

Identifying mismatch and match between clinical needs and mental healthcare use trajectories in people with anxiety and depression: results of a longitudinal study

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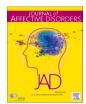
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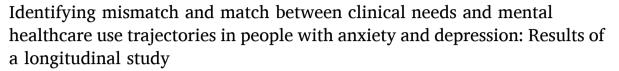
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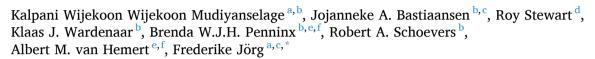
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ABSTRACT

Background: Mismatch between need and mental healthcare (MHC) use (under-and overuse) has mainly been studied with cross-sectional designs, not accurately capturing patterns of persistence or change in clinical burden and MHC-use among persons with depressive and/or anxiety disorders.

Aims: Determining and describing [mis]match of longitudinal trajectories of clinical burden and MHC-use. *Methods*: Six-year longitudinal burden and MHC-use data came from the Netherlands Study of Depression and Anxiety (n=2981). The sample was split into four subgroups: I) no clinical burden but constant MHC use, II) constant clinical burden but no MHC-use, III) changing clinical burden and MHC-use, and IV) healthy non-users. Within subgroups I)-III), specific clinical burden and MHC trajectories were identified (growth mixture modeling). The resulting classes' associations with predisposing, enabling, and need factors were investigated (regression analysis).

Results: Subgroups I-III revealed different trajectories. I) increasing MHC without burden (4.1%). II) slightly increasing (1.9%), strongly increasing (2.4%), and decreasing (9.5%) burden without MHC. III) increasing (41.4%) or decreasing (19.4%) burden and concurrently increasing MHC use (first underuse, then matched care), thus revealing delayed MHC-use. Only having suicidal ideation (p<.001, Cohen's d= .6-1.5) was a significant determinant of being in latter classes compared to underusers (strongly increasing burden without MHC-use). Limitations: More explanatory factors are needed to explain [mis]match.

Conclusion: Mismatch occurred as constant underuse or as delayed MHC-use in a high-income country (Netherlands). Additionally, no meaningful class revealed constantly matched care on average. Presence of suicidal ideation could influence the probability of symptomatic individuals receiving matched MHC or not.

1. Introduction

Despite the availability of evidence-based treatments for different severity levels of anxiety and/or depressive disorders, the type and amount of received mental healthcare (MHC) have been shown to not necessarily match a person's clinical need (Jörg et al., 2016; Jureidini

et al., 2006; Kooistra et al., 2018; Kronenfeld, 2008; Saxena et al., 2007; Verhaak et al., 2009; Demyttenaere, et al., 2004).

A cross-sectional study by the WHO showed that while about 33-50% of people with severe mental disorders, including depression and anxiety, show underuse, only 2.4-8.1% show overuse in high-income countries (HIC) (Demyttenaere, et al., 2004). In previous cross-sectional

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studies, mismatch has been defined in the following ways: on the one hand, mismatch relates to *underuse*, defined as having needs but not receiving the right type and amount of care (Verhaak et al., 2009). On the other hand, mismatch can relate to a seemingly unjustified provision of care given a low need, defined as *overuse* (Keyhani et al., 2008).

Both underuse and overuse may generate negative consequences on a personal, economic, and societal level, making it a public health concern (Armstrong et al., 2018; Mcdaid, 2011; Jörg et al., 2016; Jureidini et al., 2006; Kooistra et al., 2018; Kronenfeld, 2008; Saxena et al., 2007; Verhaak et al., 2009; Demyttenaere, et al., 2004). Underuse can lead to adverse clinical outcomes and may induce high economic burden due to, for example, the consequent loss of productivity (Mcdaid, 2011). Overuse of MHC can have negative consequences such as the deprivation of resources for those in need (Armstrong et al., 2018; Jureidini et al., 2006).

One limitation of the mismatch research that has been published so far is that results are mainly based on cross-sectional study designs (Bet et al., 2013; Verhaak et al., 2009; Demyttenaere, et al., 2004). Evaluations of the presence of mismatched MHC based on cross-sectional studies may provide only partial insight into the issue because such studies do not capture the way in which symptomatology changes over time and how treatments for anxiety and depressive disorders are carried out over longer periods of time (Blier et al., 2007; Penninx et al., 2008).

From the above-mentioned definitions of underuse and overuse that were based on cross-sectional studies, one can also derive patterns of [mis]match that could appear over time in prospective studies: (1) those without needs and no MHC-use (healthy non-users), (2) those without need but constant MHC-use (constant overusers), (3) those with constant needs but no MHC-use (constant underusers) and finally, (4) a varied group of persons with different trajectories of needs and MHC-use (changing [mis]match). It is important to note that the extent of the under- or overuse can vary, that is, MHC-use can increase or decrease among the overusers, or needs may increase or decrease among underusers. In the changing [mis]match group, the way in which the match or mismatch between needs and MHC-use changes over time can vary considerably. For instance, changes in MHC-use could largely correspond with changes in needs, but there could also be patterns where a matched situation transitions to a mismatched situation (diverging needs and MHC-use trajectories) or vice versa (converging trajectories). To prevent underuse and overuse, policymakers and clinicians can benefit from insights into the frequency and extent of different types of mismatches over time, and the underlying mechanisms.

To identify explanatory factors for [mis]match patterns, Andersen's Behavioural Model of Health Services Use (BMH; Andersen, 1968) can be used. According to the BMH, healthcare use depends on three main factors: enabling factors, predisposing factors, and need factors. Previous cross-sectional studies have investigated how these factors are associated with under-or overuse of MHC (Babitsch et al., 2012; Demyttenaere et al., 2004; Jörg et al., 2016; Verhaak et al., 2009). Enabling factors include the individual's financial resources or the structure of healthcare systems, which can make it more or less difficult to access care. Examples are the limited availability and financing of services (e.g., public or private), which have been shown to be associated with high MHC underuse, especially in middle- and low-income countries (Babitsch et al., 2012; Demyttenaere, et al., 2004). Predisposing factors include individual demographics and social influences on healthcare-seeking patterns (Babitsch et al., 2012). For example, male gender and negative attitudes towards MHC have previously been associated with MHC underuse (Mackenzie et al., 2007). Need factors can be divided into subjective and clinical needs. Subjective needs are defined as one's own perspective on having a psychological problem that warrants care. Verhaak et al. concluded that the presence of subjective needs determines whether a person received care or not (Verhaak et al., 2009). In contrast, clinical needs are defined as the objective need for (professional) treatment as determined by a clinician (Verhaak et al., 2009). The WHO study shows that when defining the clinical need as the presence of a diagnosis, overuse seems to be present (Demyttenaere et al., 2004). However, another study that included the severity in addition to the DSM-diagnosis concluded that there is no overuse (Jörg et al., 2016).

In countries with an equal-access healthcare system, such as the Netherlands, clinical needs are crucial for appropriate healthcare distribution (Kroneman et al., 2016). However, the different ways in which clinical needs were defined previously may have led to the contradictory results on the presence of overuse (Demyttenaere et al., 2004; Jörg et al., 2016). To accurately assess under-and overuse, developing a more realistic clinical need definition is important. We, therefore, intended to generate a composite clinical need measure (also called clinical burden), which includes information on the diagnosis, based on diagnostic criteria (i.e., the Diagnostic and Statistical Manual [DSM]), severity (also called symptom burden), and comorbidity. This selection is based on previous literature, showing that the symptom burden, in addition to the diagnosis, explains why people obtain care vs. no care (Jörg et al., 2016). Furthermore, because the symptom burden strongly depends on whether a person has only one or more anxiety and/or depressive disorders, we additionally considered information on the symptom burden of comorbid anxiety (two or more anxiety disorders), comorbid depression (two or more depressive disorders), and anxiety-depression disorders (one or more anxiety and depressive disorders) (Hofmeijer-sevink et al., 2012).

The aim of this study was, first, to extend the definition of under-and overuse derived from cross-sectional studies by investigating how mismatch between needs and MHC-use is presented over time. Second, we aimed to explain why people show certain mismatch patterns by describing these identified mismatch patterns with predisposing, enabling, and need factors from Andersen's BMH. We used 6-year prospective data from the Netherlands Study of Depression and Anxiety (NESDA) cohort to address these aims.

2. Methods

2.1. Sample and procedures

This study has an observational, longitudinal design, using the NESDA study data from baseline (wave one), two- (wave three), four-(wave four), and six-year follow-up (wave five). NESDA is an ongoing multisite, naturalistic cohort study examining long-term courses of people with depression and/or anxiety. In total, 2,981 participants were recruited from the general population (18.9%), primary MHC services (54%), and specialized MHC settings (27.1%). The cohort included participants with different stages of anxiety and depressive disorders: 1,701 participants with a current DSM-IV disorder of depression and/or anxiety, 907 with a life-time diagnosis or high risk for developing these disorders and 373 healthy controls. Participants not being fluent in Dutch and with a primary psychiatric diagnosis of a disorder that is not anxiety or depression were excluded. NESDA was approved by the medical ethical review boards of all participating centres. All participants signed informed consent. For a detailed description of the study rationale and methods of NESDA, see Penninx et al. (2008).

2.2. Measures

To be able to determine a [mis]match, the clinical burden and MHC-use trajectories over time were estimated and compared. To enable accurate comparison of the trajectories, we developed two standardized scales to be used in the trajectory estimations: clinical burden (Fig. 1) and MHC-use (Fig. 2).

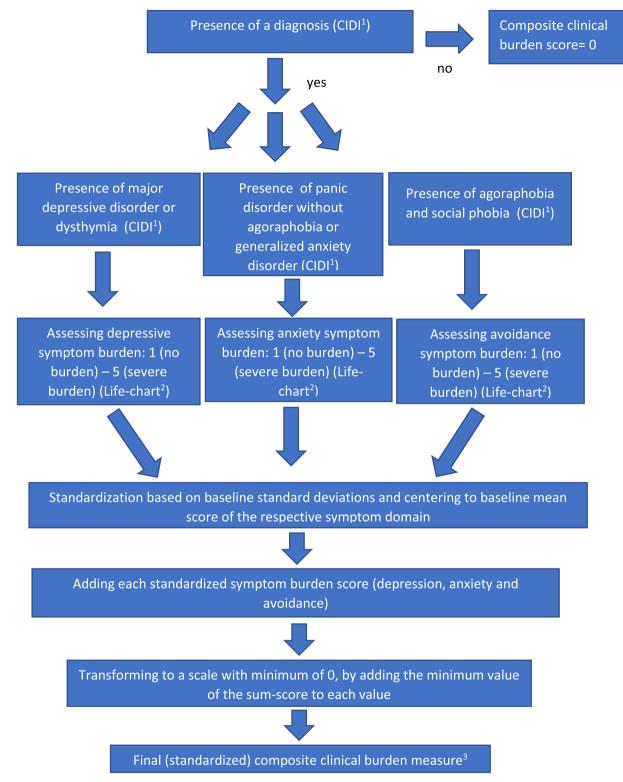
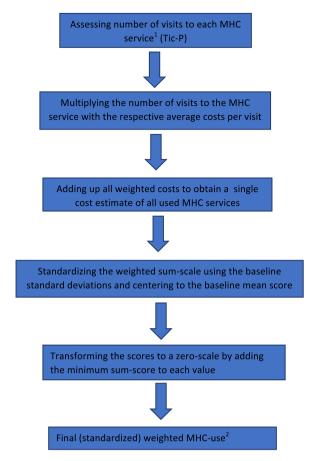


Fig. 1. Flow-chart on each process step in generating the clinical burden composite measure. 1: The CIDI (composite international diagnostic interview – lifetime version 2.1 assesses the presence of a diagnosis for the past 6 months at each wave. 2: The life-chart questionnaire retrospectively assesses symptom burden for the past 6 months at each wave. The only exception were the assessments for anxiety, depression and/or avoidance at baseline. Here a one-year burden was available, which was taken as a proxy for the 6-months burden. 3: The final composite measure of the clinical burden scale can be interpreted as follows: 0= no clinical burden and, >0 = higher scores reflect higher clinical burden of diagnosed (comorbid) disorders.



 ${\bf Fig.~2.}$ Flow-chart on each process step in generating the weighted MHC use measure

1: MHC-use refers to the past 6-months of each interview. 2: The weighted MHC-use measure can be interpreted as follows= 0 (no MHC use), >0 = higher scores reflect higher levels of MHC use (frequency of visits and type of MHC service).

2.3. Clinical burden

We created a composite clinical burden measure that includes information on the presence of a current diagnosis (6-months prevalence), symptom burden (i.e., severity of symptoms), and comorbidity. In particular, we focus on the symptom burden of single diagnosed anxiety or depressive disorders, combinations of two or more anxiety/depression disorders, and combination of one or more anxiety and depressive disorders. At each wave, the composite international diagnostic interview (CIDI)-lifetime version (Robins et al., 1988; Wittchen, 1994). was used to determine the presence of seven DSM-IV-based disorders (i.e., major depressive disorder, dysthymia, social phobia, panic disorder with and without agoraphobia, agoraphobia, and generalized anxiety disorder), in the preceding six months. Symptom burden was assessed retrospectively with the Life-chart questionnaire (Lyketsos et al., 1994;

Denicoff et al. 1997), which yields monthly scores ranging from 1 (no burden) to 5 (severe burden) for three main symptom domains: anxiety, depression, and avoidance. Similar to the time window of the CIDI, we used symptom burden scores of the preceding six months for waves 3, 4, and 5. For wave 1, only a one-year symptom burden assessment was available, which was therefore used as a proxy for the six months symptom burden. For each wave, information on all diagnoses and their associated symptom burden was combined into a single clinical burden score (see Appendix p.2 for a worked example of the calculations). On this composite continuous scale, a zero-score is interpreted as having no diagnosis (thus no clinical burden), and the higher the score, the higher the clinical burden of (comorbid) anxiety and depressive disorders.

2.4. MHC-use

We defined MHC-use as mental health-related visits to the general practitioner (GP), social worker, first-primary care psychologist, psychiatric nurse, psychotherapist, psychiatrist, MHC institutions, MHC specialists in hospitals, centers for alcohol and addiction, and mental health-related hospital admissions in the past six months at each wave, which was assessed with the Tic-P (Bouwmans et al., 2013). Furthermore, we created a weighted sum-score, using the average costs per visit, because costs are a good proxy for the level of care (see appendix p.4-7 for worked examples of this procedure). Medication use is included in visits to any (mental health) physician, including the GP, as in the Netherlands, medication needs to be prescribed and protocolled by such a professional (Kroneman et al., 2016; Magnée, 2017; Poll et al., 2020; Roijen et al., 2015). On the final weighted continuous MHC-use scale, a zero-score can be interpreted as no use, and increasing scores reflect increasing MHC-use.

2.5. Predictors

As predisposing factors, we included sex, age, and attitudes towards MHC, assessed at baseline. Attitudes towards MHC were measured with the Confidence in Help Scale, which has been previously validated and used by Verhaak et al. and consists of three domains. Two items measured the domain "confidence in professional help" (Cronbach's alpha=.46), two items measured the domain "confidence in lay help" (Cronbach's alpha=.78) and one item assessed the domain "confidence in self-help" (psychological problem are best kept to yourself). The response options on all items ranged from 1-5 (1=strongly disagree, 2=disagree, 3=no opinion, 4=agree, 5= strongly agree). For the domains, 'confidence in professional help' and 'confidence in lay help', the mean of the two items was taken. Afterward, the scores were rounded to obtain interpretable scores (Verhaak et al., 2009). Finally, for the purpose of our statistical analysis, we merged the first two and the last two options: 1=(strongly) disagree, 2=no opinion, 3= (strongly) disagree.

As enabling factors, we included socio-economic status (SES) in the form of educational level with three levels, that was assessed at baseline: 1=basic, 2=intermediate and, 3=high education.

As need factors, we included the following variables: suicidal ideation, disability, subjective need and presence of a somatic disease. The referral guidelines of the Dutch healthcare system suggest that in

addition to the presence of a diagnosis based on diagnostic criteria, the course of symptomatology, the severity of symptoms (symptom burden), and the complexity (comorbidity), also suicidality and disability play a role when deciding who will receive which type of care (Kroneman et al., 2016). The latter two could however not be included in the composite burden measure because they were not assessed on all time points and/or did not capture the same time frame (6 months prevalence). Hence, we included them as explanatory need measures. Furthermore, we used suicidal ideation as a proxy to assess suicidality. The presence of suicidal ideation was assessed for the past week of the interview (Beck et al., 1979). It is defined as having thoughts of suicide and was assessed with a shortened version of Beck's scale for suicidal ideation (SSI), which was previously found to have acceptable internal consistency ($\alpha > .74$) (Beck et al., 1979; Kivelä et al., 2019). Moreover, this variable was assessed at each wave. The four assessed suicidal ideation variables were then recoded into a single variable, that provided information on whether a person experienced suicidal ideation at least at one wave. Disability was measured using the World Health Organization Disability Assessment Schedule II, which was previously shown to have high reliability and validity (Buist-Bouwman 2008, Chwastiak, Von Korff, 2003). This interview focuses on past-month health-related disability in six different life-domains: cognition, mobility, self-care, interpersonal interactions, life activities,

participation in society. The scale at each wave ranged from 1-100 (higher scores indicating higher disability) (Mckibbin et al, 2004). To obtain a variable reflecting the total experience of disability during the follow-up time, the scores from each of the four waves were summed for each participant (range: 0-400). Participants expressed their subjective needs in the first question of the perceived need for care interview (PNCQ) and expressed if they experienced any psychological problem in the past 6 months (yes/no) (Verhaak et al., 2009). Subjective needs were assessed at each wave. We recoded these variables into a single variable, to capture the time-varying component: 1. No subjective needs, 2. Subjective needs present at $<\!50\%$ of the waves, 3. Subjective needs present at $>\!50\%$ of the waves, 3. Subjective needs present at $<\!50\%$ of the waves. Finally, we included information on whether a chronic, somatic disease was present or not (see Table 1 for an overview of the predictors).

2.6. Statistical analysis

The study protocol and analysis code were preregistered on the open science framework (Wijekoon et al., 2021). To deal with the missing values, we conducted a multiple imputation (10 imputed datasets) on the raw data using the predictive mean matching method (PMM). Furthermore, we inspected the observed characteristics of dropouts vs. completed cases with chi-square and independent t-tests.

Table 1
Description of the explanatory predictors based on Andersen's BMH.

BMH factor	Measurement instrument	Assessment time- point	Type of variable used in the analyses	Method	Citation
Predisposing factors					
Sex		Baseline	Dichotomous: female, male	SR^1	
Age		Baseline	Continuous	SR^1	
Attitudes towards	Nivel Consumer Panel Questionnaire: Confidence in	Baseline	Nominal:	Int ²	Verhaak et al.,
MHC ³	professional, lay and self help		1= (strongly) disagree		2009
			2=no opinion		
			3=(strongly) agree		
Enabling factors					
Socio-economic	SES was measured with the educational status	Baseline	Ordinal:	SR^1	
status (SES)			1=basic		
			2=intermediate		
			3=high		
Need factors					
Suicidal ideation	Shortened version of the Beck's scale for suicidal	Waves 1,3,4,5	Dichotomous: Present or absent at any	Int ²	Beck et al., 1979
	ideation		wave		
Disability	World Health Organization Disability Assessment	Waves 1,3,4,5	Continuous: 0-400 (higher scores	SR^1	Mckibbin et al,
	Schedule II		indicating greater disability)		2004
Subjective need	In the first question of the perceived need for care	Waves 1,3,4,5	Nominal:	Int ²	Verhaak, 2009
	interview (PNCQ)		1.Absent		
			2.Present at <50% of the waves		
			3.Present at >50% of the waves		
Chronic somatic		Waves 1,3,4,5	Dichotomous: Present or absent at any	SR^1	
disease			wave		

¹: SR=self-report.

²: Int=Interview.

³: The original scale of the confidence in help measurement was:1=strongly disagree, 2=disagree, 3=strongly agree, 4=no opinion. To facilitate interpretation of our statistical analysis, we first reversed the scale into 1= strongly disagree, 2= disagree, 3= no opinion, 4= agree, 5= strongly agree. Then, we combined the first two and the last two response options.

The handling of outliers and results of the missing value analysis can additionally be found in the appendix (p.9).

We first divided the NESDA sample into four groups, based on what we already know about under-and overuse from cross-sectional studies. These subgroups can then be used to extend the already established mismatch definitions by exploring how [mis]match is presented over time. Such a qualitative division of the sample, prior to the statistical analysis, helps to make sure that we build our analysis on existing definitions and concurrently avoids under-or overestimations of the presence of [mis]match. The sample was therefore split as follows: I) the overuse subgroup (n=121) with constantly no clinical burden (clinical burden at wave 1-4=0), but MHC-use present at least at one wave (MHC-use at wave x>0), II) the underuse subgroup (n=409) with constantly no MHC-use (MHC-use at wave 1-4=0) but clinical burden at least at one wave (clinical burden at wave x>0) and III) the changing [mis]match subgroup (n=1,807) with any MHC-use and clinical burden present at least at one wave (clinical burden at wave x>0; MHC-use at wave x>0), and finally, IV) the healthy non-user subgroup (n=631). Second, to further identify different patterns of [mis]match within subgroups I-III, we identified classes using a data-driven, growth mixture modeling approach (GMM) in Mplus (version 8.4) (Muthén and Muthén, 2012). The GMM helps to probabilistically classify individuals into latent classes based on their longitudinal response pattern on the clinical burden and/or MHC-use variables (Jung and Wickrama, 2008).

2.7. Trajectory analysis

Three GMM analyses were run. First, a GMM was used to identify classes with different MHC-use trajectories in the overuse subgroup. Second, GMM was used to identify classes with different clinical burden trajectories in the underuse subgroup. Third, a parallel trajectories/process GMM (pp-GMM) was used in the changing [mis]match subgroup to identify classes with different contemporaneous trajectories on both scales.

In all GMMs, models with increasing numbers of classes were fit to the data and their fit was compared based on the Akaike Information Criterion and (adjusted) Bayesian Information Criterion, with the lowest values indicating the optimal model. In addition, entropy, interpretability, and parsimony were considered as well in selecting the optimal model (Jung and Wickrama, 2008; Wright and Hallquist, 2014) . See appendix p.8-9 for more detailed model information.

2.8. Identifying mismatch and match trajectories

For each identified class in subgroups I-III, we plotted the mean trajectories over time on the clinical burden (overuse subgroup), MHC-use (underuse subgroup) or both (changing [mis]match subgroup). To identify the extent of underuse and overuse, we evaluated the growth of the single trajectories (strong vs. slight increase/decrease) of burden and MHC-use. To identify patterns of change in the changing [mis]match subgroup, we plotted the trajectories of mean burden and MHC-use scales and evaluated whether the trajectories ran parallel (match), converged (mismatch to match), or diverged (match to mismatch) over time. To determine the type of growth of each observed trajectory, the

following criteria were used: a non-significant (alpha \geq 05) slope equals a stable trajectory and significant positive and negative slopes indicate an increasing or decreasing trajectory, respectively.

2.9. Multivariate multinomial regression analysis

Regression analyses were used to investigate associations between the predictors and [mis]match class-membership. For the regression analysis, we used the pooled function in SPSS (version 27) based on the 10 imputed datasets. We first tested each predictor in a univariate analysis and then included the significant univariate predictors (p<0.1) into a multivariate model with class membership as outcome variable.

Multicollinearity of the predictors was examined using the variance inflation factor (cut-off>10), and the False Discovery Rate (FDR) was used to adjust for the effects of multiple testing (Benjamini and Hochberg, 1995). Furthermore, we converted the log odds ratio in the final model to the standardized mean difference Cohen's d (d) (Cohen, 1988). In all analyses, an alpha of 0.05 was used.

3. Results

3.1. Baseline characteristics

Table 2 depicts the baseline charactersitics of the NESDA sample. Our total baseline sample consisted of 2,981 eligible participants (66.4% females, mean age of 41.9 years). Of these, 41.7% had no current disorder (6-months prevalence) and 58.3% suffered from a current comorbid anxiety and/or depressive disorder. Additionally, the raw mean burden for anxiety, depression, and avoidance symptoms (Life-chart) in the diagnosed group was low (results of the missing value analysis can be found in the appendix on p 9-10).

Table 2Baseline characteristics¹ [N= 2981].

Sov. 04 female	66.4
Sex, % female	
Age, mean years (SD)	41.86 (13.08)
No current disorder ² , %	41.7
Comorbidity	
>1 current depressive and/or anxiety disorder, %	58.3
Symptom burden ³ , mean (SD)	
Anxiety burden	1.8 (1.78)
Avoidance burden	1.29 (1.71)
Depression burden	1.9 (1.89)
Agoraphobia, %	6.3
GAD, %	15.6
Dysthymia, %	10.2
MDD, %	37.4
Mental healthcare users	50.59

¹ The baseline characteristics refer to the total baseline sample including outliers.

² CIDI: current disorder refers to a 6-month prevalence.

³ The symptom burden was assessed by the Life-chart questionnaire.

3.2. Trajectory analysis

Based on the above-mentioned selection criteria, we selected the following class-solutions in each subgroup of the NESDA sample, excluding outliers, leaving n=2,968 (see appendix p.11-13 for more

elaborated information on the selection process of the class-solution). Fig. 3 depicts the trajectories for each class. We additionally described each identified class with Andersen's BMH factors (Table 3).

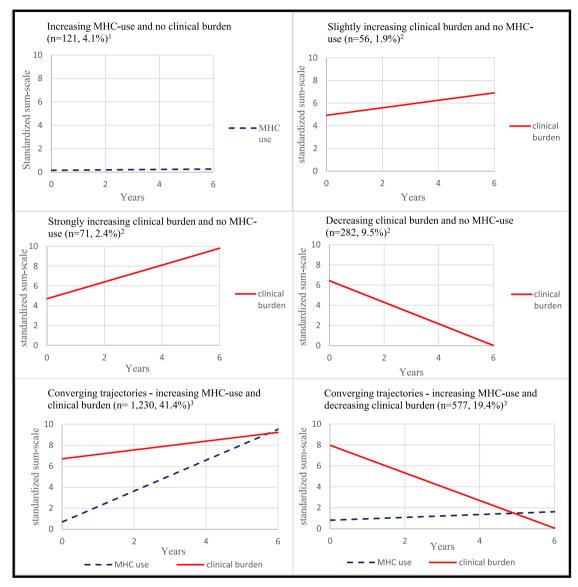


Fig. 3. MHC use and clinical burden trajectories based on single and parallel linear growth mixture models. 1. Variances for the MHC-use intercept (i_u) and slope (s_u) in the increasing MHC-use and no clinical burden class: intercept (i_u) =.32, slope (s_u) =.03. 2. Variances for the clinical burden intercept (i_b) and slope (s_b) in the strongly increasing clinical burden, slightly increasing clinical burden, and decreasing clinical burden and no MHC use were fixed to zero $(i_b$ =0, s_b =0). 3. Variances for the MHC-use intercept (i_u) and slope (s_u) and clinical burden intercept (i_b) and slope (s_b) in the Converging trajectories - increasing MHC-use and clinical burden and Converging trajectories - increasing MHC use and decreasing clinical burden: i_u =1.16 s_u =.7, i_b =5.45, i_b =0.14. All the trajectories had significant (p<.05) positive or negative slopes, indicating statistically significant increasing or decreasing trajectories in each class.

Table 3 Descriptive of BMH factors in each identified [mis]match class in each subgroup of the NESDA sample (N=2968)¹.

NESDA subgroups	Healthy non- users (N=	Overuse subgroup	Underuse su	bgroup		Changing [mis]match subgr	oup
Classes within the subgroups	631, 21.3%)	Increasing MHC use and no clinical burden (N= 121, 4.1%)	Slightly increasing clinical burden and no MHC use (N=56, 1.9%)	Decreasing clinical burden and no MHC use (N=282, 9.5%)	Strongly increasing clinical burden and no MHC use (N=71, 2.4%)	Converging trajectories: increasing MHC use and clinical burden (N=1,230, 41.4%)	Converging trajectories: decreasing MHC use and clinical burden (N=577, 19.4%)
Predisposing factors							
Age Mean (SD)	43.1 (14.25)	38.64 (12.47)	46.77 (12.02)	44.91 (13.12)	46.39 (14)	41.52 (12.51)	40.85 (12.48)
Sex (female), % Confidence in professional help ² , %	61.8	69.4	67.9	64.5	83.1	66.7	68.8
(Strongly) disagree	4.3	9.5	7.2	6.9	9.9	14.9	8.1
No opinion	11.2	12.6	21.6	16	25.9	15.9	12.7
(Strongly) agree Confidence in lay help ² , %	84.5	77.9	71.2	77.1	64.2	69.2	79.2
(Strongly) disagree	17.3	21.9	25.3	21.3	26.81	26.9	27.4
No opinion	34.3	19.7	37.8	35.3	34.4	36.9	42
(Strongly) agree Confidence in self- help ² , %	48.5	26.6	36.9	43.4	38.8	36.2	30.6
(Strongly) disagree	89.6	85.7	84	83.2	73.4	71.3	80.8
No opinion	4.8	4.5	1.8	5.7	5.2	6.4	5.6
(Strongly) agree Enabling factors Level of education, %	5.6	9.8	14.1	11.1	21.4	22.3	13.7
Basic	4	3.3	3.6	5.3	11.3	9.3	4.9
Intermediate	52.5	45.5	67.9	63.8	62	61.2	56.7
High Need factors	43.6	51.2	28.6	30.9	26.7	29.4	38.5
Subjective needs, %				10.0			
Not present Present at <50% of the waves	63.1 30.9	8.3 59.5	3.6 33.9	13.8 50.7	1.4 36.6	0 19.4	2.6 30.5
Present at >50% of the waves	6	32.2	62.5	35.5	62	72.6	66.9
Presence of chronic disease (somatic), %	39.1	60.3	76.8	74.8	81.7	87.8	73.7
Suicidal ideation, % Present at any	1.7	8.3	17.5	16	20.21	79.7	37.3
wave Disability ³ , mean (SD)	26 (23.67)	37.38 (29.76)	78.46 (43.87)	61.91 (42.69)	93.31 (52.32)	103 (55.44)	53.29

¹ These are pooled estimated based on 10 imputed datasets. The total sample in each sample, excluding outliers is N=2968.

² We merged the first two and the last two scores of the confidence in professional, lay-and self-help-scale (original reverse-scale: 1=strongly disagree, 2=disagree,3=no opinion, 4=agree 5= strongly agree).

³ Disability: the maximum score of this time-varying sum-scale for disability is 400.

(continued on next page)

3.2.1. Overuse subgroup (n=121)

In the overuse subgroup, the 1-class solution was deemed the best option.

3.2.1.1. Increasing MHC-use and no clinical burden (n=121, 4.1%). This class showed on average a low baseline MHC-use level (intercept_{MHC-use} $[i_u]$ =0.31, p<.001) that slightly increased ($slope_{MHC-use}$ $[s_u]$ =0.1, p=.002).

3.2.2. Underuse subgroup (n=409)

In the underuse subgroup, the 3-class solution was deemed the best option.

3.2.2.2. Slightly increasing clinical burden and no MHC-use (n=56, 1.9%). This group had a relatively medium clinical burden level at baseline (intercept_{clinical burden} [i_b]=4.78, p<.001) that slightly increased ($slope_{clinical burden}$ [s_b]=0.34, p<.001).

3.2.2.3. Decreasing clinical burden and no MHC-use (n=282, 9.5%). In contrast, this group showed a higher baseline clinical burden level (i_b =6.45, p<.001), that decreased (s_b =-1.07, <.001).

3.2.2.4. Strongly increasing clinical burden and no MHC-use (n=71, 2.4%). This group revealed a relatively medium baseline clinical burden level (i_b =4.9, p<.001) that increased strongly (s_b =0.81, p<.001), in comparison to the slightly increasing clinical burden and no care class.

3.2.3. Changing [mis]match subgroup (n=1807)

In the mismatch and match subgroup, the 2-class solution was deemed the best option.

3.2.3.5. Converging trajectories- increasing MHC-use and clinical burden (n=1,230, 41.4%). This class had a high baseline clinical burden level (i_b =6.81, p<.001) that increased (s_b =0.37, p<.001). Simultaneously, these participants revealed a lower baseline MHC-use level (i_u =0.69, p<.001) that increased strongly (s_u =1.55, p<.001). Hence, both trajectories show a high discrepancy between the burden and MHC-use levels in the beginning of the study that decreased with time. In other words, the trajectories converged over time, indicating a mismatch to match transition. This class is comparably the largest.

3.2.3.6. Converging trajectories- increasing MHC-use and decreasing clinical burden (n=577, 19.4%). Similarly, this class shows converging trajectories with increasing MHC-use (i_u =0.81, <.001, s_u =0.21, p<.001). However, in contrast to the first converging trajectory class, here the participants revealed a high baseline clinical burden (i_b =8.01, p<.001) that decreased (s_b =-1.33, p<.001).

3.3. Regression analysis

For the regression analysis, we chose as a reference the group with the least favourable mismatch situation: strongly increasing burden and no MHC-use (i.e., constant underuse) (Table 4). Moreover, we excluded gender from the multivariable analysis, as it was not significant (p=.01) in the univariable analysis, using the FDR-based cut-off (alpha=.002). In comparison to the reference class, the increasing MHC-use class (overuse) was significantly less likely to experience higher disability (b=-.03, p<-.001, d<0.2). However, around 59.5% of this class experienced subjective needs for care (Table 3). Furthermore, both classes with converging trajectories were significantly more likely to experience suicidal ideation (b=1.14-2.78=2.78, p<-.001, d=0.63-1.5) compared to the reference class (Table 4). There were no differences between the reference class and the other classes regarding enabling or predisposing factors (Table 4).

Results of the multinomial logistic regression: BMH factors that predict membership in the identified [mis]match classes (dependent variable)

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Predictors: BMH factors ²	p	Ъ	E^{B} (95%CI)	Cohens' d³	Predictors: BMH factors	p	Ъ	E ^b (95%CI)	Cohens' d³	
Dependent category: Healthy non-user class (n= 631, 21.3%) (Reference category: strongly increasing clinical burden and no MHC-use)	n-user class (n=	631, 21.3%) (Re	eference category: strongl	y increasing clinical b	ourden and no MHC-use).					
Enabling factors					Need factors					
SES (educational level)	.42	.124	1.53 (.89-2.62)	.23	Subjective needs					
Predisposing factors					Present at <50% of the waves	-2.94	*100.	.05 (.013)	1.6	
Confidence in professional help ⁴					Present at >50% of the waves	-4.69	<.001*	.01 (005)	2.59	
(strongly) disagree	.11	.884	1.12 (.26-4.87)	<.2	Suicidal ideation	-2.71	<.001*	.07 (.0318)	1.49	
(strongly) agree	.45	.354	1.56 (.61-4.01)	.25	Chronic somatic disease	31	.502	.73 (.3-1.82)		
Confidence in self-help ⁴					Disability	03	<.001*	(8096.) 26.	< i2	
(strongly) disagree	.22	.801	1.25 (.22-7.22)	.12						
(strongly) agree	34	.735	.71 (.1-5.11)	.19						
Confidence in lay help⁴										
(strongly) disagree	37	.418	.69 (.29-1.69)	.2						
(strongly) agree	.00	.958	1.02 (.49-2.11)	<.2						
Age	01	.595	.99 (.97-1.02)	<.2						
Dependent category: Increasing I	MHC-use and no	clinical burden	class (n= 121, 4.1%) (Re	ference category: stro	Dependent category: Increasing MHG-use and no clinical burden class (n= 121, 4.1%) (Reference category: strongly increasing clinical burden and no MHG-use)	(HC-use				
Enabling factors					Need factors					
SES (educational level)	.71	.02	2.03 (1.12-3.66)	.39	Subjective needs					
Predisposing factors					Present at <50% of the waves	23	908.	.79 (.12-5.14)	.13	
Confidence in professional help ⁴					Present at >50% of the waves	-1.1	.251	.34 (.06-2.13)	.59	
(strongly) disagree	.87	.313	2.4(.44-13.28)	.48	Suicidal ideation	49	.316	.61 (.24-1.59)	.27	
(strongly) agree	.34	.524	1.41 (.49-4.01)	.19	Chronic somatic disease	27	.575	.76 (.29-1.98)	.15	
Confidence in self-help ⁴					Disability	03	<.001*	(86-96.) 26.	< >	
(strongly) disagree	-:1	606.	.91 (.17-4.91)	<.2						
(strongly) agree	61	.53	.54 (.08-3.65)							

Table 4 (continued)

Predictors: BMH factors ²	b	P	E ^B (95%CI)	Cohens' d ³	Predictors: BMH factors	b	P	E ^b (95%CI)	Cohens' d ³
Confidence in lay help ⁴									
Strongly disagree	02	.969	.98 (.37-2.62)	<.2					
(strongly) agree	05	.896	.95 (.44-2.05)	<.2					
Age	03	.027	.97 (.9499)	<.2					
Dependent category: Slightly increase	asing clinical b	ourden and no	MHC-use class ($n=56, 1.$	9%) (Reference categ	ory: strongly increasing clinical burden	and no MHC-us	e)		
Enabling factors					Need factors				
SES (educational level)	.1	.786	1.11 (.53-2.33)	<.2	Subjective needs				
Predisposing factors					Present at <50% of the waves	3.81	.604	4.95 (0-7.02)	2.1
Confidence in professional help ⁴					Present at >50% of the waves	3.72	.616	4.15 (0-7.37)	2.05
(strongly) disagree	02	.987	.98 (.13-7.73)	<.2	Suicidal ideation	04	.944	.96 (.32-2.91)	<.2
(strongly) agree	.09	.901	1.09 (.26-4.6)	<.2	Chronic somatic disease	.28	.712	.76 (1.6-3.49)	.15
Confidence in self-help ⁴					Disability	<01	.477	.1 (.1-1.01)	<.2
(strongly) disagree	7.4	.993	16 (0-18.29)	4.08	-				
(strongly) agree	6.92	.993	12.3 (0-19.29)	3.82					
Confidence in lay help ⁴									
Strongly disagree	17	.791	.84 (.23-3.07)	<.2					
(strongly) agree	19	.699	.82(.31-2.21)	<.2					
Age	.02	.348	1.02 (.98-1.06)	<.2					
					rongly increasing clinical burden and no	MHC-use)			
Enabling factors			(,, (-		Need factors				
SES (educational level)	.13	.630	1.14 (.67-1.93)	.07	Subjective needs				
Predisposing factors	.10	.000	1111 (107 1170)	107	Present at <50% of the waves	99	.27	.37 (.06-2.16)	.54
Confidence in professional help ⁴					Present at >50% of the waves	-1.86	.032	.16 (.0384)	1.02
(strongly) disagree	.34	.612	1.4 (.38-5.17)	.19	Suicidal ideation	16	.677	.85 (.4-1.8)	<.2
(strongly) agree	.5	.29	1.65 (.65-4.15)	.28	Chronic somatic disease	2	.664	.82 (.34-2.01)	<.2
Confidence in self-help ⁴	.5	.23	1.03 (.03-4.13)	.20	Disability	01	.057	.99 (.99-1)	<.2
(strongly) disagree	2	.803	.82 (.18-3.85)	.11	Disability	01	.037	.99 (.99-1)	\.Z
(strongly) disagree	2 69	.407	.5 (.1-2.56)	.38					
(Strongry) agree	.05	. 107	.0 (.1 2.00)	.50					
Confidence in lay help ⁴									
Strongly disagree	19	.662	.83 (.35-1.94)	<.2					
(strongly) agree	.01	.975	1.01 (.5-2.05)	<.2					
Age	<.01	.948	1 (.97-1.03)	<.2					
) (Reference category: strongly increasin	a clinical burde	on and no MHC-11	se)	
Enabling factors	ajectories - inc	creasing wire-t	isc and chinear burden ci	.ass (ii= 1250, 41.470	Need factors	g chinear burde	ii and no wire-u	30)	
SES (educational level)	.25	.326	1.28 (.78-2.11)	<.2	Subjective needs				
Predisposing factors	.23	.320	1.20 (./0-2.11)	\. <u>L</u>	Present at <50% of the waves	-1.2	.187	.3 (.05-1.77)	.6
Confidence in professional help ⁴					Present at >50% of the waves	69	.417	.5 (.1-2.65)	.38
(strongly) disagree	.84	.219	2.31 (.61-8.79)	.46	Suicidal ideation	2.78	<.001*	16.04 (7.95-32.37)	1.5
(strongly) disagree	.77	.112	2.17 (.84-5.56)	.40	Chronic somatic disease	.36	<.001" .479	1.44 (.42-4)	.2
	.//	.112	2.17 (.84-3.36)	.42				, ,	
Confidence in self-help ⁴ (Strongly) disagree	19	.795	.83 (.2-3.41)	<.2	Disability	<.01	.427	1 (.1-1.01)	<.2
				<.2 .2					
(strongly) agree Confidence in lay help ⁴	39	.615	.68 (.15-3.11)	.4					
, , ,	02	054	00 (42 2 21)	. O					
Strongly disagree	02	.954	.98 (.43-2.21)	<.2					
(strongly) agree	01	.974	.99 (.5-1.97)	<.2					
Age	03	.012	.97 (.9499)	<.2					
	ajectories- inc	reasing MHC-u	se and decreasing clinica	I class (n=577, 19.4%	(Reference category: strongly increasing	ng clinical burd	en and no MHC-1	ise)	
Enabling factors SES (educational level)					Need factors				
	.43	.092	1.54 (.93-2.54)	.24	Subjective needs				

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Predictors: BMH factors ²	p	Ъ	E ^B (95%CI)	Cohens' d³	Predictors: BMH factors	þ	Ъ	E^{b} (95%CI)	Cohens' d³
Predisposing factors					Present at <50% of the waves	.03	696°	1.04 (.18-5.91)	<.2
Confidence in professional help ⁴					Present at >50% of the waves	ε.	.73	1.34 (.25-7.17)	.2
(strongly) disagree	.56	.42	1.76 (.44-6.99)	.31	Suicidal ideation	1.14	*100.	3.14 (1.56-6.32)	.63
(strongly) agree	.81	.114	2.24 (.83-6)		Chronic somatic disease	03	.954	.98 (.41-2.35)	<.2
Confidence in self-help ⁴					Disability	01	.055	.99 (.99-1)	<.2
(Strongly) disagree	32	.687	.73 (.15-3.46)	.2					
(strongly) agree	59	.467	.56 (.11-2.72)	.33					
Confidence in lay help ⁴									
Strongly disagree	06	.888	.94 (.41-2.17)	<.2					
(strongly) agree	46	.174	.63 (.32-1.22)	.26					
Age	04	.004	.96 (.9499)	<.2					

Following reference categories were chosen for each BMH variable: educational status = continuous variable; confidence in professional, self-and lay help= no opinion; age= continuous; subjective needs at <50% and These results are based on pooled estimates of 10 imputed datasets. The strongly increasing clinical burden and no MHC-use class (N=71, 2.4%) was chosen as a reference category in this regression analysis. no suicidal ideation present; chronic somatic disease= no chronic somatic disease present; disability= continuous. 50% of the waves= no subjective needs; suicidal ideation=

4 Confidence in help variable: We merged the first two and the last two scores of the confidence in professional, lay-and self-help-scale (original reversed scale: 1=strongly disagree, 2=disagree, 3=no opinion, 4=agree Cohens' d can be interpreted as follows: >=.2 (small effect),

5= strongly agree). * marks significant p-values based on an adjusted (FDR) cut-off of p=.002

4. Discussion

This longitudinal study revealed four main groups having a specific (mis)match pattern: healthy non-users, overusers, constant underusers and a group showing a changing mismatch-to-match pattern, which was the largest group (60.9%). In the latter group, MHC use increases to match high clinical burden, that increases in one subclass and decreases in the other. The constant underusers could be divided in three subclasses, with decreasing, slightly and strongly increasing clinical burden, respectively. Constant underusers (reference) and those with delayed care (mismatch-to-match) differed from each other only in the presence of suicidal ideation among those receiving delayed care. Interestingly, we did not identify any meaningful class that continuously revealed matched care on average over the six years.

4.1. Overuse

We found that the overuse class was less likely to show disability than the reference group, which underused MHC. The associated effect size was, however, very small. Despite finding no other significant differences, we could detect a large proportion with subjective needs (59.5%) in the overuse class. This finding hints on an existing misfit between subjective and clinical needs, which previous researchers have already supported (Druss et al., 2008; Fretian et al., 2020). This misfit can appear in two ways. First, there are those that have clinical needs but do not feel that they need help (Fretian et al., 2020). Second, similarly to our findings, there are those that do not have clinical needs (i.e., a diagnosis) but experience a need for help, potentially explained by other stressors (Druss et al., 2008; Jörg et al., 2016, Bloem 2012). Hence, it may be important to explore further the reasons for these types of misfits between clinical and subjective needs. Additionally, it could be that these were recovering individuals who still obtained some form of care to prevent relapse. However, because we do not have data on the actual type of received MHC (whether it is preventive or active treatment), we cannot surely say that this MHC-use was for recovering patients. Furthermore, it should be noted that the average care level in this class was quite low in comparison to those who obtained care (all underuse classes and the classes with converging trajectories). Hence, we should be cautious when labeling this class as actual overusers. We suggest that more need factors, such as subthreshold symptoms, should be included in future research to gain better insight into the mechanisms that explain this pattern. Only then could we fairly classify such patterns as signs of overuse or not.

4.2. Constant underuse

The fact that in this study only 13.8% of participants revealed constant underuse can be explained by the fact that around 80% of NESDA participants were recruited at MHC settings. When taking a closer look, the overall level of the clinical burden of the constant underuse class is not entirely different from the clinical burden of the converging classes. These findings suggest that even when the diagnosis, symptom burden and comorbidity are similar between different individuals, the presence of suicidal ideation appeared as a key determinant of who will receive care. Suicidal ideation is known to be linked to suicidality, which is mentioned as a criterion for receiving care in the Dutch guidelines for referral (Kroneman et al., 2016; Harmer et al. 2021). However, suicidal ideation is known to be very fluctuating and thus a heterogenous state, which can relate to other factors than just the presence of a diagnosis (Foster et al., 1999; Harmer et al., 2021). Thus, we recommend future researchers to explore the link between suicidal ideation, that occurs in addition to having clinical burden, and suicidality. Furthermore, future research is needed to explore how this link is related to different healthcare use patterns.

Moreover, based on previous research, we would have expected that also other BMH factors may have played a role in explaining the

different [mis]match patterns, such as gender. This is because men are known to be less likely to seek MHC compared to women (Sagar-Ouriaghli et al., 2019). However, in this study, we did not find any predisposing or enabling factors that could explain why these participants showed constant underuse compared to for example those who obtained care. A broader range of potential explanatory factors, such as mental health-related stigma, might be included and explored in future studies (Conner et al., 2010).

One class showed ameliorating clinical burden despite receiving no care. These results emphasize that underuse of common, evidence-based MHC services, does not necessarily always lead to exacerbation of clinical burden. A previous cross-sectional study showed that about 83% of recovery can be attributed to treatment-unrelated factors and spontaneous remission (Ormel et al., 2019), which could be an explanation of the presently observed pattern. Another explanation could be the usage of alternative self-help services. Hence, the question remains who will recover spontaneously and what factors facilitate recovery in the long term in these people.

4.3. Mismatch to match transition

Interestingly, two classes showed more dynamic patterns in form of converging trajectories. Both groups showed underuse in the first half of the study, which gradually changed to matched care. These mismatch to match transitions may indicate the presence of delayed access to appropriate MHC. Striking is the fact that one of the converging trajectory classes included almost half of the NESDA sample. Similarly, another study found that 80% of the participants with a lifetime disorder, did not obtain care in a timely manner (Wang et al., 2002). A consequence of delayed MHC-use is a potentially poor prognosis of the symptoms with time (Osso et al., 2012). One could argue that this may explain why especially this large group shows constantly increasing clinical burden, despite increasing care. However, as mentioned above, our study also showed that underuse does not always result in poorer outcomes. Hence, why underuse (constant or delayed MHC-use) leads to a poor clinical burden progression in some people, but not in others, remains unclear. Other factors explaining such delays may be waiting lists, which should therefore be included in future studies (Vallerand and Mclennan, 2013)

4.4. Correct users

We did not identify any class with a sufficient and meaningful sample size that revealed continuously matched care on average. There were few people that showed constantly matched care, but they did not make up a meaningful sample size. This is alarming and reveals the great extent of the mismatch problem even in a HIC, such as the Netherlands. Because most participants who eventually received matched care showed a delayed MHC-use on average, we need to develop and implement strategies that overcome such delay.

4.5. Limitations and strengths

The strengths of this study include the use of a large longitudinal dataset, that allowed for investigation of different types of underuse over time. Moreover, we used the Dutch guidelines for referral to include further explanatory clinical variables (disability and suicidality) in addition to the literature. Additionally, we used all types of regular MHC services. This approach provided a more accurate reflection on the real-world MHC needs and use, increasing our findings' generalisability.

However, some methodological limitations need to be considered. First, despite the many explanatory BMH factors, only limited associations were found with the observed mismatch patterns. Hence, other (time-varying) exploratory variables (such as stigmatization of MHC or waiting lists) should be investigated. Second, our analysis revealed that

among all the explanatory factors that were included, only one need factor (suicidal ideation) was a significant determinant for receiving care between those with similar clinical burden. This raises the question if, given the close relationship between suicidal ideation and clinical burden, these entities can indeed be seen as factors with distinct roles in healthcare delivery. Future research could look more closely into the overlap and/or distinction between need factors and components of clinical burden. Third, the approach to capture comorbid severity, while avoiding overestimations of the symptom burden, may have caused people with symptom burden scores around the average on all three symptom burden domains (anxiety, depression, avoidance) and people with symptom burden scores above and below the average to be treated as having similar clinical burden. However, the symptom burden estimates on which the scale was standardized were relatively low, still enabling us to capture people with highly comorbid disorders in the high clinical burden trajectories and people with single (less severe) disorders in the low clinical burden trajectories. Fourth, the retrospective nature of the Life-chart questionnaire may have caused recall-bias. Fifth, the fact that most participants were recruited from MHC settings ensured that there was variation in obtained MHC services but may have caused a selection bias. A general population sample could circumvent that problem but may have caused difficulties in identifying trajectory classes with sufficient group sizes. This may be especially the case for identifying less commonly found groups such as overusers. Thus, when merely focusing on underuse, we recommend that future research should use a general population sample. Sixth, the GMM classes reflected homogeneous subgroups with different levels and types of mismatches between clinical burden and MHC-use, but these bottom-up classifications are almost certainly also influenced by other sources of population heterogeneity. Still, this data-driven approach to identify these subgroups was deemed the best option to achieve the research aims, given the lack of clear existing ideas of what kinds of match- or mismatch-patterns over time exist in the real world. Finally, we only captured medication use through the visits to the MHC setting, assuming that a specialist prescribes and supervises the medication use. This, however, may have caused some bias, because for instance some people visit the specialist more often while receiving the same amount of medication, which would consequently result in a higher MHC-use score. However, because previous literature has found that a combination of psychotherapy and pharmacotherapy is more effective than only medication, the impact of this limitation on the mismatch does not seem to be large (Cuipers et al., 2009).

5. Conclusion

This paper reveals that in HIC such as the Netherlands, participants with different disease progressions show mismatch mainly in the form of constant underuse or delayed MHC-use, and no meaningful sample revealed constant matched care within six years. Interestingly, the clinical burden of people who did not use any care or had delayed care was either deteriorating or ameliorating, which emphasizes the importance to detect factors influencing the disease progression, with and without care. The presence of suicidal ideation could most prominently explain why symptomatic individuals received (delayed) care compared to those who did not receive care (underusers). Furthermore, we cautiously conclude that there was generally no mismatch in the form of overuse, given the high proportion of people with subjective needs and the relatively low average MHC-use levels obtained in this group. Therefore, in contrast to overuse, mismatch in the form of underuse still seems to be a problem, even in HIC. The additional absence of a meaningful class with constantly matched care on average is alarming. Hence, to decrease the mismatch in HIC, such as in the Netherlands, the focus should lie on identifying and targeting factors that can explain the treatment gap, especially those leading to delayed MHC.

Author contribution

KWWM, JAB and FJ came up with the study concept. KWWM conducted the data analysis with input from RS and KJW. KWWM wrote the initial draft with feedback from JAB, KJW, BWJHP, RAS, AMVH and FJ. All authors approved the final version of the article.

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Data availability statement

According to European law (GDPR) data containing potentially identifying or sensitive patient information are restricted; our data involving clinical participants are not freely available in a public repository. However, data are – under some specifications - available upon request via the NESDA Data Access Committee (nesda@ggzingeest.nl). See also our website: www.nesda.nl

Declaration of Competing Interest

BWJHP received (non-related) research grants from Boehringer Ingelheim and Jansen Research.

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