

Associations Between Personality Traits and Adherence to Antidepressants Assessed Through Self-Report, Electronic Monitoring, and Pharmacy Dispensing Data

A Pilot Study

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Abstract: Treatment with antidepressants is often compromised by substantial nonadherence. To understand nonadherence, specific medication-related behaviors and beliefs have been studied, but less is known about broader and temporally stable personality “traits.” Furthermore, adherence has often been assessed by a single method. Hence, we investigated associations between the Big Five personality traits and adherence assessed by self-report, electronic drug use monitoring, and dispensing data. Using the Big Five Inventory, we assessed the personality traits “openness,” “conscientiousness,” “extraversion,” “agreeableness,” and “neuroticism” of patients treated with antidepressants who were invited through community pharmacies. Self-reported adherence was assessed with the Medication Adherence Rating Scale (score >24), electronic monitoring with medication event monitoring system (MEMS) devices (therapy days missed $\leq 10\%$ and < 4 consecutive days missed), and dispensing data (medication possession ratio $\geq 80\%$). One hundred four women and 33 men participated (mean age, 51; standard deviation, 14). Paroxetine was most frequently prescribed (N = 53, 38%). Logistic regression analysis revealed that of the personality traits, the third and fourth quartiles of “conscientiousness” were associated with better self-reported adherence (odds ratio, 3.63; 95% confidence interval, 1.34–9.86 and odds ratio, 2.97; 95% confidence interval, 1.09–8.08; $P \leq 0.05$). No relationships were found between personality traits and adherence assessed through electronic drug use monitoring or dispensing data. We therefore conclude that adherence to antidepressant therapy seems to be largely unrelated to personality traits.

Key Words: adherence, compliance, antidepressants, personality traits, electronic drug use monitoring, self-report

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Antidepressants are often prescribed^{1,2} for various disorders that require long-term treatment.³ However, nonadherence to and premature discontinuation of antidepressant therapy have been found to be substantial.^{4–6} Nonadherence to antidepressant therapy is a serious problem because it was previously found to

be associated with an increased relapse risk.⁵ Numerous specific factors have been associated with nonadherence to antidepressant therapy including beliefs about medicines,^{7,8} experience of adverse side effects,⁹ and perceived stigma.¹⁰

By contrast, less is known about associations between nonadherence to antidepressant therapy and broader personality “traits” that are relatively stable over time, particularly during mid-life.¹¹ In the clinical and health psychology literature, consensus has been reached that the numerous individual differences can be reduced to 5 broad traits: “extraversion,” “neuroticism,” “conscientiousness,” “agreeableness,” and “openness to experience,” which collectively are known as the Big Five personality traits.¹²

Previously, in a small sample of patients with depression, Cohen et al¹³ found “extraversion” to be associated with nonadherence. Furthermore, in several other patient groups, associations were found between personality traits and nonadherence. “Conscientiousness” was found to be associated with better adherence to asthma medication,¹⁴ antibiotics,¹⁵ cholesterol lowering treatment,¹⁶ and to clinic-based rehabilitation activities,¹⁷ renal dialysis,¹⁸ as well as with an increase in number of CD4 cells and a decrease of viral load and better medication adherence in HIV patients.¹⁹ Furthermore, “openness” and “agreeableness” were found to be associated with better adherence to asthma medication in male patients,¹⁴ whereas “agreeableness” was also found to be associated with more frequent attendance to clinic-based rehabilitation activities¹⁷ and adherence to antibiotics.¹⁵ Finally, “neuroticism” was found to be associated with difficulties to develop routines of asthma medication taking²⁰ and adherence to antibiotics.¹⁵

However, a frequently encountered problem in adherence research is that the assessment of adherence is limited to a single method with its own particular flaws. Inferring adherence from electronic drug use monitoring and dispensing data is likely to be more objective than self-reported adherence which may be liable to social desirability bias.^{19,21} Yet, the latter may be useful to inform clinicians about whether nonadherence was of a more *unintentional*, for example, forgetting or *intentional* or more deliberate nature. Corroboration of an association found with 1 assessment method of adherence by another measure of adherence is therefore warranted.

After the previous findings, the aim of the present study is therefore to examine relationships between the Big Five personality traits and adherence to antidepressant therapy as assessed by 3 different measures, namely, self-report, electronic drug use monitoring, and dispensing data.

MATERIALS AND METHODS

Study Design and Setting

Participants were patients who were invited through five community pharmacies from the Utrecht University Pharmacy

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Practice Research Network.²² All pharmacies have automated dispensing records, which include information on a patient's sex, date of birth, and dispensed medicines. Information on dispensed medicines includes dispensing date, type of prescriber, type of medicine, amount dispensed, prescribed dosage regimen, and the estimated duration of use. The duration of drug use was estimated by dividing the number of dispensed units by the prescribed number of units per day. All drugs were coded according to the Anatomical Therapeutic Chemical classification index.²³

Participants

The patient selection procedure took place between April 2011 and April 2012. Patients were eligible if they were 18 years or older and if they were being treated with an antidepressant (Anatomical Therapeutic Chemical codes N06AB, N06AF, N06AG and N06AX). Depending on the number of patients in a pharmacy, every fourth or fifth patient was selected for participation. Eligible patients received an invitation to participate in the study and a questionnaire about sociodemographic characteristics (sex, age, marital status, and educational level), medication use including previous use of antidepressants, disease characteristics, the Big Five Inventory (BFI),²⁴ and the Medication Adherence Rating Scale (MARS).²⁵ Participants were asked to return the completed questionnaire within 2 weeks. In case of nonresponse, they received 3 reminders by mail. The index date was defined as the date on which the signed informed consent and the questionnaire were received. Participants were also asked to get their antidepressants dispensed in a special medication event monitoring container (MEMS; Aardex, Zug, Switzerland). The medical ethical committee of the University Medical Center of Utrecht approved the study. All participants provided written informed consent.

Adherence to Antidepressant Therapy

Adherence to antidepressant therapy was assessed through self-report, electronic drug use monitoring, and drug dispensing data. Figure 1 shows the time windows during which the data of these different adherence measures were collected. Self-reported adherence was assessed using the MARS.²⁵ The MARS consists of 5 items and asks participants to report on how frequently they engage in the following specific nonadherence behaviors: forget using antidepressants, altering the dose, stop using antidepressants for a while, deciding to skip a dose, and using less than prescribed. Each item was rated on a 5-point scale (1 = always, 5 = never). A total score of the 5 items was calculated with higher scores being indicative of better adherence (range, 5–25).

Electronic drug use monitoring was done with MEMS devices. The MEMS devices registered times and dates of moments when the medication vial had been opened. This device allowed for monitoring of participants' daily drug use. All MEMS data were downloaded at the end of the study period. From these data, we inferred 2 adherence measures. First, we assessed

the percentage of missed therapy days by dividing the number of days missed by the total duration of MEMS days multiplied with 100, thus higher percentages reflected worse adherence. Second, we assessed how many participants did not take antidepressants on consecutive days.

Information on all dispensed medication of the study population was extracted from the drug dispensing data. So-called treatment episodes were constructed for each participant in the way as described elsewhere.²⁶ As a measure of adherence assessed from the drug dispense data, we estimated the medication possession ratio (MPR) for the last treatment episode prior to the index date or the "number of days supply between the first prescription within a treatment episode and the index date" and "the number of days elapsing between the first prescription within a treatment episode and the index date." Higher MPR percentages reflected better adherence.

The BFI

Personality traits were assessed with a validated Dutch version of the BFI.²⁴ The BFI consists of 44 items with 5-point Likert scales (1, strongly disagree; 5, strongly agree) that measure the Big Five personality traits of "extraversion," "neuroticism," "conscientiousness," "agreeableness," and "openness to experience." "Extraversion" is characterized by positive emotions, pronounced engagement with the external world, and being assertive and energetic. "Neuroticism" refers to the degree to which a person responds to distress, emotional reactivity, and vulnerability to stress. People who score high on "conscientiousness" are goal-oriented, reliable, and have a preference for planned rather than spontaneous behavior. "Agreeableness" refers to the degree to which we defer to others, being tolerating and accepting, rather than being hostile and aloof. "Openness to experience" refers to how open people are to new experiences, their flexibility, and their ability to deal with chaos.²⁷

To examine whether the BFI items were measuring the personality trait they were purported to measure, BFI items were subjected to a factor analysis (varimax rotation). The factor analytic solution was reasonably consistent with the solution presented by Denissen et al.²⁴ The 5 personality dimensions explained 47% of the variance in item responses. The personality traits "extraversion" (Cronbach $\alpha = 0.82$), "neuroticism" (Cronbach $\alpha = 0.84$), "openness" (Cronbach $\alpha = 0.79$), and "conscientiousness" (Cronbach $\alpha = 0.79$) had high internal consistencies, whereas "agreeableness" (Cronbach $\alpha = 0.70$) had sufficient internal consistency. Accordingly, for every participant, total scores for the 5 personality dimensions were calculated by summing the items measuring these personality dimensions.

Statistical Analysis

Descriptive statistics were calculated for participants' sociodemographic and disease characteristics, and the adherence measures. Spearman's rank correlations (r_s) were calculated to examine

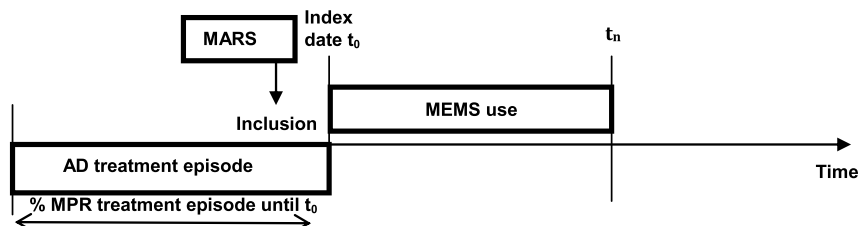


FIGURE 1. Time windows of adherence measures collected in the study population.

associations between participants' characteristics and the Big Five personality traits as well as the adherence measures.

Associations between adherence and the Big Five personality traits were examined in separate multiple logistic regression models with the adherence measures as the dependent variables and were restricted to participants who had all adherence measures available. Individual Big Five personality traits were entered as independent variables, 1 personality trait per model. For these analyses, we dichotomized all adherence measures: self-reported adherence (nonadherent score ≤ 24 vs adherent score >24), percentage of therapy days missed (adherent $\leq 10\%$ vs nonadherent $> 10\%$), number of consecutive days of therapy missed (adherent 0–3 days vs nonadherent ≥ 4 days), and the MPR (nonadherent $<80\%$ vs adherent $\geq 80\%$). To examine whether levels of personality traits were differentially associated with adherence, the personality traits were divided into quartiles and represented by dummy variables in the models. Multiple regression models were adjusted for covariates which were associated with personality traits or adherence but were only retained in final multivariate models if they remained significant.

Finally, 3 sensitivity analyses were conducted. First, we altered the cutoffs scores of adherence measures. We dichotomized the MARS total score as 23 or less (nonadherent) vs greater than 23 (adherent), percentage of therapy days missed as measured with the MEMS as 20% or less (adherent) vs greater than 20% (nonadherent), examined participants who had 3 or 5 consecutive days of therapy missed, and set the MPR threshold as less than 90% (nonadherent) versus 90% or greater (adherent). Second, we restricted the examination of associations between the Big Five

personality traits and adherence as inferred from electronic drug use monitoring to participants whose drug use had been monitored for 6 months or longer. Third, we examined whether associations between personality traits and nonadherence were significantly different for male and female participants, as well as for indication of antidepressants (depression vs anxiety, depression and concomitant anxiety, or other disorders). *P* values of 0.05 or less were considered statistically significant.

RESULTS

There were 145 participants for whom MARS, MEMS, and dispensing data were available. Of them, 121 (83%) responded immediately, whereas 24 (17%) responded after 1 to 3 reminders. After excluding 8 participants who had an incomplete BFI, data from 137 participants were included in the analysis (Fig. 2). Three quarters of the participants were women and had a spouse or partner, almost half of the participants had attained an intermediate educational level, the majority were treated with paroxetine, and about half had been treated with antidepressants before. Two fifths were treated for depression whereas the remaining participants were treated with antidepressants for anxiety, for depression with concomitant anxiety, or other disorders (Table 1).

The mean score for “extraversion” was 22.3 (SD, 5.7; minimum score, 11; maximum score, 37), for “neuroticism,” 24.5 (SD, 5.5; minimum score, 9; maximum score, 34), for “openness,” 31.5 (SD, 6.2; minimum score, 15; maximum score, 47), “conscientiousness,” 29.1 (SD, 5.2; minimum score, 13; maximum score, 41), and for “agreeableness,” 29.8 (SD, 4.6; minimum

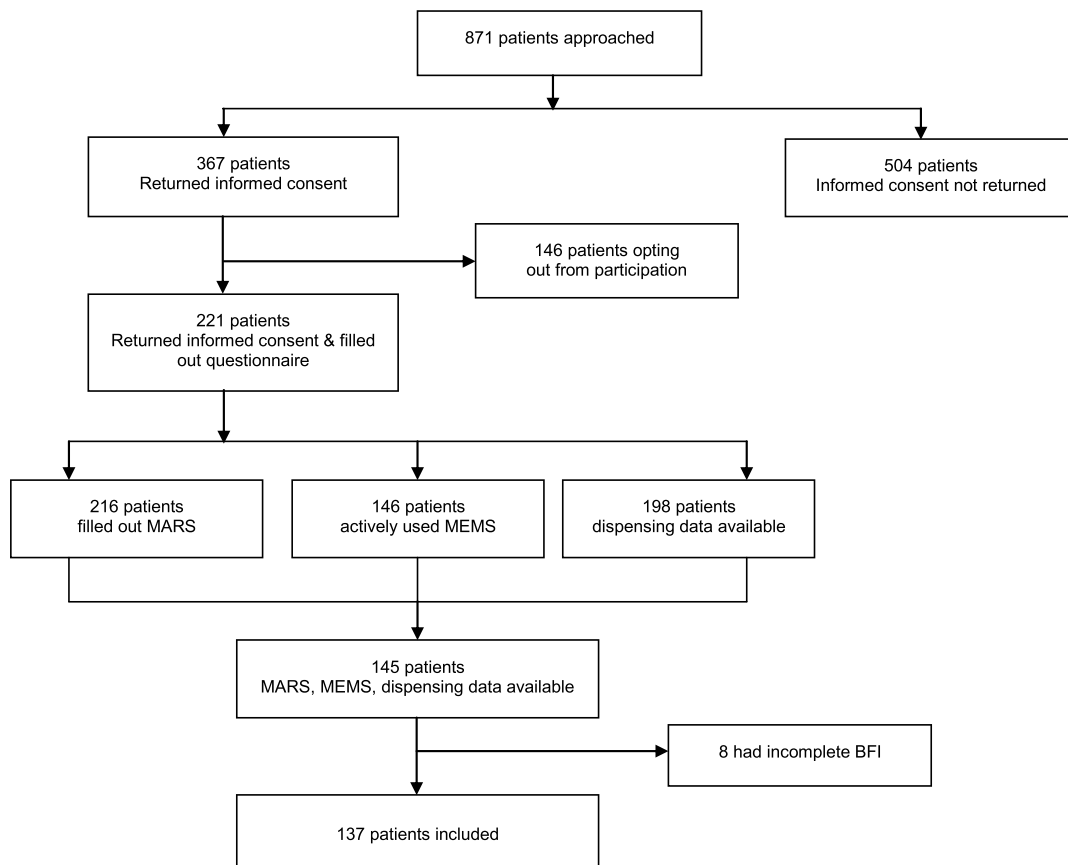


FIGURE 2. Flowchart of patient inclusion.

TABLE 1. Demographic and Clinical Characteristics of the Participants (N = 137)

Characteristics	Statistic
Women, n (%)	104 (76)
M (SD) age	51 (14)
With spouse/partner, n (%)	100 (73)
Educational level, n (%)	
Low	27 (20)
Intermediate	63 (46)
High	46 (34)
Type of antidepressant, n (%)	
Paroxetine	53 (38)
Fluoxetine	9 (7)
Fluvoxamine	3 (2)
Sertraline	5 (4)
Citalopram	28 (20)
Venlafaxine	24 (18)
Escitalopram	6 (4)
Other	9 (7)
N (%) used antidepressants before	65 (47)
Diagnosis	
Depression	57 (41)
Anxiety	31 (23)
Depression and anxiety	44 (32)
Other	5 (4)

score, 14; maximum score, 39). Being male was associated with lower levels of “conscientiousness” and “agreeableness.” Advancing age was associated with higher levels of “agreeableness,” and living together with a spouse or a partner was associated with higher levels of “extraversion.” Higher educational level was associated with higher levels of “openness.” No associations were observed between previous use of antidepressants and personality traits (see Table 2).

Based on the MARS, 66 participants (48%) were judged as adherent for a cutoff score greater than 24. Based on the percentage of therapy days missed as measured with the MEMS, 91 participants (66%) were adherent for a cutoff score of 10% or less, and 92 (67%) had not skipped antidepressants for 4 or more consecutive days. Based on the MPR, 122 (89%) were adherent if the cutoff score was set at 80% or greater. Female participants were more often adherent according to self-report than male participants (MARS > 24: 53% vs 33%, $\chi^2(df, 1) = 3.84$, $P = 0.05$). Furthermore, higher educated participants were less

often adherent according to self-report than participants with intermediate to low education (MARS > 24: 39% vs 46% and 70%, $\chi^2(df, 2) = 6.94$, $P = 0.03$).

Multiple regression analyses revealed significant associations between the third and fourth quartiles of “conscientiousness” and better self-reported adherence (MARS cutoff score >24) (Table 3). Further analyses of associations between “conscientiousness” and item specific self-reported adherence behavior showed that being conscientious was associated with not forgetting to take antidepressants: odds ratio third quartile = 4.21 (95% confidence interval, 1.53–11.60; $P = 0.006$) and odds ratio fourth quartile = 3.16 (95% confidence interval, 1.16–8.61; $P = 0.02$) but not the other self-reported adherence behaviors (all P s > 0.05). No associations were observed between personality traits and assessment of adherence through electronic drug use monitoring with MEMS (overall percentage of therapy days missed and number of consecutive therapy days missed) or MPR calculated from the dispensing data, except for an association between the third quartile of “agreeableness” and less than 4 consecutive days missed.

In the sensitivity analyses, the associations between “conscientiousness” and self-reported adherence lost their significance, whereas no other significant associations emerged (results from sensitivity analyses available on request).

DISCUSSION

We found the third and fourth quartiles of “conscientiousness” to be associated with better self-reported adherence. This finding is inconsistent with findings by Cohen et al¹³ who found “extraversion” to be associated with nonadherence, yet consistent with an accumulating body of evidence showing associations between “conscientiousness” and adherence in various patient groups.^{14–20}

However, given that this finding was not corroborated when adherence was assessed by electronic drug use monitoring with MEMS devices or by the MPR calculated from the dispensing data, and also lost significance in the sensitivity analysis, the evidence for an association between higher levels of “conscientiousness” and better adherence to antidepressant therapy is actually limited. Furthermore, unlike in other research,^{13–15,17} “extraversion,” “neuroticism,” “openness,” and “agreeableness” were not found to be associated with adherence regardless of whether adherence was measured through self-report, MEMS, or drug dispensing data. Only an association between the third quartile of “agreeableness” and less than 4 consecutive therapy days missed was observed.

Given that consensus has been reached that these personality traits cover the majority of stable individual personality differences,¹²

TABLE 2. Correlations (Spearman ρ) Between Big Five Dimensions and Participants' Characteristics

Characteristics	Extraversion	Neuroticism	Openness	Conscientiousness	Agreeableness
Male sex	−0.16	−0.03	0.10	−0.31 [†]	−0.30 [†]
Age	0.04	−0.13	0.07	0.14	0.25 [†]
Living together	0.17*	−0.03	0.02	0.12	−0.04
Educational level	−0.07	0.02	0.23 [†]	−0.01	−0.08
Previous AD use	−0.09	0.05	−0.00	0.15	0.06

* $P \leq 0.05$.

[†] $P \leq 0.01$.

AD indicates antidepressants.

TABLE 3. Multiple Logistic Regression Analysis: Associations Between Big Five Scores and Adherence as Assessed With the MARS, MEMS and the MPR

Personality Traits	Self-Report		MEMS Days Missed		MPR
	MARS > 24 (N = 66, 48%) OR (95% CI)	≤10% (N = 91, 66%) OR (95%CI)	<4 consecutive days (N = 92, 67%) OR (95%CI)	≥80% (N = 122, 89%) OR (95%CI)	
Extraversion					
First quartile	Reference	Reference	Reference	Reference	
Second quartile	1.18 (0.45–3.14)*	1.13 (0.40–3.17)	2.09 (0.75–5.86)	0.38 (0.06–2.20)	
Third quartile	1.43 (0.56–3.64)*	0.71 (0.28–1.82)	1.79 (0.69–4.63)	0.37 (0.07–2.02)	
Fourth quartile	1.74 (0.65–4.67)*	0.92 (0.33–2.57)	1.46 (0.54–3.94)	0.36 (0.06–2.12)	
Neuroticism					
First quartile	Reference	Reference	Reference	Reference	
Second quartile	0.75 (0.29–1.98)*	1.05 (0.39–2.84)	1.39 (0.50–3.89)	1.50 (0.38–5.86)	
Third quartile	0.39 (0.14–1.05)*	1.00 (0.37–2.72)	0.88 (0.33–2.36)	3.10 (0.58–16.59)	
Fourth quartile	1.00 (0.38–2.64)*	0.92 (0.34–2.46)	0.92 (0.34–2.46)	2.07 (0.47–9.03)	
Openness					
First quartile	Reference	Reference	Reference	Reference	
Second quartile	0.84 (0.33–2.09)*	1.40 (0.53–3.70)	1.08 (0.42–2.78)	0.69 (0.17–2.80)	
Third quartile	0.87 (0.33–2.33)*	0.88 (0.34–2.25)	1.30 (0.49–3.44)	0.84 (0.19–3.63)	
Fourth quartile	1.44 (0.49–4.23)*	0.86 (0.30–2.47)	0.86 (0.30–2.47)	1.19 (0.20–7.03)	
Conscientiousness					
First quartile	Reference	Reference	Reference	Reference	
Second quartile	1.55 (0.58–4.14)*	1.44 (0.54–3.84)	1.67 (0.61–4.54)	0.83 (0.19–3.61)	
Third quartile	3.63 (1.34–9.86)* [†]	1.15 (0.44–2.98)	1.50 (0.56–3.99)	0.86 (0.20–3.73)	
Fourth quartile	2.97 (1.09–8.08)* [†]	1.53 (0.56–4.19)	1.14 (0.43–3.02)	1.07 (0.22–5.17)	
Agreeableness					
First quartile	Reference	Reference	Reference	Reference	
Second quartile	0.76 (0.30–1.93)*	1.25 (0.49–3.17)	2.26 (0.87–5.91)	1.83 (0.32–10.68)	
Third quartile	0.97 (0.36–2.62)*	2.83 (0.95–8.47)	4.34 (1.38–13.66) [†]	0.53 (0.13–2.19)	
Fourth quartile	1.24 (0.48–3.21)*	1.70 (0.64–4.49)	1.81 (0.70–4.70)	0.81 (0.19–3.50)	

*Adjusted for educational level.

[†] $P \leq 0.05$.

OR indicates odds ratio; 95% CI, 95% confidence interval.

it seems plausible that personality is *largely* unrelated to adherence in patients who are treated with antidepressants. Of course, more follow-up research is needed to examine the generalizability of this finding.

Before reaching as a final conclusion that personality is largely unrelated to adherence in patients treated with antidepressants, it is important to explore alternative explanations for the absence of associations between personality traits and adherence to antidepressant therapy. First, although links between personality traits and depression and other mental disorders have been found,²⁸ restriction of range in scores of personality traits as a potential explanation was unlikely given that the standard deviations of the personality trait scores were sufficiently large. Second, selection bias was an unlikely explanation. Although selection bias with regard to adherence cannot be ruled out, that is, adherent patients were probably more likely to participate, a substantial number of participants were still nonadherent as was demonstrated by the MEMS data. Furthermore, individuals' decisions to participate in research may also have in part depended on their own personality traits. Previously, participation in research was found to be associated with higher levels of the personality traits "agreeableness" and "openness."²⁹ Again, however, the ample spread in personality trait levels, which we observed, seems not to support that selection bias with regard to personality traits played a major role.

Improving nonadherence by targeting its determinants is of crucial importance given that nonadherence to antidepressant therapy is substantial^{4,5} and was found to be associated with an increased relapse risk.⁵ The fact that we did not find personality traits to be associated with adherence is actually reassuring in this regard. After all, personality traits tend to be relatively stable across a large part of the lifespan¹¹ and would therefore constitute difficult to change inclinations that would provide little hope for adherence improving strategies. To better understand and improve adherence, specific experiences with regard to the efficacy, side effects, and practical problems of antidepressants are likely to be more relevant.^{30,31} These could be considered as "state variables" or variables which are more susceptible to change over time such as beliefs about medicines.³² As such, it would also be plausible that these variables are more susceptible to influence by interventions.

However, to know whether adherence is truly "state" driven, further research is needed about whether other relatively stable psychological characteristics of patients are associated with adherence to antidepressant therapy. Also, personality traits could moderate patients' specific experiences with regard to antidepressants which in turn could be reasons for nonadherence, for example, patients with higher levels of "neuroticism" may experience more often side effects and may therefore discontinue using antidepressants more often. Some relationships between personality traits and beliefs about medicines were found in asthma patients.³³

The most important strength of the current analysis was the use of self-report, MEMS, and drug-dispensing data to assess adherence. Adherence assessment is often limited by a single method usually the self-reported modality. Although self-reported adherence is generally believed to be less objective than electronic drug use monitoring because it is liable to social desirability bias, it may inform clinicians and researchers about whether nonadherence was unintentional, for example, forgetting or intentional, that is, of a more deliberate nature. Adoption of multiple assessment methods of adherence is therefore essential.²¹ With regard to the assessment of personality, a second important strength was the adoption of a standardized and validated²⁴ questionnaire to assess the Big Five personality traits. Furthermore, a strength with regard to the data analysis was that we examined a “dose-response” relationship between personality traits and nonadherence to take the possibility into account that there might be nonlinear associations between personality traits and nonadherence. Indeed, we saw “conscientiousness” being positively associated with better adherence but only from a certain level onward.

Some shortcomings of the study should also be mentioned. First, our sample size was moderate. Second, although adherence was measured longitudinally with pharmacy refill data and electronic drug use monitoring, personality traits were only assessed at the index date. We were therefore unable to verify the stability of the personality traits in our sample. Third, we studied a heterogeneity of antidepressants and perhaps adherence might be differentially related to different types of antidepressants. Fourth, we had no data about participants' personality levels before the onset of depression and/or anxiety. Therefore, we cannot be wholly sure about whether the BFI admixed the intended measurement of personality traits deemed to be stable over time with unintended measurement of depression or anxiety symptoms which could change over time. At the same time, to understand associations between personality traits and nonadherence, it makes more sense to study personality traits during depressive episodes when patients are treated with antidepressants rather than studying premorbid personality traits.

Taken together, we conclude that there were no clear relationships between personality traits and adherence to antidepressant therapy.

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AUTHOR DISCLOSURE INFORMATION

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The authors declare no conflicts of interest.

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