Depression and role functioning
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Explaining heterogeneity in disability with current major depressive disorder: Effects of personal and environmental characteristics

Abstract

**Background:** Major depressive disorder (MDD) is associated with disability, yet some patients function surprisingly well. The reason for this heterogeneity between patients is unclear. Building on the International Classification of Functioning (ICF) model, this study aims to examine effects of personal and environmental characteristics on disability with MDD, over and above illness characteristics.

**Methods:** Data were obtained from 573 patients with a current diagnosis of MDD. Three measures for disability were used, varying in objectivity and specificity: ‘WHODAS disability’, ‘days out of role’, and ‘work absence’. Univariate and stepwise multivariate regression analyses were conducted.

**Results:** WHODAS disability was best explained by the study variables. Illness characteristics were clearly the strongest correlates of WHODAS disability, whereas personal and environmental characteristics were less influential. Personal and, more restrictedly, environmental characteristics were almost equally important to illness characteristics in explaining days out of role and work absence. High conscientiousness, high neuroticism, low level of physical activity, and high work stress were the strongest predictors of disability among MDD patients.

**Limitations:** Due to the cross-sectional design of the present study we could not draw conclusions about causal relationships between our predictor variables and disability.

**Conclusions:** Personal characteristics appeared to be almost equally important to illness characteristics in explaining heterogeneity in disability when measured objectively and specifically (i.e., days out of role and work absence). However, personal characteristics turned out to be considerably less important to disability measured in a broad and subjective way (i.e., WHODAS disability). Environmental characteristics appeared to have little impact.
Introduction

It is well established that major depressive disorder (MDD) is associated with disability.1-7 Disability is often defined as 'any restriction or lack of capacity to perform an activity in a manner or within a range considered normal for a human being'.8 This loss of productivity is a burden for patients themselves, to their environment and a costly burden for the economy. Remarkably enough the association between MDD and disability does not hold for every MDD patient: some patients function quite well despite their depression, whereas others function very poorly.5,9,10 The reason for this heterogeneity between patients is unclear.

A number of previous studies attempted to identify characteristics that influence the association between MDD and disability. From these studies it was concluded that illness characteristics, including comorbid mental disorders, are good predictors of disability.5,11-14 In a previous paper we tried to explain heterogeneity in MDD-associated disability by assessing the effect of several illness characteristics on this disability and concluded that MDD symptom severity, age of onset of depression, comorbid agoraphobia, and alcohol dependence were significant predictors of disability.15 A considerable amount of variance (ranging from 13-42%, depending on the measure of disability) was accounted for by illness characteristics but the large amount of residual variance indicates that there must be other characteristics that affect the association.

A basis for understanding the heterogeneity in disability among patients with MDD is provided by the International Classification of Functioning, Disability and Health (ICF).16 The ICF framework assumes that personal characteristics and environmental characteristics are important to understand individual differences in disability, over and above illness characteristics.17 The present study examines the association between personal and environmental characteristics and disability among patients with MDD, over and above illness characteristics. For this purpose, we extended the ICF model by including illness characteristics as well as personal and environmental characteristics in the present study (Figure 1). Personal characteristics are defined as the particular conditions of an individual’s life and living, and are not classified in the ICF because of large social and cultural variance associated with these characteristics.18 However, the ICF offers some examples of personal characteristics which include gender, age, coping styles, social background, education, profession, overall behaviour pattern, personality, and other characteristics that influence how disability is experienced by the individual.16 Environmental characteristics make up the physical and social environment in which people live and conduct their lives. Until now, no research has examined the association between personal and environmental characteristics and disability among patients with MDD. Therefore we also included several plausible personal and environmental characteristics on an explorative basis.

To assess disability, three measures were used: (1) WHODAS disability, (2) days out of role, and (3) absence from paid work. These measures differ in specificity and subjectivity, and
consequently in their possible association with personal and environmental characteristics. WHODAS disability refers to the World Health Organization Disability Assessment Schedule.\textsuperscript{19} The WHODAS has been developed to assess activity limitations and participation restrictions experienced by an individual, irrespective of a medical diagnosis. WHODAS disability is a broad measure of disability as it assesses many aspects of functioning. Furthermore it is subjective; it does not refer to the actual time a participant was out of function, but it refers to the extent to which someone had difficulties with functioning and is scored on a four point scale, from no difficulties to many difficulties. In contrast, days out of role and absence from paid work are

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Extended version of The International Classification of Functioning model. The model acknowledges contextual characteristics, over and above illness characteristics, to be important for understanding the heterogeneity in disability of patients with MDD.}
\end{figure}
objective and specific measures because they determine the actual number of days or weeks the participant was out of function or experienced functional decline in certain activities. In sum, this study aims to identify to what extent personal and environmental characteristics, over and above illness characteristics, can explain heterogeneity in disability among patients with MDD.

Methods

Participants

Participants were derived from the Netherlands Study of Depression and Anxiety (NESDA). NESDA is a multi-centre longitudinal cohort study including 2981 individuals (18-65 years) with current or remitted depressive and/or anxiety disorder, patients at risk due to family history or subthreshold symptoms, and healthy controls. Participants were recruited at three locations in the Netherlands, in three different settings: the general population, primary care, and mental health care. The aim of NESDA is to investigate the long-term course and consequences of depression and anxiety disorders. The rationale, objectives, and methods of NESDA have been described previously.20

In the present study, data were used from the baseline measurements, conducted between September 2004 and February 2007. We only included participants with a diagnosis of current (i.e., one month) MDD, as assessed with the Composite International Diagnostic Interview (CIDI), version 2.1.21

Measures for disability

The first measure for disability we used is ‘WHODAS disability’, which was retrieved from the total score of the WHODAS. It assesses disability, as experienced by the participant, in six domains: communication, getting around, self-care, getting along with people, life activities, and participation in society. Domain scores were aggregated to a total score (range 0-100) with a good inter-item reliability (α=.95); higher scores indicated greater difficulties in functioning (α=.77 to α=.93).

WHODAS disability has some overlap with symptoms of MDD. This is for example shown by the WHODAS item “Concentrating on doing something for ten minutes”. Concentration problems can be a symptom of MDD, but it can also be an indicator of disability. To limit the influence of overlap in our results we added two other measures for disability that are more distant from MDD. Moreover, adding other disability measures gave us the opportunity to distinguish between the effect of personal and environmental characteristics on different types of functioning.
‘Days out of role’ measures the amount of days in the past month that a participant was totally unable to work or carry out normal activities; was able to work/do other activities but had to cut down on this or did not do as much as usual, and/or had to cut back on the quality or carefulness of the work. The total score was constructed by adding the scores on these items, with the latter two questions weighing half. Eventually the scores were recoded into a scale (α=.75) that ranged from 0-100. For working participants, in the present study defined as having a paid job of eight or more hours a week (N=265), we composed the disability measure ‘work absence’.

For this variable the number of days absent from work during the last six months was divided by the number of workdays the participant was supposed to work in the last six months. This resulted in a measure for the number of workweeks a participant was absent from work during the last six months.

**Predictor variables**

*Personal characteristics.*

Age in years and gender were taken into account when assessing the effects of personal characteristics on disability. The number of years of education was calculated based on the highest level of education a participant completed. Personality was measured using the NEO Five-Factor Inventory (NEO-FFI): a short version of the Revised NEO Personality Inventory (NEO PI-R), consisting of 60 items. With this questionnaire the most important domains of personality of adults were measured: neuroticism (N), extraversion (E), openness (O), agreeableness (A) and conscientiousness (C). Chronic diseases were measured by counting the number of chronic somatic diseases a participant was diagnosed with, such as heart disease, osteoarthritis, diabetes, and cancer. Physical activity was measured using the International Physical Activity Questionnaire and expressed in three categories (low, moderate, and high physical activity) based on the resting metabolic rate multiplied by minutes of physical activity per week as reported by the participant. At last, first degree family history of depression was derived from the family tree inventory.

*Environmental characteristics*

Childhood trauma was assessed retrospectively using the childhood trauma interview. A cumulative index (childhood trauma index) was calculated as the sum of experienced number and frequency of childhood trauma for each participant. Information on emotional neglect, psychological and physical abuse, and sexual abuse in the participant’s first sixteen years of life was derived. To measure the influence of adverse life events on disability with MDD, we measured the number of adverse life events a participant had experienced in the past year. We measured twelve different events from the List of Threatening Experiences by Brugha.

In addition, we constructed variables indicating the level of social support. We assessed
social network size by asking with how many relatives, friends, and others the participant has regular and important contact. Through the Close Person Inventory/Questionnaire (CPI), social support was measured by asking the amount of social support the participant received from the partner (if present), and up to two friends (over 18 years old, no housemates) with whom the participant has important contact on a regular basis. A total of four questions about emotional support, such as “how often do you trust him/her with your most private problems” were answered with the possibility to give a maximum of 5 points per item, ranging from no support up to high support (α= .77). Two separate variables, a partner support and a friend support variable, were constructed based on z-scores: no partner/friend, low support (< -1 SD), moderate support (-1 through 1 SD), and high support (> 1 SD).

Household income was assessed with 24 categories, from an income of less than € 500,- a month up to an income of over € 5000,- a month. The participant was allocated the mean of his income category to create a continuous variable.

By means of the Job Content Questionnaire we assessed whether the participant experienced stress at work. For each negative answer (i.e., leading to stress at work) the participant was scored 1 point and for positive answers no points were given. By summing up the scores and dividing them by the number of items we calculated a total score (26 items; α=.81) which was subsequently divided into four groups, based on z-scores: no work stress (i.e., people without a job), low work stress (< -1 SD), moderate work stress (-1 through 1 SD), and high work stress (> 1 SD). In the analyses with work absence as a measure of disability we excluded the “no work stress” group because people without a job were excluded in these analyses anyway.

**Illness characteristics**

Additionally, we included the illness characteristics that were found to be significantly associated with disability in a previous paper on the same study population. These consisted of MDD symptom severity (measured with the 28-item Inventory of Depressive Symptoms), age of onset of depression, and a diagnosis of comorbid agoraphobia and alcohol dependence. The latter three were measured with the CIDI.

**Statistical analyses**

To study the strength of the association between our predictors and disability, we conducted univariate regression analyses. To assess the effect of the predictors on disability simultaneously, and the change in effect after adding new variables to the model, we conducted stepwise multivariate regression analyses and estimated five models. In the first model we included all personal characteristics, in the second model we assessed the effect of all environmental characteristics and in the third model we looked at the effect of all illness characteristics. Furthermore, we estimated a fourth model with all personal and
environmental characteristics together. In the fifth and most extensive model we added the personal, environmental, and illness characteristics simultaneously. In model one, two, and three we assessed the effect of the different groups of characteristics separately whereas in model four and five we assessed the effect of different groups of characteristics together, while adjusting for confounding effects by the characteristics from the other group(s).

Statistical significance of individual predictor variables in the different models was used to conclude about their effect on disability. In addition, the measure of explained variance ($R^2$) was used to assess the strength of the effects of personal, environmental, and illness characteristics on disability.32

Multicollinearity could be a problem with multivariate analyses; it may influence the reliability of the results. We checked our analyses for multicollinearity by using the variance inflation factor (VIF). To minimise the effects of missing values we used different strategies. Missing values (varying per variable, max. 9%) on all the predictors were replaced by the sample mean of that particular predictor. To compensate missing values in the WHODAS domains we replaced missing values with the participant’s mean of that domain (N=72). When participants had more than one answer per domain missing, WHODAS disability was not calculated. For the three-item days out of role and one-item work absence outcome we did not impute missing values because of the small number of items. To ensure that the same source population was used in all analyses, participants with missing values on one or more measures for disability were case wise deleted from our sample (N=34). By doing so we assessed the effect of all variables under study, in all models, on the same participants.

Results

Our final sample consisted of 573 participants with a mean age of 41 years. 66.2% of our participants were females. Population characteristics and ranges of all variables are shown in Table 1.

WHODAS disability was best explained by all predictor variables together ($R^2=.48$). The VIF values of all models were below 2.5, indicating no sign of multicollinearity. The univariate and multivariate associations of personal, environmental, and illness characteristics with three types of disability are reported in Tables 2, 3, and 4. Illness characteristics ($R^2=.42$) were clearly the strongest predictors for WHODAS disability (Table 2) in both the univariate and multivariate models. Personal and environmental characteristics ($R^2=.26$, without illness characteristics in the model) were considerably less influential. Moreover, personal and environmental characteristics explained only an extra 5.7% of the variance after the inclusion of illness characteristics in the model. Although small, this difference was significant (p-value $R^2$ change < .001 for the model with illness characteristics versus the model with illness, personal, and environmental characteristics). Environmental characteristics
appeared to be least important with regard to WHODAS disability. Conscientiousness and household income were significantly associated with disability in both the univariate and the multivariate model. Patients with high conscientiousness and high household income had less WHODAS disability than patients with a lower score on conscientiousness or household income, independent of illness characteristics. A higher score on WHODAS disability was found for patients scoring high on neuroticism, suffering from chronic diseases, and high work stress. A lower score on WHODAS disability was associated with high extraversion and high physical activity. However, the latter effects did not remain significant after adding illness characteristics to the model.

For the variance in disability measured with days out of role (Table 3) the personal and environmental characteristics together ($R^2=.12$) were almost equally important as illness characteristics ($R^2=.14$). Nevertheless, our results clearly show that personal characteristics are considerably more important than environmental characteristics in explaining heterogeneity in days out of role. Personal characteristics accounted for eight percent of variance between participants whereas environmental characteristics explain half of this amount (4%). Further, the environmental characteristics did not add significantly to the explained variance (p-value $R^2$ change >.05). We were able to explain up to 24% of variance in days out of role with personal and environmental characteristics and illness characteristics assessed simultaneously. The personality traits neuroticism, openness, and conscientiousness, and a high level of physical activity were associated with reduced days out of role. In contrast, more years of education and high work stress were associated with more days out of role. These results were found in both the univariate model and the multivariate models, except for neuroticism which did not remain associated after adding illness characteristics to the model.

The explained variance of work absence (Table 4) showed the same pattern as the explained variance of days out of role. Personal and environmental characteristics accounted for 17% of variance in work absence between patients whereas illness characteristics explained 13% of variance. Again, the effect of environmental characteristics was considerably smaller than that of the other characteristics ($R^2=.07$ versus $R^2=.12$ for personal characteristics and $R^2=.13$ for illness characteristics; adding the environmental characteristics to personal characteristics the $R^2$ change was non-significant (p>.05)). Simultaneously assessing all study variables we could explain up to 24% of variance in work absence. Patients scoring high on neuroticism and conscientiousness, and patients with high regular physical activity had less work absence compared to patients with low scores on these variables, irrespective of the characteristics of MDD. In contrast, high work stress was associated with more work absence. Again, neuroticism appeared to be significantly associated with work absence only after adding illness characteristics to the model. In contrast, the decreasing effect of extraversion on work absence did not hold after adding illness characteristics to the model.
For the environmental characteristics childhood trauma, adverse life events, and social support as well as for age and gender, we found no significant association with any type of disability (see Table 2, 3, and 4).

Table 1. Characteristics of the study population

<table>
<thead>
<tr>
<th>Disability measures</th>
<th>Mean (SD)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>WHODAS disability (0-100)</td>
<td>45.1 (15.8)</td>
<td></td>
</tr>
<tr>
<td>Days out of role (0-100)</td>
<td>41.5 (28.6)</td>
<td></td>
</tr>
<tr>
<td>Work absence (0-26)</td>
<td>9.0 (10.5)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Personal characteristics</th>
<th>Mean (SD)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
<td>41.9 (12.0)</td>
<td></td>
</tr>
<tr>
<td>Gender (female)</td>
<td>381 (66.5)</td>
<td></td>
</tr>
<tr>
<td>Years of education (0-18)</td>
<td>11.3 (3.2)</td>
<td></td>
</tr>
<tr>
<td>- neuroticism</td>
<td>44.0 (6.3)</td>
<td></td>
</tr>
<tr>
<td>- extraversion</td>
<td>31.7 (6.7)</td>
<td></td>
</tr>
<tr>
<td>- openness</td>
<td>37.4 (6.1)</td>
<td></td>
</tr>
<tr>
<td>- agreeableness</td>
<td>42.0 (5.7)</td>
<td></td>
</tr>
<tr>
<td>- conscientiousness</td>
<td>38.3 (6.6)</td>
<td></td>
</tr>
<tr>
<td># chronic diseases</td>
<td>1.1 (1.2)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Physical activity:</th>
<th>Mean (SD)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>- low</td>
<td>159 (27.7)</td>
<td></td>
</tr>
<tr>
<td>- moderate</td>
<td>261 (45.5)</td>
<td></td>
</tr>
<tr>
<td>- high</td>
<td>153 (26.7)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Family history of MDD</th>
<th>N (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>501 (87.4)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Environmental characteristics</th>
<th>Mean (SD)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Childhood trauma index (0-4)</td>
<td>1.4 (1.3)</td>
<td></td>
</tr>
<tr>
<td>No of adverse life events</td>
<td>0.8 (1.1)</td>
<td></td>
</tr>
<tr>
<td>Social network size (# persons)</td>
<td>2.3 (0.9)</td>
<td></td>
</tr>
<tr>
<td>Support by partner:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- no partner</td>
<td>N (%)</td>
<td>219 (38.2)</td>
</tr>
<tr>
<td>- low support</td>
<td>N (%)</td>
<td>51 (8.9)</td>
</tr>
<tr>
<td>- moderate support</td>
<td>N (%)</td>
<td>253 (44.2)</td>
</tr>
<tr>
<td>- high support</td>
<td>N (%)</td>
<td>50 (8.7)</td>
</tr>
<tr>
<td>Support by friend(s):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- no friend(s)</td>
<td>N (%)</td>
<td>157 (27.4)</td>
</tr>
<tr>
<td>- low support</td>
<td>N (%)</td>
<td>63 (11.0)</td>
</tr>
<tr>
<td>- moderate support</td>
<td>N (%)</td>
<td>291 (50.8)</td>
</tr>
<tr>
<td>- high support</td>
<td>N (%)</td>
<td>62 (10.8)</td>
</tr>
<tr>
<td>Household income (Euros)</td>
<td>Mean (SD)</td>
<td>1934.34 (1039.94)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stress at work</th>
<th>Mean (SD)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>- no job</td>
<td>N (%)</td>
<td>265 (46.2)</td>
</tr>
<tr>
<td>- low stress</td>
<td>N (%)</td>
<td>53 (9.2)</td>
</tr>
<tr>
<td>- moderate stress</td>
<td>N (%)</td>
<td>200 (34.9)</td>
</tr>
<tr>
<td>- high stress</td>
<td>N (%)</td>
<td>55 (9.6)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Illness characteristics</th>
<th>Mean (SD)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>MDD symptom severity (0-69)</td>
<td>38.4 (10.6)</td>
<td></td>
</tr>
<tr>
<td>Age of onset of depression (in years)</td>
<td>27.0 (12.4)</td>
<td></td>
</tr>
<tr>
<td>Agoraphobia (yes)</td>
<td>N (%)</td>
<td>45 (7.9)</td>
</tr>
<tr>
<td>Alcohol dependence (yes)</td>
<td>N (%)</td>
<td>124 (21.6)</td>
</tr>
<tr>
<td>Total</td>
<td>N (%)</td>
<td>573 (100)</td>
</tr>
</tbody>
</table>

a 36 items only applicable if participant is employed (≥ 8h/wk), otherwise 32 items
b only applicable if participant is employed (≥ 8h/wk)
### Table 2. Stepwise regression analysis WHODAS disability in a MDD sample.

<table>
<thead>
<tr>
<th>WHODAS disability</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>M 1&lt;sup&gt;t&lt;/sup&gt;</td>
</tr>
<tr>
<td>β</td>
<td>β</td>
<td>β</td>
</tr>
</tbody>
</table>

**Personal characteristics**
- **Age**: -0.006, -0.003, .003, -0.002
- **Gender**: 0.017, 0.012, -0.013, 0.025
- **Years of education**: -0.108<sup>*</sup>, -0.040, 0.002, 0.017
- **Personality**: 
  - **neuroticism**: 0.398***, 0.305***, 0.280***, 0.043
  - **extraversion**: -0.320***, -0.150**, -0.138**, -0.023
  - **openness**: -0.090*, -0.033, -0.062, -0.037
  - **agreeableness**: -0.061, 0.031, 0.034, 0.055
  - **conscientiousness**: -0.246***, -0.100*, -0.108*, -0.161***
- **Chronic diseases**: 0.109**, 0.138**, 0.145***, 0.050
- **Physical activity**: 
  - **low**
  - **moderate**: -0.102*, -0.073, -0.057, -0.009
  - **high**: -0.166**, -0.093*, -0.092*, -0.049
- **Family history**: 0.001, 0.033, 0.025, 0.018

**Environmental characteristics**
- **Childhood trauma**: 0.169***, 0.137**, 0.089*, 0.046
- **Adverse life events**: 0.079, 0.064, 0.025, 0.004
- **Social network size**: -0.136**, -0.093*, -0.092*, -0.049
- **Partner support**: 
  - **no partner**
  - **low support**: -0.036, -0.009, -0.033, -0.068
  - **moderate support**: -0.053, 0.022, 0.006, 0.004
  - **high support**: -0.041, 0.001, 0.022, 0.044
- **Friend support**: 
  - **no friends**
  - **low support**: 0.022, -0.019, -0.030, -0.002
  - **moderate support**: -0.077, -0.081, -0.047, 0.020
  - **high support**: -0.016, -0.030, -0.019, 0.022
- **Household income**: -0.140**, -0.118*, -0.125**, -0.091*
- **Stress at work**: 
  - **no job**
  - **low stress**: -0.092*, -0.064, -0.013, 0.035
  - **moderate stress**: -0.101*, -0.044, 0.052, 0.067
  - **high stress**: 0.065, 0.094*, 0.099*, 0.061

**Illness characteristics**
- **MDD symptom severity**: 0.639***, 0.624***, 0.568***
- **Age of onset of MDD**: -0.014, -0.017, -0.017, 0.016
- **Agoraphobia**: 0.173***, 0.116***, 0.117***
- **Alcohol dependence**: 0.113**, 0.066*, 0.057

<table>
<thead>
<tr>
<th>R²</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>.225</td>
<td>573</td>
</tr>
<tr>
<td>.080</td>
<td>573</td>
</tr>
<tr>
<td>.426</td>
<td>573</td>
</tr>
<tr>
<td>.256</td>
<td>573</td>
</tr>
<tr>
<td>.483</td>
<td>573</td>
</tr>
</tbody>
</table>

<sup>t</sup> Model 1: Personal characteristics; <sup>u</sup> Model 2: Environmental characteristics; <sup>v</sup> Model 3: Illness characteristics; <sup>w</sup> Model 4: Personal & Environmental characteristics; <sup>x</sup> Model 5: Personal, Environmental & Illness characteristics.

*36 items only applicable if participant is employed (≥ 8h/wk), otherwise 32 items.

* p <.05, ** p <.01, *** p <.001
Table 3. Stepwise regression analysis of Days out of role in a MDD sample.

<table>
<thead>
<tr>
<th>Days out of role</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M 1</td>
<td>M 2</td>
</tr>
<tr>
<td><strong>β</strong></td>
<td><strong>β</strong></td>
<td><strong>β</strong></td>
</tr>
<tr>
<td>Personal characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>.034</td>
<td>-.026</td>
</tr>
<tr>
<td>Gender</td>
<td>-.032</td>
<td>-.023</td>
</tr>
<tr>
<td>Years of education</td>
<td>.013</td>
<td>.084</td>
</tr>
<tr>
<td>Personality:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>neuroticism</td>
<td>.068</td>
<td>.001</td>
</tr>
<tr>
<td>extraversion</td>
<td>-.146***</td>
<td>-.098*</td>
</tr>
<tr>
<td>openness</td>
<td>-.111**</td>
<td>-.113*</td>
</tr>
<tr>
<td>agreeableness</td>
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<td>.041</td>
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<tr>
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* Model 1: Personal characteristics;  ** Model 2: Environmental characteristics;  *** Model 3: Illness characteristics;  **** Model 4: Personal & Environmental characteristics;  ***** Model 5: Personal, Environmental & Illness characteristics.

*p <.05, **p <.01, ***p <.001
Table 4. Stepwise regression analysis of work absence* in a MDD sample.

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<tr>
<td>β</td>
<td>β</td>
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**Personal characteristics**
- Age: .134 | .092 | .093 | .054
- Gender: -.082 | -.023 | -.034 | -.012
- Years of education: -.095 | -.054 | -.011 | .000

**Personality:**
- neuroticism: .048 | -.019 | -.078 | -.179*
- extraversion: -.203*** | -.164* | -.152* | -.113
- openness: -.094 | -.036 | -.065 | -.056
- agreeableness: -.004 | .046 | .044 | .035
- conscientiousness: -.094 | -.063 | -.091 | -.124*
- Chronic diseases: .136* | .090 | .091 | .058

**Physical activity**
- low: Ref
- moderate: -.034 | -.029 | -.013 | .009
- high: -.220** | -.180* | -.150* | -.137*

**Family history**
- low: -.141* | -.085 | -.079 | -.042

**Environmental characteristics**
- Childhood trauma: .015 | .018 | .046 | .040
- Adverse life events: .070 | .101 | .067 | .053
- Social network size: -.047 | -.022 | .001 | .005

**Partner support**
- no partner: Ref
- low support: .051 | .078 | .039 | .003
- moderate support: .091 | .122 | .080 | .054
- high support: -.007 | .025 | .000 | -.001

**Friend support**
- no friends: Ref
- low support: -.099 | -.129* | -.115 | -.091
- moderate support: -.029 | -.032 | .004 | .065
- high support: -.098 | -.110 | -.071 | -.028

**Household income**
- low: -.067 | -.120 | -.121 | -.083

**Stress at work**
- low stress: Ref
- moderate stress: .056 | .089 | .134 | .101
- high stress: .168* | .197** | .216** | .155*

**Illness characteristics**
- MDD symptom severity: .309*** | .300*** | .282***
- Age of onset of MDD: .170** | .163** | .080
- Agoraphobia: .086 | .062 | .067
- Alcohol dependence: -.009* | -.003* | .006

<table>
<thead>
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<th>R²</th>
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</table>

*Model 1: Personal characteristics; "Model 2: Environmental characteristics; "Model 3: Illness characteristics; "Model 4: Personal & Environmental characteristics; "Model 5: Personal, Environmental & Illness characteristics.

* p < .05, ** p < .01, *** p < .001

* only applicable if participant is employed (≥ 8h/wk)
Discussion

In the present study we tried to disentangle the heterogeneity in disability among patients with MDD. By doing so we investigated the effect of several personal and environmental characteristics, over and above illness characteristics. We used three types of disability to differentiate the effect of the variables under study on various aspects of disability, as documented earlier. Our study suggests that personal characteristics are important when explaining heterogeneity in disability among MDD patients, over and above illness characteristics. Although environmental characteristics are associated with disability, these effects are considerably smaller in magnitude. Still, illness characteristics, in particular MDD symptom severity, appeared to be the best predictors for all three types of disability. Personal characteristics were found to be almost equally important as illness characteristics when disability was objectively and specifically measured (i.e., days out of role and work absence) but appeared considerably less important for disability when measured in a broader and more subjective way (i.e., via WHODAS disability).

Among the personal characteristics, personality seemed to be involved in the way someone is able to maintain functioning despite of MDD. In particular, a higher level of conscientiousness showed a consistent association with lower disability, even after controlling for 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. In addition, high neuroticism was associated with fewer days out of role and work absence but this effect emerged only after adjustment for illness characteristics. This finding is in contrast to previous research. Cuijpers et al. recently described that in the general population neuroticism is associated with high nonmedical costs caused by the high amount of work absence in persons scoring high on neuroticism. In a recent study among patients with MDD, Rhebergen and colleagues showed that neuroticism proved to be a significant predictor of both lower social functioning, as well as lower physical functioning among which role functioning. A possible explanation for the effect we found in the present study may be that, with regard to functioning, neuroticism has a positive and negative aspect. The negative effect indicates vulnerability for common mental illness among high neurotic patients. Because this negative effect is controlled for by MDD severity and comorbidity, other effects on behaviour become visible. The positive aspect could be that high neuroticism scores may reflect awareness of 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. Due to these features these patients may tend to continue functioning despite their feeling of disability. For WHODAS disability there was no association with neuroticism after adjustment for illness characteristics, probably because disability as defined by the WHODAS is not sensitive to possible effects of neuroticism. Last, we found that high regular physical activity
is associated with reduced days out of role and work absence. This confirms the 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{38,39}

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{40,41} However, the association with WHODAS disability was not significant after adjustment for illness characteristics, probably because WHODAS disability is less related to work than the other two disability measures. A separate analysis for the effect of work stress on the domains of WHODAS among participants with a job revealed that only the ‘participation in society’ domain was significantly affected by high work stress (β=.24, p=.002) but this effect did not remain significant (though borderline) after adding illness characteristics to the model (β=.13, p=.052). This suggests that among people with paid jobs high work stress leads to reduced participation compared to people with low work stress, but illness characteristics account largely for this effect. Thus, the reduced participation among working MDD patients with high work stress may actually be caused by the characteristics of their MDD (e.g. severity of depression).

Remarkably, we found differences in the magnitude of the association of personal and environmental characteristics with disability between the disability measures. Overall, the more objective and specific measures days out of role and work absence showed a similar pattern, whereas WHODAS disability showed somewhat distinct (less significant) associations. In general, days out of role and work absence could be mostly explained by both personal characteristics and illness characteristics, whereas WHODAS disability was undoubtedly best explained by illness characteristics. Possible explanations may be the operational overlap between the measures of WHODAS disability and depression severity and the fact that days out of role and work absence are more distant from MDD. This is illustrated by the finding that after adjustment for illness characteristics, most of the significant effects of personal and environmental characteristics did not hold in explaining WHODAS disability. These findings emphasise the importance of using a suitable disability measure that meets the type of disability of interest. If we had only chosen the general WHODAS disability, we would have falsely concluded that personal and environmental characteristics are not important in explaining heterogeneity in disability with MDD.

We did not find an association between social support and disability, in contrast to what we had expected and to what has been found in previous research.\textsuperscript{42,43} Janowski and colleagues\textsuperscript{37} found that social support plays a protective role and buffers negative effects from MDD on disability. Furthermore, in elderly it appeared that social support and social networks are associated with functional decline.\textsuperscript{44,45} It might be that the effect of social support differs
depending on, for example, gender and age. The lack of significant effects of environmental characteristics supports our conclusion that the environment is less important in explaining heterogeneity in disability with MDD than illness and personal characteristics. Future studies might do well to investigate possible modifiers of the effect of social support on disability among patients with MDD.

The present study has several advantages over previous studies. To our knowledge we are the first to study personal, environmental, and illness characteristics simultaneously to assess their unique effect on disability among MDD patients. The size of the sample provided the chance to include multiple domains of personal and environmental factors in one comprehensive model. Our findings highlight the importance of taking personal factors into account when explaining disability with MDD and may thus be important for clinical practice in the sense that managing the important predictors can lead to less disability. Efforts can be taken to reduce work stress and improve physical activity. Personality is harder to tackle but addressing, during treatment, the role of personality factors on disability may have some effect. If the therapist is aware of the existence and effect of some personally trait on a patient’s functioning, this may get an important role in the treatment procedure and can in that way benefit prevention or reduction of disability. Thus, it is important that the functioning of patients with these characteristics is monitored more closely and perhaps addressed more explicitly during early treatment than usually.

Another strength is the use of multiple measures of disability that address different types of disability. We used WHODAS disability as a general, subjective measure for perceived disability. A more objective and specific measure of disability was provided by the number of days a participant was out of role and was absent from work. Our results showed that different characteristics accounted for different measures of disability. In future studies it is thus very important to choose the disability measure carefully, when taking the aim of the study and the predictors into account.

This study has limitations too. Due to the cross-sectional nature of our study we cannot make conclusions about causal relationships between the predictors and disability. This is an important limitation because causal relations provide information that can be used for reducing and preventing disability among patients with MDD. Recently, Rytsälä and colleagues studied long-term work disability in a prospective setting and concluded that many sociodemographic and clinical factors clearly predict long-term work disability among patients with MDD. Even after adjusting for clinical variables the effect of older age and lack of vocational education predicted disability pension. This study emphasises that longitudinal research on disability of patients with MDD is important and can help to determine whether the significant predictors in our study are also causal risk factors for disability. Another limitation is that only self-reported measures of disability were used in the present study, whereas reports of family, friends, et cetera would have provided additional information, and reduce shared-method bias. Furthermore it could be a methodological limitation that
we ascribed importance of the different groups of predictors by comparing models using $R^2$. Although comparing $R^2$ across models has some limitations, for example because $R^2$ is influenced by among other things measurement error and can therefore be misleading, it is a commonly used method in all fields of research.\textsuperscript{47,48}

To conclude, personal characteristics should be taken into account in explaining heterogeneity in disability of patients with MDD, over and above illness characteristics. Illness characteristics are in general the most important predictors in explaining heterogeneity in disability in the MDD population, whereas personal characteristics are good predictors of objective functioning as measured by days out of role and work absence. Environmental characteristics, except work stress, do not seem to be associated with MDD-associated disability. High conscientiousness, high neuroticism, regular physical activity, and low to moderate work stress are independently associated with less disability suggesting that they may co-determine whether a depressed patient is able to maintain functioning at a higher level than the average MDD patient.
References


