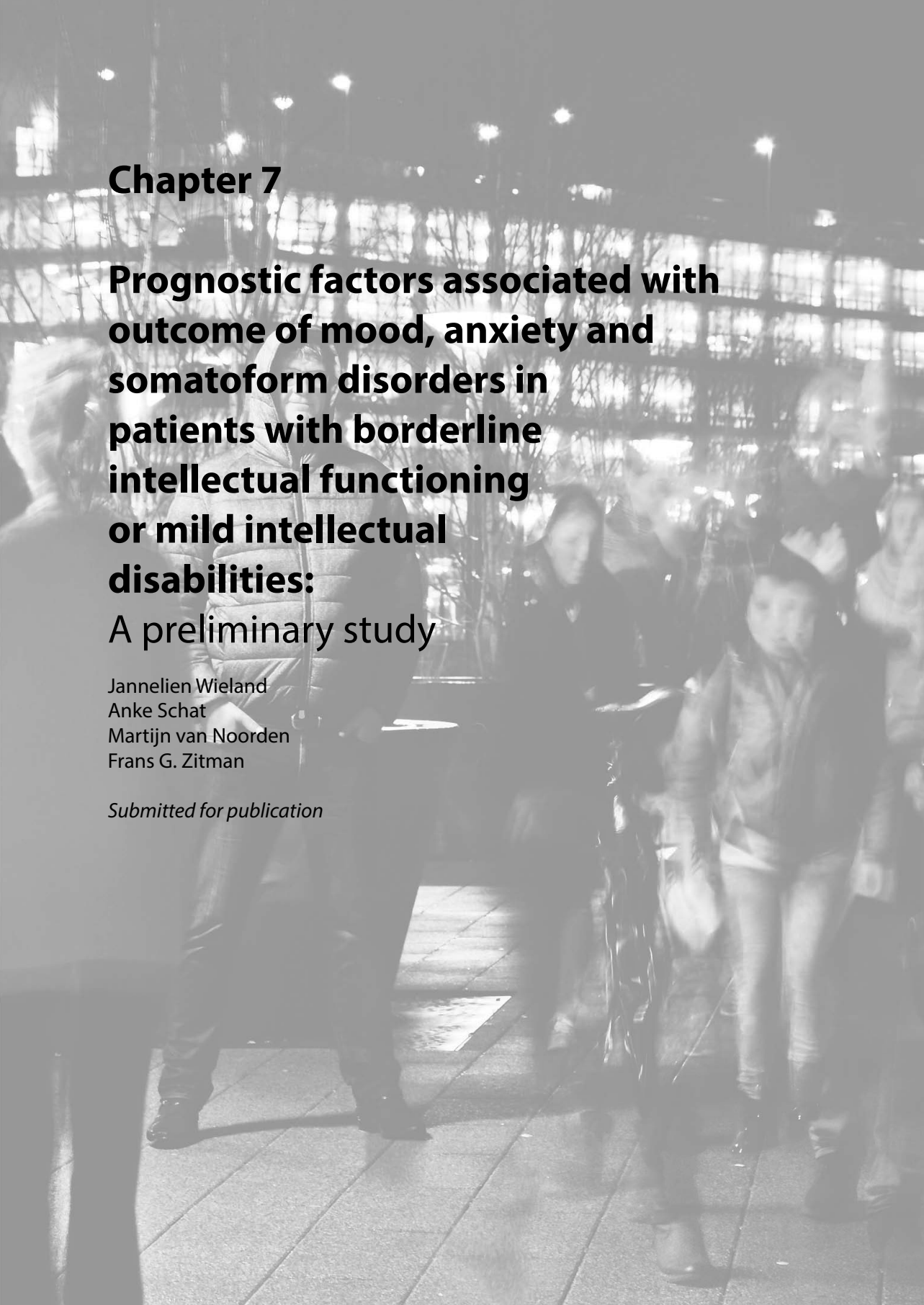

Chapter 7

Prognostic factors associated with outcome of mood, anxiety and somatoform disorders in patients with borderline intellectual functioning or mild intellectual disabilities: A preliminary study

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Abstract

Introduction Mood, anxiety and somatoform (MAS) disorders are considered to be highly prevalent among people with borderline intellectual functioning (BIF) or intellectual disability (ID), but there has not been a wealth of published research. Treatment protocols of MAS disorders in patients with BIF or ID mostly do not differ from general treatment protocols. In nondisabled MAS outpatients, age and cluster B personality traits were found to be associated with an adverse treatment outcome in routine clinical practice. The aim of the present preliminary study was to explore whether gender, age, level of ID and cluster B personality disorders (PD) is associated with treatment outcome.

Methods We used a naturalistic cohort of 93 adult outpatients referred to one of the two centres for psychiatry and intellectual disabilities of Rivierduinen (a large regional mental health care provider in the Netherlands) between 2007 and 2012, with a follow-up of up to 2 years. Outcome was measured using the Brief Symptom Inventory. Cox regression models were used to analyse gender, age, level of ID and cluster B PD as prognostic factors associated with outcome.

Results Although we found no statistically significant differences, results suggest that there may be an associations between treatment result and gender, age and cluster B PD. Hazard Ratios could be interpreted as an indication that females, young adults and people with a cluster B PD, may respond less favourable to treatment. Having either BIF or mild ID did not seem to be associated with treatment response.

Discussion This study is a first exploration into the prognostic factors associated with outcome in outpatients with MAS disorders and either BIF or mild ID. Major limitation of the present study is the limited sample size. Future studies are needed to replicate these findings in larger samples and to identify other possible associated factors influencing outcome in MAS disorders and in other psychiatric disorders in patients with BIF or ID.

Introduction

Mood, anxiety and somatoform (MAS) disorders are considered to be highly prevalent among people with borderline intellectual functioning (BIF)(Total Intelligence Quotient (TIQ) 70-85) or mild intellectual disability (ID) (TIQ 50 -70 and concurrent deficits or impairments in present functioning).[1–4] Both BIF and ID have been identified as risk factors for the development of MAS disorders in both men and women.[3,5–7] According to the normalized intelligence quotient (IQ) distribution, up to 15% of the population has a TIQ of 1 to 3 standard deviations (SD) below average, e.g. a TIQ of 50 -85; BIF or mild ID. People with BIF or mild ID participate in society up to a great extent. For instance, they generally have work, have relationships, and in contrast to people with more severe ID (TIQ< 50) they have minimal care and have to fulfil high expectations. It is important to know how to treat MAS disorders in these patients and which factors are associated with treatment outcome in daily clinical practice.
However, even though MAS disorders are prevalent in patients with BIF and ID, there is no wealth of published research on the subject. There have only been a few clinical trials concerning the treatment of MAS disorders in patients with ID, using mainly self-report questionnaires is advocated but rare and there are no studies on the treatment of MAS disorders in BIF.[8–10] In most countries, people with BIF are not considered a separate group in mental health care. BIF is not a focus of attention and patients are treated according to the same guidelines as patients with average or above average IQs. Likewise in daily clinical practice most treatment protocols in patients with MAS disorders and co-morbid ID do not differ from general treatment protocols.[11]
We know most of these treatments to be evidence based in nondisabled (non-ID) patients, and we know that outcome in non-ID MAS outpatients in naturalistic settings is associated with a number of factors, among others whether someone is married and employed.[12-15] In addition, a lower level of education[16] and having a co-morbid personality disorder[17–21] were associated with an adverse treatment outcome. To the best of our knowledge there are no published naturalistic studies on prognostic factors associated treatment outcomes in patients with either BIF or ID and MAS disorders. For patients with BIF or ID this means, when it comes to treating MAS disorders, there is a large group of patients being treated with uncertainty about the level of evidence of most of these treatments. And it is virtually unknown which factors predict the outcome of these treatments.
In a recent naturalistic cohort study of 892 regular mental health care (RMHC) outpatients with MAS disorders and a large independent replication cohort of 1392 RMHC outpatients from the Leiden Routine Outcome Monitoring (ROM) study, it was found that older age, MAS co-morbidity, a somatoform disorder and high scores on cluster B personality disorder traits (affective lability, intimacy problems and self-harm) were independently associated with poor treatment outcome.[22]

The aim of the present preliminary study was to explore whether some of these factors were also associated with treatment outcome in a naturalistic cohort study of outpatients with MAS disorders and BIF or mild ID. Following the study of van Noorden et al.[22] next to gender and age, we explored the association with treatment outcome of cluster B personality disorder (PD). Furthermore, because both BIF and ID are considered to be a risk factor for the development of MAS disorders, we explored level of ID, BIF versus mild ID, as a prognostic factor of treatment outcome.

Methods

Routine Outcome Monitoring

Routine Outcome Monitoring (ROM) is a method for the systematic collection of relevant treatment data, using reliable and valid assessment instruments.[23] The goal of ROM is to assess treatment effectiveness in naturalistic setting by collecting data about nature and severity of psychiatric symptoms in every day clinical practise. Primarily, ROM is intended to provide direct feedback on diagnoses and treatment results to the psychiatrist and the patient. Furthermore, ROM is used for benchmarking procedures and research purposes. If ROM data is used in research patient-identifiable data are removed from the database in order to secure patients' confidentiality. The use of these anonymised data for research purposes has been approved by the Ethical Review Board of the LUMC.

ROM is used for all outpatients referred for treatment of a MAS disorder to Rivierduinen (RD), a large regional mental health care provider in the Netherlands and the Leiden University Medical Centre. The Leiden ROM consists of an extensive psychometric battery of self-report and observer-rated measures administered at intake and at follow-up, every 3-4 months. In the two outpatient Centres for Psychiatry and Intellectual Disability (CPID) of RD (Kristal, Locations Leiden and Gouda) a much leaner ROM test-battery is administered, at intake and follow up every 4-6 months. ROM consists mostly of self-report questionnaires.

In the CPID, ROM-assessments are completed in an assisted fashion. Kellett et al.[24,25] described this "assisted completion format" using the Symptom Checklist-90 (SCL-90; a widely used self-report instrument evaluating a broad range of psychological problems and symptoms of psychopathology[26] and concluded that the assisted completion format was shown not to influence respondents' ratings of symptoms excessively and did not affect the psychometric properties of the test.[24,25] The assisted administration consists of the following: The assessment is conducted in a one-to-one setting. Both the instruction and the items of assessment instruments are either read together with the respondent or verbatim to the respondent. The answer feedback sheet contains both written and numerical representations. Patients with more severe ID (e.g. moderate to severe ID; TIQ< 50 and concurrent deficits or impairments in present adaptive functioning) are as a rule not included in ROM because there is no research

into reliability and validity of the self-report assessment instruments used in ROM in patients with more severe ID and because practical utility of these instruments these patients is unknown.

Patients

We used a cohort of adolescent and adult outpatients (aged 16 to 61) referred to one of the two CPID between 2007 and 2012. The cohort consisted of patients diagnosed with (a) MAS disorder(s) and either BIF or mild ID, who were included in ROM with at least one BSI. Flowchart of in- en exclusion is shown in figure 1. Diagnoses were the official diagnoses as recorded in the registration system of the electronic patient file, based on the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition*, Text Revision (DSM-IV-TR). DSM-IV-TR diagnoses were formulated using the Diagnostic Manual-Intellectual Disability (DM-ID) criteria[27] and based on the integrative approach of Došen.[28–30] The DM-ID provides guidelines for making accurate psychiatric diagnoses in patients with various levels of IDs and where necessary offers adaptations of DSM-IV-TR diagnostic criteria. The integrative assessment considers the developmental perspective as a fourth dimension, in addition to the three dimensions of the bio-psychosocial model. Patients were assessed multidisciplinary by at least an experienced psychiatrist, an experienced mental health psychologist and an experienced psychiatric community worker.

Level of intellectual functioning was based on IQ testing, using the Wechsler Adult Intelligence Scale (WAIS-III-NL).[31–33] Based on DSM-IV-TR criteria participants were divided into two groups: BIF and mild ID. Psychiatrists and mental health psychologists of the CPID provided treatment according to Dutch evidence-based treatment guidelines; adapted where needed (preferably evidence-based and otherwise practice-based) to the special needs of patients with BIF or ID. Treatment consisted mainly of psychotherapy, pharmacotherapy or a combination of both, often together with treatment supporting management. The goal of this treatment supporting management is to facilitate, among others, psycho-education, therapy adherence, generalization and crisis management.

The predictive value of baseline, treatment-independent patient characteristics were the focus of the present analyses. Therefore management, treatment and therapist characteristics were not taken in to account.

Assessment of outcomes

Primary outcome for the present study was severity of psychopathological symptoms assessed at baseline and follow-up using our main screener for psychopathology and general outcome measure the BSI.[26] The BSI is essentially the brief form of the SCL-90-R.[34,35] It is a self-report (or interview administered) symptom scale consisting of 53 items, covering nine symptom dimensions: *Somatisation* (SOM), *Obsession-Compulsion* (O-C), *Interpersonal Sensitivity* (I-S), *Depression* (DEP), *Anxiety* (ANX), *Hostility* (HOS),

Phobic anxiety (PHOB), *Paranoid ideation* (PAR) and *Psychoticism* (PSY). Rankings characterize the intensity of distress during the past seven days.
Each item is ranked on a 5-point Likert scale ranging from 0 (not at all) to 4 (extremely). Scores can be calculated for the nine symptom dimensions and for 3 global indices of severity of psychopathology: The average score on all 53 items together, the number of items with non-zero responses (or: the number of symptoms experienced by the respondent) and the severity of the existing symptoms (or: the total score divided by the number of symptoms experienced by the respondent).[36] Several studies support the use of the BSI in patients with BIF and mild ID.[25,37,38] The BSI has adequate internal to excellent internal consistency with Cronbach's alphas ranging from the Dutch BIF or mild ID population from 0.70 to 0.96.38 Using normal varimax rotation Kellett et al.37 derived 8 interpretable factors. Confirmatory factor analysis showed that the underlying structure of the BSI could be described by the same 9-factor structure of the original BSI.[38] Response was defined as at least 50% improvement on the BSI.[22,39]

Prognostic factors of 2-year outcome

Because of the limited number of patients in our cohort we could only explore a small number of prognostic factors. Following the results from the naturalistic cohort study of Van Noorden et al.[22] in two large cohorts of non-ID MAS outpatients and knowing that ID is considered a risk factor for the development of MAS disorders, the prognostic factors taken into account were gender, age, level of ID and cluster B PD.
Because the transition from late adolescence into young adulthood is seen as a high-risk developmental period in BIF and mild ID[40,41], age was divided into young adults (age < 24), adults (age 24-40) and older adults (age > 40). Level of ID was divided into borderline intellectual functioning and mild ID.[42] Cluster B PD consist of antisocial PD, borderline PD, histrionic PD and narcissistic PD.[42] In the analyses, presence of cluster B PD was dichotomous variable.

Statistical analysis

Baseline characteristics are presented as number and percentage (categorical variables). or as mean (± SD) together with the interquartile range (IQR) (continuous variables). In- and excluded patients were compared on gender, age, level of ID, prevalence of cluster B PD and baseline total BSI using chi-square for the categorical variables gender and cluster B PD and independent samples t-test of the continuous variables age and baseline total BSI.
Follow-up was censored at 24 months. Because the exact point in time of achieving response is unknown, the moment of response was defined as the midpoint between the assessment at which response was registered and the assessment before that one. Associations between time to response and the predictor variables gender, age, level

of ID and cluster B PD were examined with Cox proportional hazards analysis. Univariate hazard ratios (HR) and 95% confidence intervals (CI) for response (50% improvement relative to baseline scores on the BSI) were computed for baseline categorical and continuous predictor variables Kaplan-Meier survival curves were constructed for all variables. Kaplan-Meier analysis was used to calculate the percentage of cumulative response in the total sample, the median duration of follow-up was assessed using the reverse Kaplan Meier method.[43] All tests were two-tailed with $p < 0.05$ denoting statistical significance. IBM SPSS for Windows 19.0 was used for data analysis (IBM Corp. Armonk, NY).

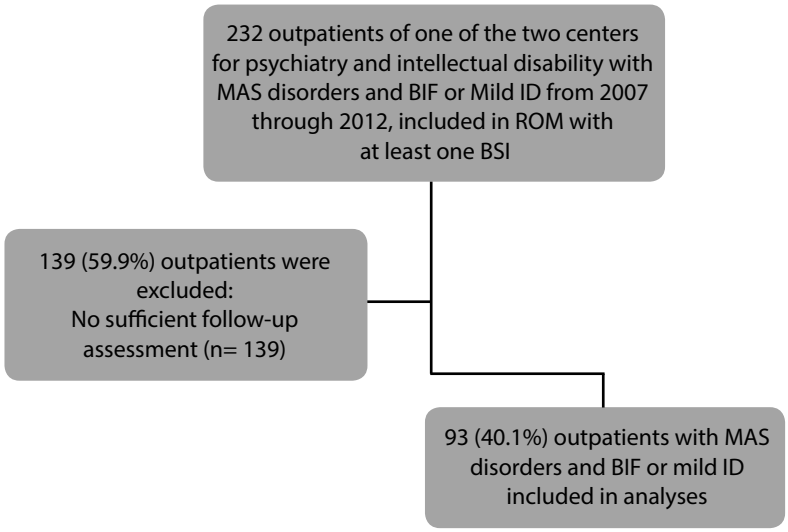


Figure 1. Flowchart of inclusion and exclusion.
MAS= Mood, Anxiety and Somatoform. ROM= Routine Outcome Monitoring. BIF= borderline intellectual functioning. ID= intellectual disabilities. BSI= Brief Symptom Inventory

Results

Sample and demographic characteristics

From 2007-2012, 232 patients diagnosed with one of more MAS disorders and BIF or mild ID, were included in ROM with at least one BSI. A total of 139 patients were excluded because they did not have (sufficient) follow-up assessment. A total of 93 outpatients (40.1%) were included in the analyses. There was no difference between the included and excluded patients in the presence of the different MAS disorders and co-morbidity ($p= 0.46$), the level of ID ($p= 0.16$), age ($p= 0.49$), prevalence of cluster B PD ($p= 0.18$) and total BSI score ($p= 0.50$) at baseline. There was a trend towards

significance for gender (24.7% men in the included group versus 35.5% in the excluded group; χ^2= 3.57, p= 0.06).
Baseline sample characteristics, including predictor variables and DSM-IV-TR diagnoses of the 93 patients included in the study are presented in table 1. The majority of the cohort consisted of females (75,3%). Mean age was 32.9 (SD= 12.1). Most patients had BIF (68.8%). Mild ID was present in 31.2% of the sample. A single anxiety disorder was the most common MAS disorder (54.8%). A single mood disorder was prevalent in 18.3% of the sample. Single somatoform disorders were seen in 7.5% of the sample. MAS comorbidity was present in 19.4% of the sample.

Table 1. Baseline characteristics of 93 outpatients diagnosed with a MAS disorders.

Categorical variables	**n**	**%**
Female gender	70	75.3
Single DSM-IV-TR Mood disorder	17	18.3
Single DSM-IV-TR Anxiety disorder	51	54.8
Single DSM-IV-TR Somatoform disorder	7	7.5
MAS comorbidity	18	19.4
Cluster B PD co-morbidity	12	12.9
Comorbid Alcohol abuse or dependence	6	6.5
Comorbid Drug abuse or dependence	1	1.1
BIF (TIQ 70-85)	64	68.8
Mild ID (TIQ 50-70 and concurrent deficits or impairments in present functioning)	29	31.2
Continuous variables	**Mean (SD)**	**IQR**
Age	32.9 (12.2)	21.5-42
BSI Total score	1.35 (0.69)	0.82-1.85

DSM-IV-TR= Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (Text Revision).
MAS= mood, anxiety and somatoform. PD= personality disorder. BIF= borderline intellectual functioning.
ID= intellectual disability. TIQ= total intelligence quotient. BSI= Brief Symptom Inventory.
SD=standard deviation. IQR= inter quartile range

Univariate prognostic factors of response

The median follow-up was 504 days (IQR = 278-730). At 2 years, 35 patients (37.6 %) had reached an endpoint, 15 patients (16.1%) still continued treatment. Gender, age, level of ID and having a cluster B PD as predictors of response are shown in Table 2.

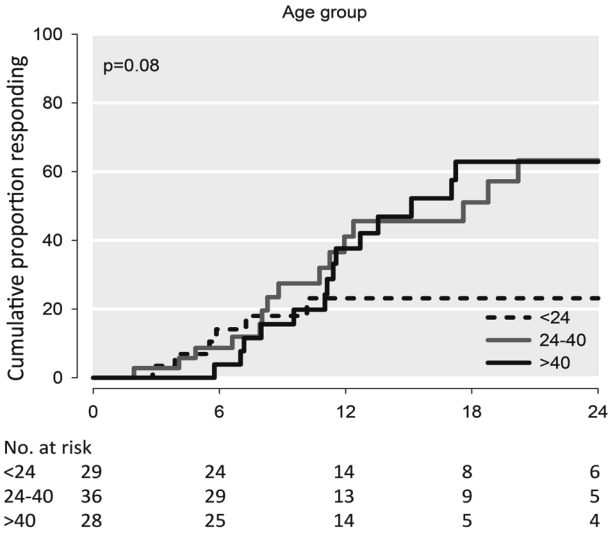
Table 2. Univariable hazard ratios of response according to the baseline predictor variables age, gender and cluster B personality disorders of 93 patients with MAS disorders and borderline intellectual functioning or mild to moderate intellectual disabilities.

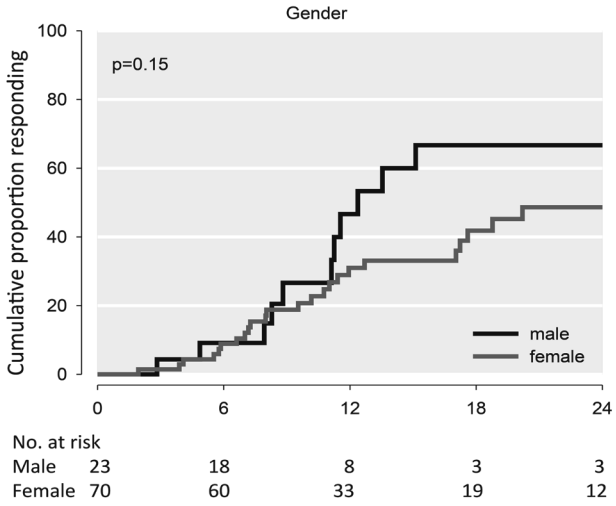
Predictor variables (categorical and continuous)	HR (95% CI)	p-value
Gender		
Female	1.00	
Male	1.69 (0.83-3.46)	0.15
Age		
> 39 years	1.00	
24-39	0.99 (0.5-2.0)	0.98
< 24 years	0.43 (0.16-1.1)	0.08
Level of ID		
BIF	1.00	
Mild ID	0.87 (0.44-1.7)	0.99
Cluster B PD	0.21 (0.03-1.5)	0.12

MAS= mood, anxiety and somatoform. HR= Hazard Ratio. CI= confidence interval. BIF= borderline intellectual functioning. ID= intellectual disability. PD= personality disorder. Response was defined as ≥ 50% reduction on the Brief Symptom Inventory

HR's for response over the 2-year follow-up were 1.69 (95% CI 0.83-3.46) for the male gender, 0.43 (95% CI 0.16-1.1) for young adults, 0.87 (95% CI 0.44-1.7) for mild ID and 0.21 (95% CI 0.03-1.5) for cluster B PDs. Results failed to reach statistical significance, indicating reliability of findings is insufficient to meet the criterion of $p< 0.05$.[44] However, the magnitude of the differences between groups could be interpreted as an indication that a difference in treatment response between the groups for gender, age and cluster B PD might exist. Analyses should be repeated in a larger sample in order to gain more reliable results. Level of ID (BIF versus mild ID) does not appear to be a predictor of treatment outcome. Figure 1 shows the Kaplan-Meier survival curves for the predictors gender, age, level of ID and cluster B PDs of naturalistic treatment response over the 2-year period of follow-up.

Figure 2. Kaplan Meier curves for response according to the baseline predictor variables age, gender and cluster B personality disorders of 93 patients with MAS disorders and borderline intellectual functioning or mild intellectual disabilities.





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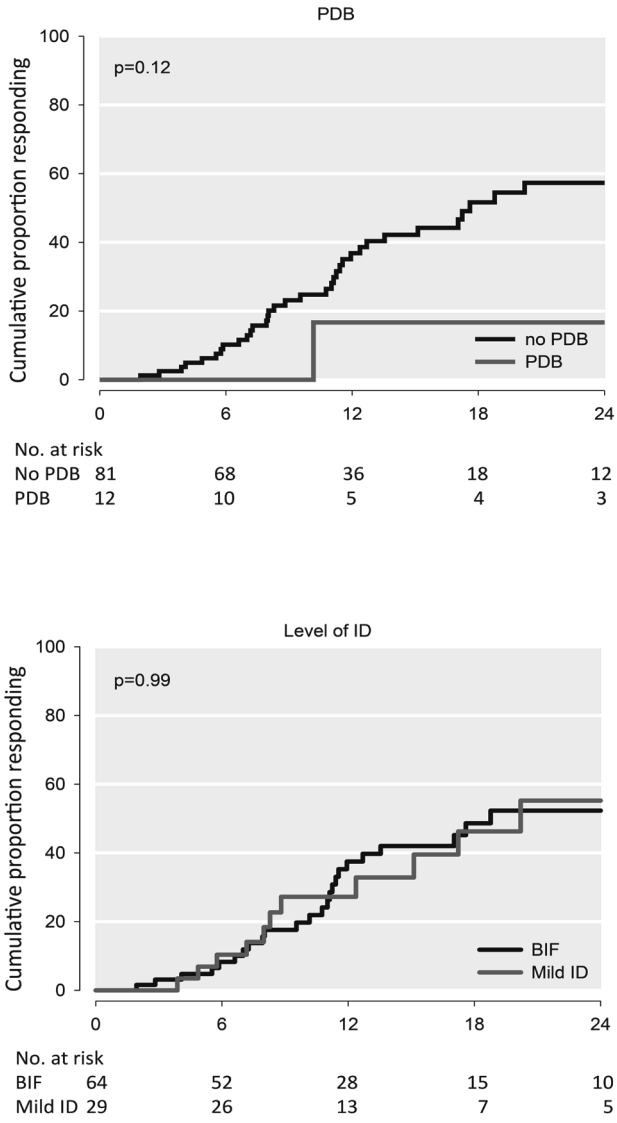

PDB= cluster B personality disorders. BIF= borderline intellectual functioning. ID= intellectual disabilities

Discussion

This study is a first exploration into the prognostic factors associated with outcome in outpatients with MAS disorders and either BIF or (mild) ID. The results suggest that there may be an associations between treatment result and gender, age and cluster B PD. The confidence intervals of our results were wide and included 1, but HRs could be interpreted as an indication that females, young adults and people with a cluster B PD, may respond less favourable to treatment. Level of ID did not play a role.
In the Leiden Routine Outcome Monitoring Study, Van Noorden et al.[22] found no difference in treatment effect between males and females in a naturalistic psychiatric outpatient setting of non-ID MAS disorder patients. Older age and several cluster B PD traits (affective lability, intimacy problems and self-harm) were associated with poor outcome. However, their study did not include patients with BIF or mild ID.
To our knowledge, this study is the first study on prognostic factors associated with treatment outcome in outpatients with MAS disorders and co-morbid BIF or mild ID. Strengths of this study lie in the well-defined patient group with MAS disorders and the carefully applied label of BIF and mild ID using extensive IQ testing. Another strength is the use of ROM and the use of a proven reliable en valid self-report questionnaire, the BSI.

Apart from the relatively small sample size, which limited the numbers of prognostic factors that could be explored, this study had several potential limitations. The design may be subject to selection bias. The CPID of RD treat patients with all levels of intellectual disability, but patients with more severe ID (e.g. moderate to severe ID) are mostly not included in ROM. Also, because ROM had a working-up phase there was a loss in follow-up during the first years after the start of data collection. Referral pathways are well established and there is a focus on patients with BIF as a separate group. Referral of patients with BIF and psychiatric disorders to specialized mental health care is the default procedure. Even so there might be patients with (unknown) higher IQs in the BIF range in regular mental health care. This means that patients included in ROM might differ from patients not included in ROM. Second, as in other naturalistic studies involving ROM[22,39], attrition is high and even though we know that this is at least in part due to absence of follow-up in the ROM implementation phase, we do not know the reasons for loss to follow-up in later stages during the study. Third, treatment consisted of either psychotherapy, pharmacotherapy or a combination of both, following existing guidelines from regular psychiatry and our own adapted care programs, but we did not include information on the specific types of treatment. Fourth, the BSI may not be specific enough to fully capture clinical changes in all MAS disorders. Even though they were not very prevalent, this might especially hold true for somatoform disorders.[44] Finally, due to the design of the study exact point of response could not be inferred and patients who did not reach the response criteria in 2 years were labelled as non-responders. Also possible relapse after initial response was not taken into account.

In summary, this study is a first exploration into the prognostic factors associated with outcome in outpatients with MAS disorders and either BIF or mild ID. Even though CI's were wide and all included 1, HR's seem could be interpreted to indicate that being female, being a young adult and having a cluster B PD is associated with decreased chances of treatment response. Having either BIF or mild ID does not seem to be associated with treatment response. Since in our CPID the same essential treatment protocols are used but adapted to level of cognitive functioning, this might mean that when patients are treated according to their cognitive abilities, it does not matter for treatment outcome whether they have BIF or mild ID.
Future studies are needed to replicate these findings in larger sample sizes and to identify other possible associated factors influencing outcome in MAS disorders and in other psychiatric disorders in patients with BIF or an ID. In the absence of further data, the results suggest that practitioners should be aware that patients with the characteristics mentioned above need extra attention.

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