol dependence predicted more days out of role. In conclusion, disability associated with current episodes of MDD is for a limited part accounted for by characteristics of MDD and comorbid mental disorders. This implies that a considerable part of the variation in disability remains unexplained by these factors, supporting the ICF model that proposes that in addition to illness characteristics also contextual factors (personal and environmental factors) play an important role in the disablement process.

In an attempt to explain this residual variance in disability, in our next study we targeted selected contextual factors. These contextual factors encompassed personal characteristics including the big five personality traits, physical activity, and environmental characteristics including work stress and social support (Chapter 5). High scores on conscientiousness were associated with less WHODAS disability, days out of role, and work absence independent of illness characteristics. People with high conscientiousness are known for their high levels of self-regulation, persistence, impulse control, achievement orientation, and self-discipline. These characteristics may account for the finding that patients with high conscientiousness remain functioning despite their depression. The personality trait openness was also associated with reduced days out of role. Individuals scoring high on neuroticism had less work absence compared to patients with low scores on these variables, irrespective of the characteristics of MDD. This finding is in contrast to previous research, but may be explained by a potential positive impact that neuroticism has on functioning. This positive impact could be that high neuroticism scores may reflect awareness of and fear for possible negative consequences of absenteeism from work or failing to carry out daily activities (e.g., being fired, loss of sympathy and support) among persons scoring high on neuroticism.
Consequently, these persons may tend to continue functioning despite their feeling of disability. Furthermore, we found that high regular physical activity is associated with reduced days out of role and work absence. This confirms findings from other studies that showed that vigorous activity helps preventing work absence and contributes to better work ability in the general working population.\textsuperscript{27,28} Last, although the total contribution of environmental characteristics was small, high work stress appeared to be an important explanation of disability in days out of role and work absence, even after adjusting for illness and personal characteristics. This is in line with previous research that revealed that exposure to work stressors is associated with an increase in absenteeism from work among persons with depressive symptoms.\textsuperscript{29,30} To follow up on these findings, in Chapter 6 we attempted to explore which factors account for the fact that while in most depressed patients disability recovers in proportion with the degree of improvement in MDD symptom severity, this does not occur in all patients. Disability was assessed using the total WHODAS disability score and the WHODAS subdomains. We identified four groups of potential moderators, based on the findings of the studies that were described in Chapter 4 and 5: (1) demographic factors; (2) clinical factors; (3) personality; and (4) contextual factors. MDD symptom severity and WHODAS disability were measured at three time-points: at baseline and after 1 and 2 years. Change in depression severity and disability over time was calculated. Only patients with a diagnosis of MDD at baseline who decreased in MDD symptom severity over time were included in the study.

We found strong synchrony of change between decreasing severity of depressive symptoms and disability in general and the domains of disability. However, this synchrony of change was weaker for depressed patients of older age and for unemployed depressed patients. The effects of age were particularly apparent in the domains of getting around and household activity. It is plausible that functioning becomes more difficult with increasing age because of physical impairments that usually accompany getting older. Therefore, recovery of functioning in the domains that are associated with physical impairment (i.e., getting around and household activities) become relatively insensitive to depression severity changes. Work stress played a major role in the domains of getting around, household activities, and participation. It appeared that having a job, and in particular a job that is experienced as causing at least moderate work stress, is beneficial for improving functioning among patients whose severity of depressive symptoms decreases. This seems counterintuitive, but there are several plausible explanations. For example, high demanding jobs may encourage motivation, having the obligation to go to work may be a driving force for getting out of bed and partaking in normal daily activities, contact with colleagues may be valuable because of social support or pressure, and a demanding work life may distract from depressed feelings that may hinder functioning. With these findings, we identified two groups (older patients, unemployed patients, or patients with low work stress) that are vulnerable to postmorbid disability. Nevertheless, it should be noted that the current findings also show that severity of depressive symptoms is such a strong predictor of recovery in disability that the impact of other factors is small or limited in a domain of functioning.
In sum, illness characteristics, psychiatric comorbidity, as well as personal characteristics should be taken into account in explaining heterogeneity in disability of patients with MDD. These findings are in line with the ICF model. Illness characteristics are in general the most important predictors of disability in the MDD population, whereas personal characteristics are good predictors of objective functioning such as days out of role and work absence. Environmental characteristics, except for work stress, do not seem to be associated with disability in MDD patients.

How do the findings from adolescence and adulthood relate?

Our studies showed that depression and role functioning are strongly associated in our sample of adolescents as well as in our sample of adults and that the ICF model is applicable to both groups. Nonetheless, it seems that there are also differences between adolescents and adults in the domains of functioning that are affected. However, it should be noted that we can only speculate about the relation between our TRAILS and NESDA findings, as TRAILS is a population sample and NESDA is mostly a clinical sample. In adolescents, particularly social domains of functioning were affected by depressive problems, while academic performance was affected to a lesser extent and only in girls. Contrastingly, in adults, functioning in the work domain was strongest affected by MDD. This difference between adolescents and adults seems plausible. Adolescents devote most of their time to social relationships whereas in adulthood work becomes more important and more time-consuming. Although adolescents spent a considerable amount of time at school, classrooms are inherently social places where adolescents pursue both social and academic goals, and especially in early adolescence social goals may be more on the foreground. In addition, social relationships are very important for adolescents from a developmental point of view. For example, social interaction influences adolescents’ self-perception, school adjustment, and academic performance. During adulthood, however, a large part of life is generally spent at the workplace. Although there is social interaction at most workplaces, this may be of somewhat lesser importance. Second, although social interactions during adulthood are important, the impact of social contacts on life will be smaller than during adolescence as the developmental effect that is present in adolescence is not applicable anymore during adulthood.

As longitudinal data from adolescence into adulthood were not available, we could not investigate whether depressive problems at young ages affect role functioning into adulthood. However, if we extrapolate our findings, it is tempting to speculate that negative effects of psychopathology on adolescents’ functioning at school do not only have crucial short-term, but also long-term consequences. More specifically, direct consequences of poor academic performance such as low grades and school drop-out may lead to poor social and economic outcomes, for example to lower earnings and wages, and unemployment.
In addition, poor academic achievement may place adolescents at risk for depression or other internalising problems during adulthood. Social problems during adolescence are associated with externalising problems at later age. Due to poor social preference or peer rejection, adolescents may receive less social correction and guidelines for normal social behaviour than adolescents with regular social interaction, which could lead to problem behaviour in the future.

Methodological issues of the conducted studies

Differences between informants of psychopathology problems in TRAILS

Apart from the main findings on the association between depression and role functioning in adolescents and adults, also other findings beg further attention. In the TRAILS study of Chapter 2, we found large differences between reports on psychopathology from different informants. The explained variance was highest when both psychopathology and functioning were reported by the same informant, likely due to a shared-method effect. The low explained variance in functioning by child-reported psychopathology calls for a discussion on how reliable and valid these self-reported psychopathology data are in preadolescence. It also shows that information provided by multiple informants can provide different conclusions than reports from just one informant. The great difference between informants emphasises that, in future studies, researchers should consider carefully who informs on which measure of functioning and psychopathology.

To address these issues regarding the use of data from multiple informants, we decided to combine child- and parent-reported depressive problem data in Chapter 3. We did so because we think no informant is inherently superior to another in identifying whether depressive problems are present or not. By combining the reports, we took into account the unique views from the two important informants. We believe that if at least one informant reports depressive problems, it is useful to take this report into account as it may reflect part of the adolescent’s functioning. In addition, the reliability of the reports by child and parent may differ depending on the child’s age. Young adolescents may be less able to rate their own behaviour and compare themselves to others than older adolescents are. Consequently, child reported depressive problem scores may be less accurate at younger ages than at older ages. In contrast, parents may be better able to report their children’s depressive problems when they are younger. When adolescents get older they are more likely to be independent of their parents and develop their own lives.

Subjectivity and specificity of the disability measures

We learned from our NESDA studies that it strongly depends on the subjectivity and specificity of the disability measure how much variation in disability is accounted for by
illness, personal, and environmental characteristics. Possible explanations may be the operational overlap between the measures of WHODAS disability and depression severity, whereas the days out of role and work absence measures are more distant from MDD. Consequently, the severity of depression was most strongly linked to WHODAS disability and least strongly associated to the days out of role and work absence. These findings emphasise the importance of using a disability measure that meets the type of disability of interest.

**Clinical implications of the findings**

The findings in this thesis hold considerable value for clinical practice and interventions to reduce the burden of depression on role functioning. Most importantly, findings suggest that prevention interventions, in adolescents and adults, should not only address depression or functioning in general, but should also focus on particular domains of functional problems. More specifically in adolescence, interventions targeting depressive problems may particularly improve functioning in the social domain but not academic performance. Furthermore, the variation in the association between psychopathology and functioning between gender and primary and secondary school points out that interventions should be tailored to target adolescent boys and girls, and primary and secondary school students differently. For example, interventions for girls should target the impact of depressive problems on academic performance as well as social functioning, while interventions targeting academic problems as a consequence of depressive problems will be less effective in boys. Also, the results emphasise that depressive problems and functional problems during adolescence should be tackled as soon as they appear, to avoid negative short- and long-term consequences. Interventions that decrease depression severity in adults will have more success in decreasing WHODAS disability than on the number of days a person will be out of role or on work absence.

Our findings in adults are particularly valuable for the identification of risk factors that speed up or complicate recovery from disability in patients who are recovering from depression, and are, from a clinical point of view, important for several reasons. Identification of risk factors may point to specific groups (e.g., older patients, unemployed patients) at risk for more severe disability than the other patients, or patients at risk of slower or incomplete recovery of functioning after a (major) depressive episode. Consequently, these patients should be monitored more closely to decrease the impact of depression on their functioning. In addition, efforts can be made to reduce or remove the burden of the identified risk factors, reducing the risk of disability during or after the depressive episode. Tackling harmful characteristics that are associated with disability may also help prevent recurrence of depression, given that persistence of disability predicts recurrence. However, also buffering factors such as physical activity were identified that can be used to decrease the impact of depression on role functioning. The strong synchrony of change between severity
of depressive symptoms and disability suggests that adequate treatment of depression is indispensable; not only to decrease severity of the depressive symptoms, but also to restore functioning with benefits for patients, their environment and the economy.

**Directions for future research**

Although we extended previous research by showing that there is a strong link between depressive problems and functioning during adolescence, and by identifying factors that explain heterogeneity in disability in adults with MDD, there are still gaps in the knowledge that should be addressed in future studies.

As we emphasised throughout this thesis, identification of factors that explain heterogeneity in disability associated with depression is important. Nonetheless, such factors have not been studied in adolescent samples so far. Hence, testing mediational processes is suggested in order to provide extra care to adolescents at greater risk, or to reduce the burden of such risk factors. The family environment may be one of the most important factors that determine functioning in depressed adolescents, as it has been repeatedly shown that parental support is beneficial for adolescents’ psychosocial adjustment, academic performance, and mental health status, while the reverse, no support from parents, is true as well.  

In addition, familial adversities can trigger problems indirectly by influencing other risk factors of depression or poor functioning, such as maternal emotional problems in single-parent families. Another important factor that may mediate the path from depression to functioning may be coping with stressful situations. As proposed by the competency-based model of depression, the relationship between poor functioning and depressive problems may be mediated by negative self-perception. A recommendation for future research would thus be to assess the effect of, among other things, family environment and coping with stressful life events on the relationship between depressive problems and poor functioning in adolescents.

To our knowledge, no studies of the longitudinal bidirectional relationships between depression and functioning in adults have been conducted. We showed that MDD is associated with disability, but disability is also associated with MDD (Chapter 6). It would valuable to see whether depressive problems precede functional problems or whether it is the other way around, as we investigated in adolescents (see Chapter 3). This would provide information as to whether depression or functional problems should be tackled in the first place.

We were fortunate to have the large longitudinal datasets of TRAILS and NESDA, but a limitation of these studies is that they followed the participants through either adolescence or adulthood. It would be very valuable to study depressive problems and functional problems during both periods of life, i.e. from (early) childhood into adulthood (i.e. at least 30 years).
With such a dataset it would be possible to more thoroughly investigate the relationship between depression and functioning, and answer questions such as whether depressive or functional problems come first and what the long-term effects of both depressive and functional problems are.

**Conclusion**

The main findings of this thesis point out that there is a strong relationship between depression and role functioning disability in both adolescents and adults. In adolescents, depressive problems precede subsequent poor functioning, mainly in the social domain, but poor functioning precedes subsequent depressive problems as well. In adults with MDD, severity of depressive symptoms is the best correlate for disability, while it also shows synchrony of change with disability. Several illness characteristics, comorbid mental disorders, and personal and environmental characteristics influence the extent to which severity of depressive symptoms leads to disability. Findings from our research describe why disability appears in some depressed persons and not in others; and it identifies some triggering as well as buffering factors for disability in this group.
References


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