Personality Modulates the Efficacy of Treatment in Patients With Major Depressive Disorder

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ABSTRACT

Objective: Effects of depression treatment are obscured by heterogeneity among patients. Personality types could be one source of heterogeneity that explains variability in treatment response. Clinically meaningful variations in personality patterns could be captured with data-driven subgroups. The aim of this study was to identify such personality types and to explore their predictive value for treatment efficacy.

Method: Participants (N = 146) in the current exploratory study came from a randomized controlled trial in primary care depressed patients, conducted between January 1998 and June 2003, comparing different treatments. All participants were diagnosed with a major depressive disorder (MDD) according to the *DSM-IV*. Primary (care as usual [CAU] or CAU plus a psychoeducational prevention program [PEP]) and specialized (CAU + PEP + psychiatric consultation or cognitive-behavioral therapy) treatment were compared. Personality was assessed with the Neuroticism-Extraversion-Openness Five-Factor Inventory (NEO-FFI). Personality classes were identified with latent profile analysis (LPA). During 1 year, weekly depression ratings were obtained by trimonthly assessment with the Composite International Diagnostic Interview. Mixed models were used to analyze the effects of personality on treatment efficacy.

Results: A 2-class LPA solution fit best to the NEO-FFI data: Class 1 (vulnerable, n = 94) was characterized by high neuroticism, low extraversion, and low conscientiousness, and Class 2 (resilient, n = 52) by medium neuroticism and extraversion and higher agreeableness and conscientiousness. Recovery was quicker in the resilient class (class × time: $P < .001$). Importantly, specialized treatment had added value only in the vulnerable class, in which it was associated with quicker recovery than primary treatment (class × time × treatment: $P < .001$).

Conclusions: Personality profile may predict whether specialized clinical efforts have added value, showing potential implications for planning of treatments.

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Although treatments for depression are available, their efficacy has been found inconsistent.[1,2] This could be caused by the heterogeneity of depression[3] and the dependence of treatment efficacy upon more specific patient characteristics, such as symptom patterns, severity, and sociodemographic factors. In addition, predisposing factors may play a role in treatment response. Personality is likely to be such a factor.[4]

Personality is usually operationalized with a range of stable personality traits.[5] Widely used traits are defined in the "Big Five" model: neuroticism, extraversion, openness, agreeableness, and conscientiousness.[6] Interindividual variations on these traits have been shown to be associated with depression: especially a combination of high neuroticism and low extraversion constitutes a depression-prone personality profile.[4,7] A meta-analysis[8] showed that major depressive disorder (MDD) and dysthymic disorder were associated with increased neuroticism, decreased extraversion, and decreased conscientiousness. Personality traits have also been observed to predict depressive course. For instance, decreased extraversion was found to predict more chronicity[9] and increased neuroticism and decreased extraversion were found to predict an unfavorable course of depression, dysthymia, and chronic depression.[10]

Personality has been found to predict treatment response in depressed patients[11] but findings have been inconsistent. Some studies found little association between personality and treatment response.[12] Others observed certain personality traits to be associated with lower treatment response to pharmacotherapy[13] and pharmacotherapy with cognitive-behavioral therapy (CBT).[14] Conversely, increased extraversion has been shown to predict a better response to pharmacotherapy[15] and cognitive therapy[16] and decreased neuroticism has been shown to predict better response to CBT.[17] The issue is complicated because the role of personality could be treatment-specific. For instance, one study found that patients with personality problems responded better to CBT than to interpersonal therapy[18] and another found that patients with high neuroticism responded better to antidepressants than to CBT.[19] Apart from true associations, the variability in these findings could arise from different study designs (eg, open label[12,13] vs randomized controlled[18]), personality definitions/measurements (eg, Neuroticism-Extraversion-Openness Five-Factor Inventory [NEO-FFI][12] vs rating scales[16]), and depression outcome evaluations. These differences imply that the perceived role of personality might depend on study design and context.

When evaluating the association of personality with treatment response in the context of primary care where the majority of MDD patients receive their treatment, 2 aspects are important to address. First, personality variations should be operationalized in a way that is translatable to the clinical context. Personality traits could be useful for this because they capture the normal personality variations encountered in primary care. In research, however, traits are mostly adjusted for each other's effects in multivariate models. The resulting independent effects are scientifically informative, but translate poorly to individual patients. Ideally, trait scores

Clinical Points

- Normal variations in personality among primary care depressed patients can be captured by 2 empirically based, yet clinically meaningful, subtypes: "vulnerable" and "resilient."
- Depressed patients with a vulnerable personality pattern show slower recovery of depressive symptomatology over time but a stronger response to specialized treatment than those with a resilient personality pattern.
- Assessing the personality subtype of a depressed patient may help to predict whether specialized treatment (eg, CBT) will be worthwhile.

should be combined with clinically appealing categories to define subgroups with different *personality profiles*. Second, evaluations of treatment outcome should be conducted frequently and for a long enough period of time to detect all relevant fluctuations.

Building on these 2 points, the current exploratory study employed latent profile analysis (LPA)[20] to identify subgroups with different patterns on the Big Five personality traits and compared their response to treatment using a year of weekly follow-up assessments. The used data were sourced from a large trial[21] in primary care MDD patients comparing the effects of treatments with different intensities. Based on the above-mentioned previous work,[8,9,11] we hypothesized that personality subtypes with different levels of depression-proneness and different treatment responses would be found.

METHOD

Participants and Procedures

The data used for the current study came from a randomized controlled trial[21,22] in primary care depressed patients conducted between January 1998 and June 2003 (all participants diagnosed with a MDD according to the *DSM-IV*). After inclusion, patients were randomly allocated to 1 of 4 treatment conditions by a ratio of 2:3:1:1 for care as usual (CAU), the psychoeducational prevention program (PEP), psychiatric consultation plus PEP (PC + PEP), and CBT plus PEP (CBT + PEP).[21] Randomization was stratified by antidepressant use.

Participants were recruited from 49 general practices in the Netherlands. Inclusion criteria were receiving current treatment for a major depressive episode (MDE) and a history of depression. Exclusion criteria were life-threatening somatic disorders, psychotic disorder, bipolar disorder, dementia, primary alcohol/drug dependency, and receiving psychotherapy. In total, 397 patients were referred by their general practitioner (GP) and approached for a telephone screening. After receiving verbal and written information about the study, eligible patients were asked to provide written informed consent. After screening, patients were interviewed with the Composite International Diagnostic Interview (CIDI)[23] to check the inclusion and exclusion criteria. Eventually, 267 participants (67.3%) were included. The study was approved by the medical ethical committee of the University Medical Center Groningen.

Participants were included in the current analyses if they completed the NEO-FFI at baseline, still met criteria for a MDE at baseline, and completed 1 year of follow-up assessments. Two hundred fifty-one (94.0%) completed the NEO-FFI. Of these, 146 (54.7%) had a MDE at baseline and completed 1 year of followup. Included and excluded participants did not differ in mean age ($t = -1.15$; $P = .25$) and years of education ($t = 1.0$; $P = .31$). There were more women in the included compared to the excluded group (69.2% vs 57.9%). This difference was borderline significant ($\chi^2 = 3.69$; $P = .06$).

Treatment Conditions

In all treatment arms, patients received CAU, consisting of care by a GP according to national guidelines (brief counseling, antidepressants, and/or referral). The PEP arm consisted of three 90-minute sessions to formulate a prevention plan with a trained practitioner, followed by trimonthly telephone followups. The accompanying intervention book and video were based on an existing method.[24] The PC + PEP arm consisted of a 1-hour session with a psychiatrist, who thereupon advised the GP to optimize antidepressant treatment, followed by PEP. The CBT + PEP arm consisted of 10–12 sessions of CBT, followed by PEP. CBT was manual guided and focused on (social) activation, restructuring of dysfunctional thoughts/cognitions, and improvement of social skills. Previously, no efficacy difference was found between CAU and PEP, nor between PC + PEP and CBT + PEP on interview-based outcomes.[21] Therefore, pooled primary treatment (CAU and PEP; n = 99, 67.8%) and specialized treatment (CAU + PC + PEP and CAU + CBT + PEP; n = 47, 32.2%) groups were used in the present study to preserve power. Note that the employed selection procedure compromised the original randomization, making the data suitable only to explore, and not to experimentally confirm personality effects on treatment.

Measures

Participants were assessed with the lifetime CIDI at baseline, followed by trimonthly follow-up assessments. At every follow-up, an adapted version of the CIDI was used to assess the 9 *DSM-IV*–criterion symptoms for MDD in the current and the 12 preceding weeks, resulting in 52 consecutive weekly symptom counts.[25] Baseline symptoms were also divided into more specific "somatic" (appetite/weight, sleep, energy, and psychomotor) and "cognitive/affective" (sadness, anhedonia, worthlessness/guilt, cognitive, and suicidality) symptoms. The NEO-FFI[26] was administered at baseline and at follow-up. Follow-up duration varied across patients with 24-month (15.2%), 27-month (4.5%), 30-month (6.1%), 33-month (5.3%), and 36-month (68.9%) followups. The mean follow-up duration was 33.2 months (SD = 4.6).

At baseline, the CIDI was used to assess the number of prior depressive episodes. The Beck Depression Inventory (BDI)[27] was administered to assess depression severity, and its cognitive/affective (items 1–14) and somatic (items 15–21) subscales were computed. The Symptom Checklist-90 (SCL-90)[28] was administered to assess overall psychopathology, and the Medical Outcomes Study Short-Form-36 Health Survey (SF-36)[29] to assess health-related quality of life. Antidepressant use, age, gender, years of education, employment status, and social status (having a partner or not) were also assessed.

Statistical Analyses

Latent profile analysis was used to identify the optimal number of latent classes to describe the heterogeneity in NEO-FFI profiles. Models with increasing numbers of classes were compared and the optimal model was selected using the Akaike information criterion (AIC) and Bayesian information criterion (BIC), with the lowest values indicating the best fit.[30] In addition, the bootstrapped likelihood ratio test (BLRT) was used to assess if adding a *k*th class significantly improved model fit.[30] Out of practical considerations, the minimum class size was also considered for each model. Latent profile analysis was conducted with Mplus 5.0[30] on baseline data and again on follow-up data to evaluate model stability.

Cross-sectional differences on baseline characteristics were investigated with *t* tests, χ^2 tests, or nonparametric alternatives. The longitudinal course of depression was investigated with linear mixed models using depressive symptom count as the dependent variable and time as predictor variable. Time was centered at the first observation. Random intercepts and slopes were estimated and removed if proven redundant. In addition, different covariance structures were tested and the best option was selected with the AIC and BIC. All analyses were bootstrapped 50 times to produce unbiased standard errors. In preliminary analyses, the AIC and BIC were used to evaluate if a linear, logarithmic (with ln[time]) or quadratic (with time and time-squared) model best fit the data. In the first main analysis, course trajectory differences between the personality classes were tested by inclusion of a class variable (0/1) and the "class × time" interaction (or its nonlinear counterpart, if applicable). In the second analysis, differences in treatment effect across classes were investigated by inclusion of a discrete treatment-variable (0 = primary/1 = specialized) and all applicable 2- and 3-way interactions of class, treatment, and time. A significant class × treatment × time interaction would indicate different treatment-specific course trajectories for each personality class. All analyses were adjusted for the following covariates: baseline severity, antidepressant use (0/1), gender (0/1), and age. A history with ≥ 3 prior depressive episodes (0/1) was added since previous work showed treatment to be effective only in those with 3 or more prior episodes.[21] Analyses were conducted with XTMIXED in Stata 12.0 (StataCorp, College Station, Texas).

RESULTS

Baseline Characteristics

Sample characteristics at baseline are shown in Table 1. Of the sample, 69.2% was female, 63.7% was employed, and 70.5% was married/in a relationship. The mean age was 43.5 years (SD = 10.8), and the mean years of education was 12.3 (SD = 3.5), the mean number of MDE-criteria was 6.9 (SD = 1.3), the median number of previous depressive episodes was 2 (IQR, 0–4), and 113 participants (77.4%) used antidepressants. A mean BDI score of 19.6 (SD = 9.1) indicated moderate depression severity.[31] Neuroticism was moderately correlated with the BDI ($\rho = 0.44$; $P < .001$) and the CIDI depression rating ($\rho = 0.37$; $P < .001$).

Latent Profile Analyses

The LPA results are shown in Table 2. The BIC was lowest for the 2-class model. A significant BLRT *P* value indicated that this model fit better than a 1-class solution and both classes were sufficiently sized for further analyses. The personality profiles of the 2 classes are displayed in Figure 1A. Class 1 (n = 94, 64.4%) constituted a *vulnerable* class, which was characterized by high neuroticism, low extraversion, and low conscientiousness, compared to class 2 (n = 52, 35.6%), which was labeled *resilient*.

At follow-up, a 2-class model again seemed most optimal when class sizes were considered in addition to the BIC and BLRT. The personality profiles were very similar to those at baseline (Figure 1B), except for lower neuroticism scores in both classes, most likely reflecting recovery effects.[32] Due to these recovery effects and the large time lag, it was unlikely that the model was measurement invariant. Still, to get an idea of model stability, class transitions were investigated in those with 2 assessments (n = 132, 90.4%). Forty-nine of 83 (59.0%) stayed in the vulnerable class and 39 of 49 (79.6%) stayed in the resilient class.

Together, these results indicated that a distinction could be made between 2 personality classes, reflecting stable traits but also containing a state aspect, which could explain class transitions.

Personality Class Characteristics

The baseline characteristics of the classes are shown in Table 1. There were no differences on demographic characteristics. Depression severity (BDI) and several SCL-90 domains (depression, anxiety, somatization, interpersonal sensitivity, and hostility) were higher for the vulnerable class. Interestingly, there were no differences in CIDI- and BDI-assessed somatic symptoms, whereas cognitive/affective symptoms were higher in the vulnerable class. The resilient class scored higher on the SF-36 subscales social functioning, vitality, and mental health. Treatment condition, baseline antidepressant use, and treatment adherence did not differ between classes.

To check the extent to which class membership simply reflected quantitative differences in depression severity rather than qualitative differences in personality, the ability

Table 1. Total Sample and Class-Specific Demographic and Clinical Characteristics at Baseline (Total N = 146)

Variable	Class 1, Vulnerable	Class 2, Resilient	Test Statistic	*P* Value	Total Sample
Number	94	52			146
Gender, female, n (%)	66 (70.2%)	35 (67.3%)	0.13	.72	101 (69.2%)
Age, mean (SD), y	43.0 (10.2)	44.2 (11.8)	−0.61	.55	43.5 (10.8)
Years of education, mean (SD)	12.5 (3.8)	12.1 (3.1)	0.52	.61	12.3 (3.5)
Unemployment, n (%)	38 (40.4%)	15 (28.8%)	1.9	.16	53 (36.3%)
Social status; married/relationship, n (%)	65 (69.1%)	38 (73.1%)	0.3	.62	103 (70.5%)
NEO-FFI scale scores, mean (SD)					
Neuroticism	46.3 (4.7)	37.3 (5.3)	10.6	<.001	43.1 (6.5)
Extraversion	29.3 (5.4)	36.9 (6.0)	−7.8	<.001	32.0 (6.7)
Openness	37.0 (5.9)	34.6 (5.6)	2.4	.02	36.2 (5.9)
Agreeableness	43.4 (5.6)	46.3 (5.1)	−3.1	.003	44.4 (5.6)
Conscientiousness	37.7 (4.8)	43.8 (4.9)	−7.2	<.001	39.8 (5.7)
CIDI-based baseline symptoms, mean (SD)					
Total symptoms	7.2 (1.3)	6.4 (1.2)	3.8	<.001	6.9 (1.3)
Cognitive/affective symptoms	4.3 (0.7)	3.6 (0.8)	5.4	<.001	4.1 (0.8)
Somatic symptoms	2.9 (0.8)	2.8 (0.9)	0.8	.43	2.9 (0.8)
Previous depressive episodes, median (IQR)	3.0 (1.0–5.0)	2.0 (0.0–4.0)	M-W	.01	2.0 (0.0–4.0)
SCL-90 scales, mean (SD)					
Depression	49.1 (12.0)	38.5 (9.8)	5.4	<.001	45.3 (12.3)
Anxiety	24.8 (8.7)	20.8 (7.0)	2.9	.004	23.4 (8.3)
Agoraphobia	14.4 (6.8)	11.5 (4.8)	3.1	.003	13.4 (6.3)
Somatic complaints	30.0 (10.0)	24.8 (7.6)	3.5	.001	28.2 (9.6)
Interpersonal sensitivity	42.0 (13.4)	29.2 (8.2)	7.1	<.001	37.4 (13.3)
Hostility	11.5 (4.8)	9.0 (2.3)	4.3	<.001	10.6 (4.2)
Sleep problems	9.2 (3.3)	8.1 (3.7)	1.9	.07	8.8 (3.5)
BDI scales, mean (SD)					
Total scale	24.6 (8.9)	17.8 (6.7)	4.6	<.001	19.6 (9.1)
Cognitive affective	16.5 (6.4)	10.3 (5.2)	5.8	.03	12.6 (7.0)
Somatic	8.4 (3.6)	7.5 (2.8)	1.6	.11	7.3 (3.2)
Physical health and functioning, mean (SD)					
Number of chronic diseases	1.6 (1.2)	1.4 (1.2)	0.90	.37	1.5 (1.2)
SF-36, social functioning	36.8 (21.8)	46.6 (17.5)	−2.8	.006	40.3 (20.9)
SF-36, physical functioning	71.6 (22.7)	77.6 (21.3)	−1.6	.12	73.8 (22.3)
SF-36, mental health	34.1 (16.1)	41.0 (13.6)	−2.6	.01	36.5 (15.6)
SF-36, vitality	23.7 (14.8)	28.8 (12.7)	−2.2	.04	25.5 (14.3)
Treatment condition, n (%)					
Primary	60 (63.8%)	39 (75.0%)	1.91	.17	99 (67.8%)
Specialized	34 (36.2%)	13 (25.0%)			47 (32.2%)
Antidepressant use, n (%)	72 (76.6%)	41 (78.8%)	0.10	.76	113 (77.4%)
Treatment adherent, n (%)	88 (93.6%)	48 (92.3%)	0.09	.76	136 (93.2%)

Abbreviations: BDI = Beck Depression Inventory, CIDI = Composite International Diagnostic Interview, IQR = interquartile range, M-W = Mann-Whitney *U* test, NEO-FFI = Neuroticism-Extraversion-Openness Five-Factor Inventory, SCL-90 = Symptom Checklist-90, SF-36 = Medical Outcomes Study Short-Form 36 Health Survey.

Table 2. Indices of Fit for 1–4 Class Latent Class Models, Based on the NEO-FFI Personality Scales in Patients With Major Depressive Disorder

Characteristic	Model	*df*	AIC	BIC	aBIC	BLRT *P* Value	Smallest Group, n (%)[a]
Baseline	1-class	10	4,714	4,744	4,713	—	—
(n = 146)	2-class	16	4,679	4,726	4,676	<.001	52 (35.6%)
	3-class	22	4,672	4,738	4,668	.05	10 (6.8%)
	4-class	28	4,670	4,753	4,664	.31	5 (3.4%)
Follow-up	1-class	10	4,343	4,372	4,340	—	—
(n = 132)	2-class	16	4,274	4,320	4,270	<.001	59 (44.7%)
	3-class	22	4,245	4,308	4,239	<.001	11 (8.3%)
	4-class	28	4,229	4,310	4,221	.01	4 (3.0%)

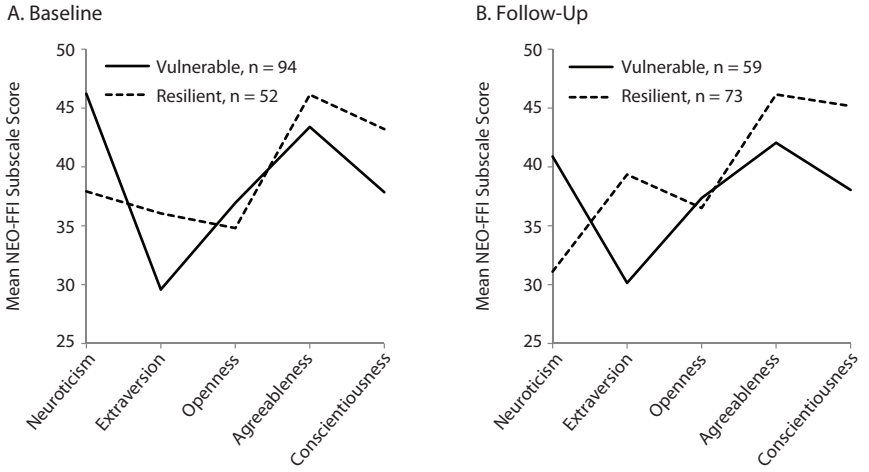
[a]Based on most likely posterior class-membership.
Abbreviations: aBIC = adjusted BIC, AIC = Akaike information criterion, BIC = Bayesian information criterion, BLRT = bootstrapped likelihood ratio test, NEO-FFI = Neuroticism-Extraversion-Openness Five-Factor Inventory.

of depression severity to predict class membership was evaluated with receiver operating characteristic curves. The area under the curve (AUC) indicated limited predictive ability for the baseline CIDI depression rating (AUC = 0.67; 95% confidence interval [95% CI], 0.58 to 0.76) and somewhat better predictive ability for the baseline BDI (AUC = 0.73; 95% CI, 0.63 to 0.82), in line with its higher correlation with neuroticism (see above). This indicated that, although class membership could be predicted to an extent by depression severity, membership did not merely reflect quantitative depression variation. All subsequent analyses were adjusted for baseline severity.

Class-Specific Depression Course

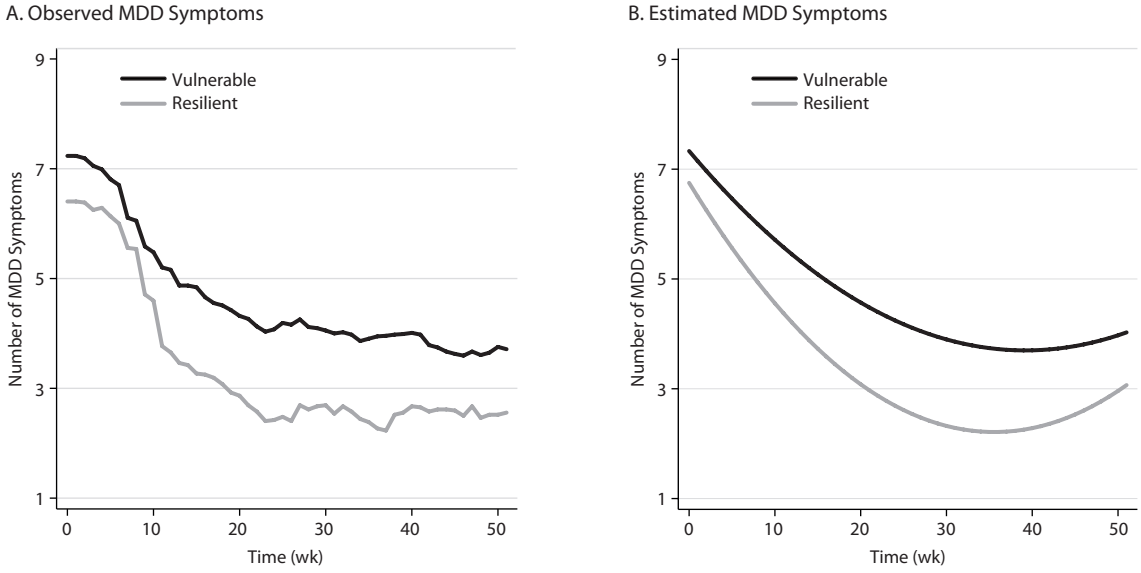
In a preliminary analysis, the best function to model the trajectories was selected. A quadratic (AIC = 25,321; BIC = 25,425) function fit better than a linear (AIC = 28,193;

Figure 1. Class-Specific Personality Profiles for the 2 Selected Latent Class Models at Baseline (A, n = 146) and Follow-Up (B, n = 132) in Outpatients With a Major Depressive Episode at Baseline



Abbreviation: NEO-FFI = Neuroticism-Extraversion-Openness Five-Factor Inventory.

Figure 2. Observed (A) and Estimated (B) Course of Depressive Symptoms Over a 52-Week Period in the Vulnerable and Resilient Personality Groups



Abbreviation: MDD = major depressive disorder.

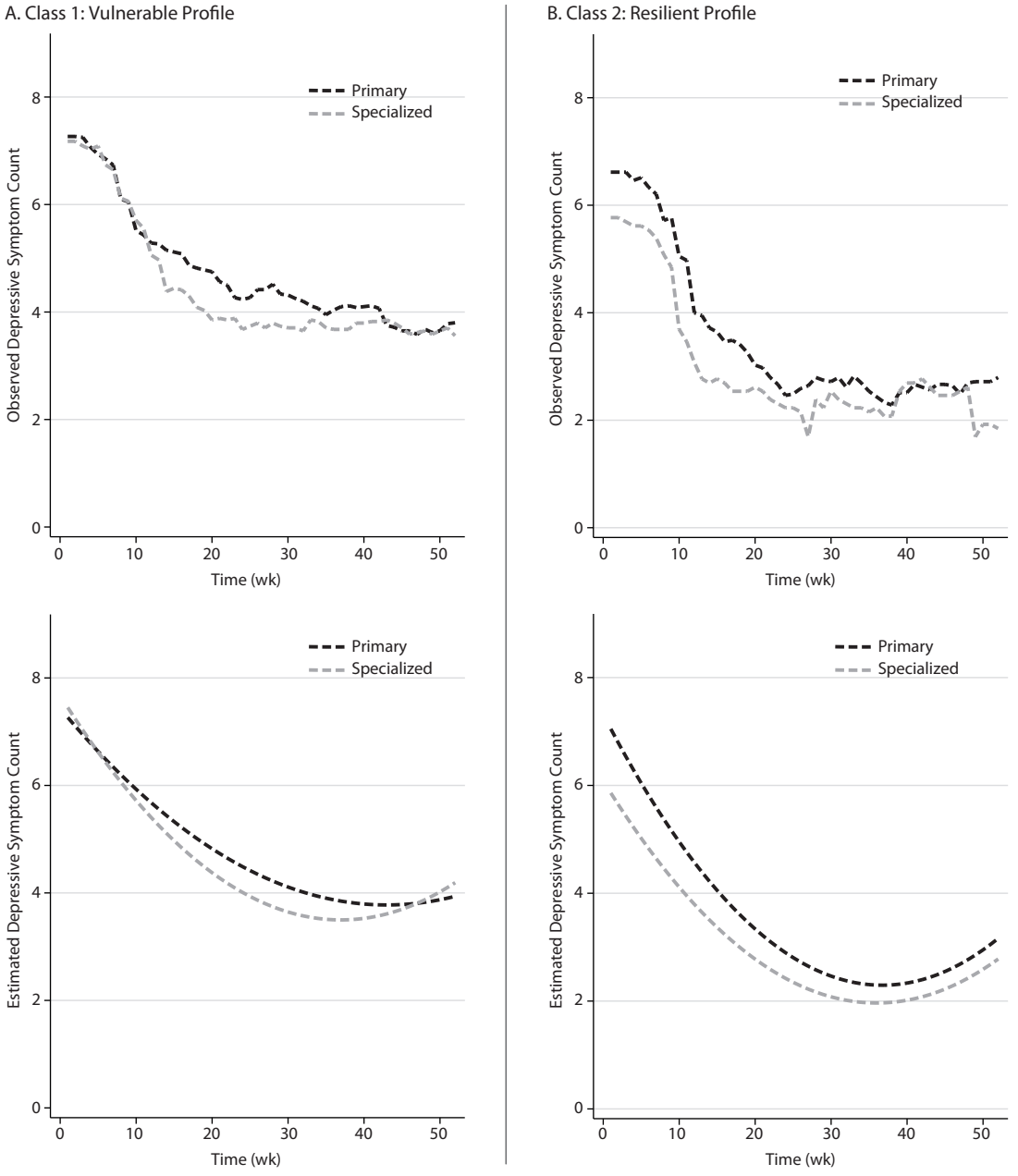
BIC = 28,276) or logarithmic function (AIC = 27,591; BIC = 27,674). Further model optimization suggested retention of random intercepts and slopes (time and time-squared) and the use of an unstructured covariance matrix (AIC = 24,972; BIC = 25,097).

The class-specific course trajectories are shown in Figure 2. The analyses on the course differences between personality classes showed significant interactions, indicating that symptom severity decreased more quickly in the resilient class than in the vulnerable class (class × time: B = −0.07; 95% CI, −0.05 to −0.09; $P < .001$, and class × time-squared: B = 0.0012; 95% CI, 0.0009 to 0.0016; $P < .001$).

Class-Specific Treatment Effects

Treatment effects differed across personality classes (see Figure 3): interactions between class, treatment, and time were significant (class × treatment × time: B = 0.10; 95% CI, 0.07 to 0.13; $P < .001$; class × treatment × time-squared: B = −0.0016; 95% CI, −0.0010 to −0.0022; $P < .001$). Stratified analyses showed that in the vulnerable class, the specialized treatment group's symptoms decreased more steeply (treatment × time: B = −0.05; 95% CI, −0.04 to −0.07; $P < .001$) and with stronger curvature (treatment × time-squared: B = 0.0011; 95% CI, 0.0008 to 0.0014; $P < .001$) than did those of the primary treatment group. In the resilient class, the

Figure 3. Different Effects of Treatment Condition on the Course of Observed and Estimated Depressive Symptom Counts in the Vulnerable and the Resilient Classes[a]



[a]The interactions "class × treatment × time" and "class × treatment × time-squared" were both significant at $P < .001$.

symptoms of the specialized treatment group decreased at a slower rate than did those of the primary treatment group (treatment × time: B = 0.04; 95% CI, 0.02 to 0.07; $P = .001$) and there was only a borderline significant difference in curvature (treatment × time-squared: B = −0.0005; 95% CI, −0.0011 to 0.0001; $P = .06$). These results indicated that the added value of specialized treatment was specific to the vulnerable class.

Although treatment subgroups were quite small in the specialized treatment group, we reran the analyses excluding CBT to investigate if CBT explained the observed effects. Here, the interaction effects of interest were smaller and only borderline significant (class × treatment × time: B = 0.06; 95% CI, 0.00 to 0.13; $P = .054$; class × treatment × time-squared: B = −0.0011; 95% CI, −0.0023 to 0.0001; $P = .08$). Stratified analyses showed that the specialized treatment group again showed a quicker decrease in symptomatology in the vulnerable class (n = 79; treatment × time: B = −0.07; 95% CI, −0.04 to −0.09; $P < .001$; treatment × time-squared: B = 0.0013; 95% CI, 0.0009 to 0.0017; $P < .001$). In the resilient group (n = 44), both interactions were nonsignificant (treatment × time: B = −0.02; 95% CI, −0.047 to 0.045; $P = .94$; treatment × time-squared: B = 0.0001; 95% CI, −0.001 to 0.001; $P = .70$). This indicates that the specific added value

of specialized treatment in the vulnerable group persisted when CBT was excluded.

DISCUSSION

The current study was aimed to explore the role of personality subtypes in depressive course and treatment effects. Latent profile analysis showed that personality variations could be described by 2 data-driven classes: a vulnerable class with high neuroticism, low extraversion, and low conscientiousness and a resilient class with comparatively lower neuroticism, higher extraversion, and higher conscientiousness. Comparing course trajectories, severity was found to decrease more slowly in the vulnerable class, in line with previous findings.[8,9] Investigation of treatment effects showed that only in the vulnerable class did specialized treatment lead to quicker recovery than primary treatment. No differences were seen in the resilient class, indicating that this group gained less from specialized treatment. Differential treatment effects were not explained by the selective effects of CBT.

The finding that people with a vulnerable personality profile benefit more from specialized interventions is of clinical interest and could have several explanations. First, there may be more room for improvement in vulnerable patients, who can therefore benefit more from specialized treatments than from primary treatments. Second, primary treatments might lack the power to affect vulnerable patients, resulting in comparatively slow recovery. Third, vulnerable patients may benefit more from specialized efforts because they need more focused/specific interventions to affect their dysfunctional, personality-based predisposition. Closer inspection of the personality profiles could help to explain the underlying mechanisms. High neuroticism is marked by high sensitivity and nervousness and the tendency to experience negative affect.[26] Cognitive-behavioral therapy is aimed to affect emotional dysregulation through behavioral and cognitive pathways by stimulating behavioral activation, leading to a more rewarding life and bolstering of self-esteem.[33,34] In addition, patterns of biased and dysfunctional cognitions and schemata are targeted.[35] However, the effect of specialized treatment was not solely explained by CBT, suggesting that psychiatric consultation must be effective as well. Psychiatric consultation was aimed at psychopharmacologic fine-tuning, which has been shown to have beneficial effects on long-term outcomes[36] and could have structural effects on emotional dysregulation and negative affect.[37] The latter could explain why in the current study, specialized treatment was effective, irrespective of treatment type. This is in line with work showing well-managed pharmacotherapy to be equally as effective as CBT.[38] However, we were unable to investigate longer-term efficacy differences.[39]

The presented classes are of clinical interest. Previous studies showed the importance of personality traits for depression treatment,[8,10,15–19] but did not directly translate this to clinically useful groups. The current findings show that the predictive value of personality traits can also be captured with clinically appealing personality profiles that can serve as prototypes against which clinicians can compare their patients.

Strengths of this study included its intensive, high-resolution follow-up and its diverse treatment arms. However, there were some limitations. First, the study was purely observational. Second, participant exclusion may have caused selection bias. Third, LPA models provide raw, discrete approximations of reality, and their interpretability is limited by assuming no (co)variance within classes (local independence). Fourth, sample attrition prevented a full investigation of LPA-model invariance. Fifth, the number of GP visits was not recorded, so comparison of CAU characteristics across conditions was impossible. Sixth, previous work showed that PEP may worsen the outcome in severe patients, which might explain why the vulnerable group recovered better with enhanced treatment. Seventh, the limited sample size prevented thorough comparisons across different types of specialized treatment. Future experimental studies could address this interesting issue.

In conclusion, the current study showed that simple data-driven personality profiles can be used to differentiate between those patients that will and those that will not benefit from specialized interventions. These findings illustrate the importance of accounting for interindividual heterogeneity when planning treatment. In addition, the findings indicate that patients with a vulnerable predisposition may have a relatively increased need for specialized treatment.

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