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Personality traits and polypharmacy: meta-analysis of five samples

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ABSTRACT

Objective: The present study examined the prospective relationship between personality traits and the risk of polypharmacy.

Methods and Measures: Participants (age range: 16–101 years; $N > 15{,}000$) were from the English Longitudinal Study of Ageing (ELSA), the Midlife in the United States Study (MIDUS), the Health and Retirement Study (HRS), the Wisconsin Longitudinal Study of Aging (WLS), and the Longitudinal Internet Studies for the Social Sciences (LISS). In each sample, personality traits and demographic factors were assessed at baseline. Number of medications was obtained from 2 to 20 years later.

Results: Random-effect meta-analyses revealed that higher neuroticism was related to a higher risk of polypharmacy (Odd Ratio = 1.30; 95% CI 1.17–1.46) and excessive polypharmacy (Odd Ratio = 1.44; 95% CI 1.18–1.77) whereas higher conscientiousness (Odd Ratio = 0.84; 95% CI0.74–0.95) and extraversion (Odd Ratio = 0.85; 95% CI 0.73–0.98) were associated with a lower risk of polypharmacy. Openness and agreeableness were unrelated to polypharmacy. Body mass index, number of chronic conditions, and depressive symptoms partially mediated the association between personality and the number of medications.

Conclusion: The present study provides replicable and robust evidence that neuroticism is a risk factor for simultaneous use of multiple medications, whereas conscientiousness and extraversion may play a protective role.

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1. Introduction

Polypharmacy, which refers to concurrent use of five or more medications by one individual (Masnoon et al., 2017), is a critical public health issue across adulthood. Although medication addresses the healthcare needs of patients, the simultaneous use of several mediations has a range of deleterious implications due to drug-related side effects, drug-drug interactions or drug-disease interactions (Masnoon et al., 2017).

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Indeed, higher polypharmacy has been associated with a higher risk of incident frailty (Saum et al., 2017), falls (Dhalwani et al., 2017), cognitive impairment (Niikawa et al., 2017; Rawle et al., 2018), hospitalization (Chang et al., 2020), and all-cause mortality (Huang et al., 2022). Given these implications, there is a need to better understand the factors that are associated with the risk of polypharmacy. Studies have found that older age, higher body mass index (BMI), worse mental health, and a higher number of chronic health conditions are related to a higher risk of polypharmacy (Midão et al., 2018; Rieckert et al., 2018; Slater et al., 2018; Ye et al., 2022). The present study focused on the role of psychological factors, by examining whether personality traits, which are enduring patterns of thoughts, feelings, and behaviors, are related to polypharmacy.

There is consistent evidence for an association between the personality traits defined by the Five-Factor model (McCrae & John, 1992) and health across adulthood (Aschwanden et al., 2021; Strickhouser et al., 2017). In particular, higher neuroticism (the propensity to experience negative emotions) and lower conscientiousness (the tendency to be self-disciplined and responsible) have been associated with worse overall health (Leger et al., 2021; Strickhouser et al., 2017), including a higher risk of chronic conditions (Weston et al., 2020), obesity (Sutin & Terracciano, 2016), higher depressive symptoms (Hakulinen et al., 2015), poor cognitive functioning and steeper cognitive decline (Sutin et al., 2023), higher risk of dementia (Aschwanden et al., 2021), and ultimately heightened mortality risk (Graham et al., 2017). To a lesser extent, higher extraversion (the tendency to be sociable and energetic) and openness (the tendency to be curious and imaginative) have been associated with better overall health (Strickhouser et al., 2017), such as a lower risk of obesity (Sutin & Terracciano, 2016), better functional health (Canada et al., 2021; Stephan et al., 2017, 2022), and lower risk of depressive symptoms (Hakulinen et al., 2015). Less consistent evidence exists for the link between agreeableness (the tendency to be cooperative and trusting) and health and cognition in adulthood (Aschwanden et al., 2021; Canada et al., 2021; Leger et al., 2021).

The consistent association between personality and physical and mental health suggests that it may be associated with medication use. And indeed, higher neuroticism, and lower extraversion and conscientiousness have been related to opioid use (Sutin et al., 2019) and mental healthcare use, including psychiatric medications (Goktan et al., 2022). Furthermore, neuroticism has been associated with increased use of analgesic, anti-depressant, and sedative medication (Langvik et al., 2019). Despite this evidence, few studies have examined personality and polypharmacy, that is the simultaneous use of multiple medicines. In a sample of 836 older individuals, Yoshida et al. (2022) found a relationship between higher neuroticism and higher risk of polypharmacy in men, whereas higher extraversion was related to a lower risk of polypharmacy in women. In contrast, another study found that neuroticism was unrelated to polypharmacy in a sample of 803 older adults (Wongpakaran et al., 2018). In a sample of 89 patients with bipolar disorders, Sachs et al. (2014) found that individuals with lower openness used more current psychotropic medications, whereas lower extraversion and lower conscientiousness were related to higher lifetime medication use. In contrast, no association was found with neuroticism. Therefore, the relationship between personality and polypharmacy is mixed and remains relatively unclear. The inconsistent findings could be explained by the focus of existing research on small and/or clinical samples, or on men and women separately. Furthermore,

some studies examined only one trait. In addition, existing research has been cross-sectional, and no research has yet examined the prospective association between personality and polypharmacy. To the best of our knowledge, no large-scale study has yet examined the link between the full FFM personality traits and polypharmacy. In addition, no research has tested whether personality traits were related to excessive polypharmacy, defined as the use of 10 or more medications (Masnoon et al., 2017).

Based on five large longitudinal samples of middle-aged and older adults, the present study examined the prospective association between personality and polypharmacy. Given the consistent association with worse physical and mental health (Hakulinen et al., 2015; Leger et al., 2021; Strickhouser et al., 2017; Sutin & Terracciano, 2016; Weston et al., 2020), it was hypothesized that higher neuroticism would be related to a higher risk of polypharmacy and excessive polypharmacy. In contrast, higher extraversion, openness and conscientiousness are related to better overall physical and mental health (Strickhouser et al., 2017; Sutin & Terracciano, 2016; Weston et al., 2020) and were expected to relate to lower risk of polypharmacy and excessive polypharmacy. No associations between agreeableness and either polypharmacy or excessive polypharmacy were expected. Individuals who take more medications tend to be less healthy, and the number of medications may track closely the number of clinical conditions. Personality could be associated with polypharmacy because of its association with multimorbidity, but traits could also be related with the tendency to use more or less medications compared to others with similar health conditions. To evaluate to what extent health conditions account for associations between personality and polypharmacy, additional analyses tested whether clinical (number of chronic conditions and BMI) and psychological (depressive symptoms) factors mediated these relationships. Given the reported sex differences and the importance of aging in polypharmacy (Midão et al., 2018), exploratory analyses tested whether age and sex moderate the association between personality and polypharmacy.

2. Methods

2.1. Participants

Participants were from the English Longitudinal Study of Ageing (ELSA), the Midlife in the United States Study (MIDUS), the Health and Retirement Study (HRS), the Wisconsin Longitudinal Study of Aging (WLS), and the Longitudinal Internet studies for the Social Sciences (LISS). Written informed consent was obtained from all participants in all samples.

ELSA is a panel study of a representative cohort of men and women living in England aged 50 years and over. Data on personality traits and demographic covariates (age, sex, education, and race) were obtained at Wave 5 (2010/2011) from 8117 participants. From this sample, 6157 participants (55% women, Mean age = 66.29, SD = 8.28) provided complete data on number of medications used in Wave 6 (2012/2013). Complete data on mediators (BMI, depressive symptoms, number of conditions) were available at Wave 5 and Wave 6 from 5931 individuals.

The MIDUS is a longitudinal study of non-institutionalized, English-speaking US adults. Data on personality and demographic factors were obtained from 6116 participants in

1995–1996 (MIDUS I). Of this sample, a total of 2584 participants (55% women; Mean Age = 46.57; SD = 11.24) had data on medications used in 2013–2014 (MIDUS III). Complete data on mediators were obtained in 2004–2006 (MIDUS II) from 2351 participants.

The HRS is a nationally representative longitudinal study of individuals 50 years and older and their spouse. A total of 13,141 participants had complete data on personality traits and demographic factors in 2008 and 2010. Data on polypharmacy were obtained from around a 10% random sample of the core interview in a 2016 experimental module. From the baseline sample, 1237 participants (58% women; Mean Age = 68.64; SD = 7.13) provided data on number of medications used in 2016. Of this sample, 1062 participants had complete data on mediators in 2012 (for the 2008 sample) and 2014 (for the 2010 sample).

The WLS is a longitudinal study of a random sample of individuals who graduated from Wisconsin high schools in 1957 and their selected siblings. A total of 10,072 participants had complete data on personality and demographic factors in 1992–1994. Of this sample, 5434 individuals (55% women, Mean age = 53.12, SD = 3.68) also had complete data on number of medications used in 2011. Mediators were obtained in 2003–2007 from 4773 participants.

The LISS panel is a representative longitudinal sample of Dutch individuals. At the first wave (2008), 6780 participants provided data on personality and demographic factors. Of this sample, 1832 participants (52% women, mean age = 47.86, SD = 13.25) provided data on number of medications used at the 15th wave (2022). Data on mediators were from the 8th wave (2015) on 1743 participants.

2.2. Measures

2.2.1. Personality

In ELSA, MIDUS, and HRS, personality traits were assessed using the Midlife Development Inventory (MIDI) (Zimprich et al., 2012). A 25-item version was used in the MIDUS and a 26-item version was used in HRS and ELSA. Participants were rated how well adjectives described them on a scale from 1 (*not at all*) to 4 (*a lot*). Example adjectives are: worrying (neuroticism), outgoing (extraversion), curious (openness), warm (agreeableness), and responsible (conscientiousness). A 29-item version of the Big Five Inventory (John et al., 1991) was used to measure personality in the WLS. Participants were asked to rate the extent to which they see themselves as someone: "who gets nervous easily?" (neuroticism), "who generates a lot of enthusiasm?" (extraversion), "who has an active imagination?" (openness), "who likes to cooperate with others?" (agreeableness) and "who does things efficiently?" (conscientiousness). Answers were given on a 6-point scale from 1 (*disagree strongly*) to 6 (*agree strongly*). The International Personality Item Pool was used in the LISS (Goldberg et al., 2006). Participants were asked to rate how accurately 50 items described themselves on a scale from 1 (*very inaccurate*) to 5 (*very accurate*). Example items are: "worry about things" (neuroticism), "talk to a lot of different people at parties" (extraversion), "have a vivid imagination" (openness), "sympathize with others' feelings" (agreeableness), and "like order" (conscientiousness). Mean scores for each trait were calculated in each sample, with higher scores indicative of higher neuroticism, extraversion, openness, agreeableness, and conscientiousness.

2.2.2. Polypharmacy

In ELSA, participants were asked whether they were currently taking or using any medicines, pills, syrups, ointments, puffers, or injections prescribed for them by a doctor. In the MIDUS, participants were asked to indicate whether they have taken prescription medicines for various health conditions in the last 30 days. The total number of prescription medicines taken was recorded, resulting in maximum of 9 medicines. In the HRS, participants reported how many different prescription medications they used in the last month, with up to 28 medications reported. A maximum of 27 medications was recorded. In the WLS, participants were asked to list all medications they were currently taking, including both prescription medication and over-the-counter medications. Up to 26 medications were recorded. Finally, participants in the LISS indicated whether they were currently taking medicine at least once a week for different conditions. The total number of medicines taken was computed, resulting in a maximum of 15 medicines. Based on an established definition (Masnoon et al., 2017), polypharmacy was defined as taking ≥ 5 medications and coded 1 (vs. 0 for 0–4 medications) and excessive polypharmacy was defined as taking ≥ 10 medications (coded 1 vs. 0 for 0–4 medications).

2.2.3. Mediators

BMI, number of chronic conditions and depressive symptoms were included as mediators in additional analyses. BMI was computed in kg/m^2 using objective assessments of weight and height in ELSA and HRS and participant-reported weight and height in MIDUS, WLS, and LISS. In the five samples, the number of conditions was the sum of diagnosed diseases and conditions (see Supplementary material for the complete list of conditions assessed in each sample). In ELSA and the HRS, depressive symptoms were assessed using an 8-item version of the Center for Epidemiologic Studies Depression Scale (CES-D) (Wallace et al., 2000). Participants were indicated whether they experienced eight symptoms during the past week. Answers were summed with higher scores indicating higher depressive symptoms. The full 20-item CES-D version was used in the WLS (Radloff, 1977). Items were averaged, with higher scores indicating higher depressive symptoms. The MIDUS used the Composite International Diagnostic Interview Short Form (CIDI-SF) (Kessler et al., 1998). Participants indicated the extent to which they experienced depressive symptoms that lasted for two weeks during the last 12 months. A composite score was computed with higher values indicating higher depressive symptoms. The 5-item subscale of the MOS 36-item short form health survey (Ware & Sherbourne, 1992) was used in the LISS. Respondents rated their mental health during the past month on 6-point Likert scales (0 = never to 5 = continuously). The mean was computed, with higher scores indicating higher anxiety and depressive symptoms.

2.2.4. Covariates

Age (in years), sex (1 = female and 0 = male), and education were controlled in the five samples. Race was controlled in HRS and MIDUS (1 = African American and 0 = other) and ELSA (1 = non-white and 0 = other). Ethnicity (1 = Hispanic and 0 = not Hispanic) and year of personality assessment (1 = 2008 and 0 = 2010) were also included

as covariates in the HRS. Education was measured in years in the HRS and the WLS and reported on a scale from 1 (no grade school) to 12 (doctoral level degree) in the MIDUS, from 1 (primary school) to 6 (University) in the LISS, and from 1 (no qualification) to 7 (NVQ4/NVQ5/Degree or equivalent) in ELSA.

2.3. Data analysis

Logistic regression was used to examine whether personality was related to risk of polypharmacy in the five samples. Separate analyses were conducted for each personality trait, standardized to z-score. Demographic factors were included as covariates. Year of personality assessment was also included in the HRS analysis. The same analysis was conducted with excessive polypharmacy as the outcome. Estimates from each sample were combined in a random-effect meta-analyses conducted with the Comprehensive Meta-Analysis software. Additional linear regression analyses were conducted with the continuous measure of number of medications as the outcome.

The mediating role of BMI, number of conditions and depressive symptoms in the association between personality and the number of medications was tested using the PROCESS macro (Hayes, 2018), with 5000 bootstrapped samples and 95% bias-corrected confidence intervals. The continuous measure of the number of medications was the outcome. The three mediators were included simultaneously, and each personality trait was examined in separate analyses. Demographic factors were included as covariates. The continuous measures were standardized.

Additional analyses tested whether age or sex moderated the relationship between personality and polypharmacy by including an interaction between either age or sex and each personality trait. Supplementary logistic regression analyses were also conducted to examine the association between personality traits and the likelihood of using medications for specific (group of) conditions (Supplementary Material). These analyses were conducted in the MIDUS, HRS, and LISS. Information about the conditions connected to medication use was not available in ELSA and the WLS.

3. Results

Descriptive statistics are in Table 1. The proportion of individuals with polypharmacy was 30, 4, 41, 54, and 6% in ELSA, MIDUS, HRS, WLS, and LISS, respectively. The meta-analysis indicated that higher neuroticism was related to a higher risk of polypharmacy at follow-up, whereas higher extraversion and conscientiousness were associated with a lower risk of polypharmacy (see Table 2). The association between neuroticism and polypharmacy was found in the five samples, whereas the association with extraversion and conscientiousness was observed in three out of the five samples. For every one standard deviation (SD) increase in neuroticism, the risk of polypharmacy increased between 14 and 48% across the samples. In contrast, a one SD higher extraversion and conscientiousness was related to 22–35% and 19–30% lower risk of polypharmacy, respectively. There was little replicable for openness or agreeableness and polypharmacy (Table 2). The only exception was the association between higher openness and a lower risk of polypharmacy in ELSA (Table 2). A one SD higher

Table 1. Descriptive statistics for the five samples.

	ELSA		MIDUS		HRS		WLS		LISS	
Variables	*M*/%	*SD*	*M*/%	*SD*	*M*/%	*SD*	*M*/%	*SD*	*M*/%	*SD*
Age (Years)	66.29	8.28	46.57	11.24	68.64	7.13	53.12	3.68	47.86	13.25
Sex (% women)	55%	–	55%	–	58%	–	55%	–	52%	–
Race (% African American/ Black)	2%[a]	–	3%	–	12%	–	0%	–	–	–
Ethnicity (% Hispanic)	–	–	–	–	6%	–	0%	–	–	–
Education	4.22	2.22	7.34	2.45	13.19	2.62	13.96	2.44	3.55	1.47
Neuroticism	2.09	0.59	2.22	0.66	1.97	0.59	3.19	0.97	2.55	0.68
Extraversion	3.15	0.56	3.20	0.56	3.22	0.56	3.82	0.90	3.27	0.63
Openness	2.89	0.55	3.02	0.51	2.96	0.56	3.65	0.78	3.54	0.50
Agreeableness	3.51	0.48	3.47	0.49	3.54	0.48	4.75	0.73	3.92	0.49
Conscientiousness	3.30	0.49	3.47	0.43	3.42	0.45	4.85	0.68	3.79	0.50
Polypharmacy (%)	30%		4%		41%		54%		6%	
Excessive Polypharmacy (%)	6%		–		8%		16%		–	

Note. ELSA: $N = 6157$; MIDUS: $N = 2584$; HRS: $N = 1237$; WLS: $N = 5434$; LISS: = 1832.
[a]Percent of non-white participants. See the method section for differences in measures across the samples.

Table 2. Summary of logistic regression analysis predicting follow-up polypharmacy from baseline personality traits.

	Polypharmacy (≥ 5 Medications)						
	ELSA[a]	MIDUS[b]	HRS[c]	WLS[d]	LISS[e]	Random Effect	Heterogeneity I^2
Neuroticism	1.24*** (1.17–1.32)	1.48*** (1.22–1.80)	1.17** (1.04–1.31)	1.14*** (1.08–1.20)	1.84*** (1.51–2.25)	1.30*** (1.17–1.46)	85.16
Extraversion	0.74*** (0.70–0.78)	0.77** (0.64–0.93)	0.93 (0.82–1.04)	0.98 (0.93–1.04)	0.82* (0.67–1.00)	0.85* (0.73–0.98)	91.90
Openness	0.87*** (0.82–0.92)	0.87 (0.72–1.05)	0.99 (0.88–1.12)	1.02 (0.96–1.08)	0.93 (0.76–1.15)	0.94 (0.86–1.03)	74.52
Agreeableness	1.03 (0.97–1.09)	0.93 (0.76–1.13)	1.01 (0.90–1.14)	1.00 (0.95–1.06)	1.21 (0.97–1.50)	1.02 (0.98–1.06)	0
Conscientiousness	0.77*** (0.72–0.81)	0.77** (0.64–0.92)	0.84** (0.75–0.95)	0.97 (0.92–1.02)	0.84 (0.68–1.03)	0.84** (0.74–0.95)	89.97

[a]Adjusted for age, sex, education, and race; $N = 6157$.
[b]Adjusted for age, sex, education, and race, $N = 2584$.
[c]Adjusted for age, sex, education, race, ethnicity and wave of personality assessment; $N = 1237$.
[d]Adjusted for age, sex, and education; $N = 5434$.
[e]Adjusted for age, sex, and education; $N = 1832$.
$^*p < .05$, $^{**}p < .01$, $^{***}p < .001$.

openness was associated with about 15% lower risk of polypharmacy. The overall pattern of relationship was supported in additional analyses predicting the continuous measure of number of medications used (Supplementary Table S1).

Analyses on the link between personality and excessive polypharmacy were conducted in ELSA, HRS, and the WLS. The proportion of individuals with excessive polypharmacy was 6, 8 and 16% in ELSA, HRS, and the WLS, respectively. Similar to polypharmacy, higher neuroticism was related to a higher risk of excessive polypharmacy in the three samples and the meta-analysis (Table 3). A one SD higher neuroticism was related to 24–65% higher risk of excessive polypharmacy. Furthermore, higher extraversion and conscientiousness were associated with lower risk of excessive polypharmacy in two samples but not in the meta-analysis (Table 3). For every one SD higher extraversion and conscientiousness, the risk of excessive polypharmacy decreased by 28–75% and by 27–56%, respectively. Openness and agreeableness were unrelated to excessive polypharmacy (Table 3).

Table 3. Summary of logistic regression analysis predicting follow-up excessive polypharmacy from baseline personality traits.

	Excessive polypharmacy (≥ 10 medications)				
	ELSA[a]	HRS[b]	WLS[c]	Random Effect	Heterogeneity I^2
Neuroticism	1.65*** (1.47–1.85)	1.49*** (1.22–1.83)	1.24*** (1.24–1.34)	1.44*** (1.18–1.77)	87.91
Extraversion	0.57*** (0.52–0.64)	0.78* (0.63–0.95)	0.94 (0.87–1.02)	0.75 (0.53–1.06)	96.01
Openness	0.78*** (0.70–0.87)	1.03 (0.83–1.28)	1.03 (0.95–1.13)	0.93 (0.76–1.15)	87.21
Agreeableness	0.96 (0.86–1.07)	1.11 (0.90–1.39)	0.99 (0.92–1.08)	0.99 (0.93–1.06)	0
Conscientiousness	0.64*** (0.58–0.71)	0.79* (0.65–0.97)	0.96 (0.88–1.03)	0.79 (0.59–1.05)	94.70

[a]Adjusted for age, sex, education, and race; $N = 4670$.
[b]Adjusted for age, sex, education, race, ethnicity and wave of personality assessment; $N = 832$.
[c]Adjusted for age, sex, and education; $N = 3359$.
*$p < .05$, **$p < .01$, ***$p < .001$.

The mediation analyses indicated that the association between neuroticism and the higher number of medications used was mediated in part by a higher number of conditions in the five samples (Table 4). Higher depressive symptoms partially mediated the association between neuroticism and a higher number of medications in three out of five samples (Table 4). The association between higher extraversion and lower number of medications was mediated in part by lower depressive symptoms in ELSA, MIDUS, HRS, and the LISS. Furthermore, lower number of conditions mediated this association in ELSA, MIDUS, and HRS, and lower BMI was a significant mediator in ELSA (Table 4). Finally, the link between conscientiousness and lower number of medications was explained in part by lower depressive symptoms, lower BMI, and lower number of conditions in ELSA, MIDUS, and HRS (Table 4).

There was no replicable evidence for moderation by age or sex. The few interactions that were significant did not replicate across samples (Supplemental Material). Supplementary analysis revealed that higher neuroticism and lower extraversion and conscientiousness were associated with using medications for different conditions and were not restricted to medication for one particular (group of) condition (Tables S2–S4). As would be expected, however, neuroticism had stronger associations with medications for anxiety and depression as compared to most other conditions.

4. Discussion

Based on five longitudinal samples including more than 15,000 participants, the present study examined whether personality was associated with polypharmacy. The meta-analysis indicated that higher neuroticism was related to a higher risk of polypharmacy and excessive polypharmacy, whereas higher extraversion and conscientiousness were associated with a lower risk of polypharmacy. Openness and agreeableness were unrelated to polypharmacy. The association between personality and polypharmacy was robust because it replicated across five samples from countries with different healthcare systems, using different personality and medications measures, and over follow-ups that ranged from 2 to 20 years. Furthermore, the present study found a mediating role of clinical and psychological factors in the association

Table 4. Summary of bootstrap analysis.

	Bootstrap analysis[a]				
Variables	Neuroticism	Extraversion	Openness	Agreeableness	Conscientiousness
ELSA					
Depressive Symptoms	.037(.027; .047)	−0.025(−0.032; −0.018)	−0.016(−0.021; −0.011)	−0.008(−0.013; −0.005)	−0.02(−0.026; −0.014)
BMI	−0.00(−0.005; .001)	−0.004(−0.007; −0.0009)	.00(−0.002; .004)	.004(.001; .008)	−0.008(−0.012; −0.005)
Number of Conditions	.069(.055; .083)	−0.076(−0.090; −0.063)	−0.031(−0.045; −0.018)	−0.00(−0.014; .013)	−0.07(−0.084; −0.056)
Direct effect[b]	.010	−0.04***	−0.016	.02	−0.03*
MIDUS					
Depressive Symptoms	.007(−0.0008; .015)	−0.003(−0.008; −0.0001)	.00(−0.002; .003)	.002(−0.0004; .004)	−0.003(−0.008; −0.0002)
BMI	.008(−0.002; .019)	−0.007(−0.016; .0005)	−0.010(−0.021; −0.0002)	−0.000(−0.009; .008)	−0.02(−0.031; −0.0116)
Number of Conditions	.057(.041; .075)	−0.026(−0.040; −0.015)	−0.016(−0.028; −0.004)	−0.006(−0.019; .009)	−0.03(−0.044; −0.016)
Direct effect[b]	.09***	−0.05**	−0.05*	.00	−0.016
HRS					
Depressive Symptoms	.026(.010; .044)	−0.013(−0.023; −0.004)	−0.006(−0.014; .004)	−0.004(−0.012; .002)	−0.009(−0.020; −0.002)
BMI	.002(−0.005; .009)	−0.004(−0.012; .002)	.006(−0.001; .014)	.00(−0.007; .008)	−0.008(−0.016; −0.001)
Number of Conditions	.053(.022; .088)	−0.037(−0.068 − 0.008)	−0.002(−0.032; .029)	.00(−0.031; .032)	−0.061(−0.092; −0.030)
Direct effect[b]	.02	.004	−0.003	.00	−0.008
WLS					
Depressive Symptoms	.009(−0.0009; .019)	−0.006(−0.010; −0.0015)	−0.004(−0.008; −0.001)	−0.009(−0.014; −0.003)	−0.009(−0.015; −0.003)
BMI	−0.002(−0.008; .004)	.008(.002; .0140)	−0.005(−0.0106; .0012)	−0.003(−0.009; .002)	−0.02(−0.024; −0.012)
Number of Conditions	.034(.026; .043)	−0.008(−0.016; −0.012)	.012(.004; .020)	−0.017(−0.025; −0.009)	−0.02(−0.029; −0.013)
Direct effect[b]	.04**	−0.008	.008	.03	.02
LISS					
Depressive Symptoms	.06(.033; .090)	−0.02(−0.033; −0.011)	−0.009(−0.017; −0.0018)	−0.010(−0.019; −0.003)	−0.02(−0.033; −0.012)
BMI	.004(−0.0009; .0103)	.004(−0.0015; .0100)	.00(−0.005; .006)	.00(−0.0047; .0063)	−0.005(−0.012; .0003)
Number of Conditions	.08(.055; .104)	−0.002(−0.024; .020)	−0.005(−0.031; .019)	.02(−0.0042; .043)	−0.025(−0.048; −0.003)
Direct effect[b]	.02	−0.03	−0.00	.03	.02

[a]Bootstrap estimates and 95% bias-corrected confidence interval for indirect effects of personality traits on number of medication through depressive symptoms, BMI, and number of conditions, controlling for age, sex, education, and race (except for the WLS and the LISS).

[b]Direct effect of personality traits on number of medications adjusted for mediators, age, sex, education, and race (except for the WLS and the LISS); Coefficients are standardized regression coefficient.

*p<.05; **p<.01;***p< .001.

ELSA: N = 5931; MIDUS: N = 2351; HRS: N = 1062; WLS: N = 4773; LISS: N = 1743.

between personality and the number of medications used. Taken as a whole, the present study advances existing knowledge by providing replicable evidence for an association between personality and polypharmacy and by testing mediators to better understand potential mechanisms of this association.

Neuroticism was the most consistent and strongest personality correlate of polypharmacy and excessive polypharmacy. This finding is broadly consistent with evidence for higher neuroticism and worse physical and mental health (Leger et al., 2021; Strickhouser et al., 2017). The current finding clarifies the mixed results of previous studies (Sachs et al., 2014; Wongpakaran et al., 2018; Yoshida et al., 2022). The differences across previous studies were possibly due to statistical power, study design, or features of the samples examined. The use of five well-powered, longitudinal studies in the present study brings coherence to this literature by identifying a replicable association between neuroticism and polypharmacy.

The basic tendencies of neuroticism may explain in part the association with polypharmacy. Indeed, neuroticism is characterized by a higher propensity to experience distress and negative emotions, and a higher vulnerability to stress, which may result in the use of a higher number of medications. This association may also operate through indirect pathways. Neuroticism, for example, is related to clinical and psychological factors that have been implicated in polypharmacy and excessive polypharmacy, such as higher risk of obesity (Sutin & Terracciano, 2016), depressive symptoms (Hakulinen et al., 2015), and chronic conditions (Leger et al., 2021). Consistent with this hypothesis, the present study found replicable evidence that the association between neuroticism and a higher number of medications was explained in part by its link with more chronic conditions and to a lesser extent by higher depressive symptoms. In addition to clinical factors assessed in the present study, other health-related factors may potentially explain the link between neuroticism and polypharmacy and excessive polypharmacy. For example, neuroticism has been related to higher fatigue (Stephan et al., 2022), chronic pain (Sutin et al., 2019), lower physical function (Stephan et al., 2022), and higher utilization of mental healthcare services (Goktan et al., 2022), which together may increase the likelihood of simultaneous use of multiple medications. Behavioral pathways are also likely to explain in part these associations. For example, higher neuroticism is associated with higher physical inactivity (Sutin et al., 2016) and smoking (Hakulinen et al., 2015), which have been related to a higher risk of polypharmacy (Abolhassani et al., 2017; Bielemann et al., 2020).

As expected, conscientiousness was related to a lower risk of polypharmacy. A similar pattern was also found for extraversion, for which we had a more tentative hypothesis. Both traits were unrelated to excessive polypharmacy. These associations align with the literature on these two traits and better overall health (Leger et al., 2021; Strickhouser et al., 2017). Furthermore, these findings support past research on clinical samples that found an association between these traits and polypharmacy (Sachs et al., 2014) but contrast with research that found no association (Yoshida et al., 2022). Furthermore, the present study found that the clinical and psychological profiles associated with both conscientiousness and extraversion may explain in part their relationship with polypharmacy. Indeed, lower BMI, lower chronic conditions, and less depressive symptoms mediated part of the association between higher

extraversion and conscientiousness and the use of fewer medications. These traits have also been associated with higher energy (Terracciano et al., 2013), lower fatigue (Stephan et al., 2022), lower chronic pain (Sutin et al., 2019), and better physical function (Stephan et al., 2022), which may reduce the likelihood of medication use and the risk of polypharmacy. Finally, extraversion and conscientiousness are associated with a more physically active lifestyle (Sutin et al., 2016), which may lead to lower medication use (Bielemann et al., 2020).

Unexpectedly, openness was unrelated to polypharmacy in the meta-analysis. This finding is in contrast with one clinical sample (Sachs et al., 2014), but consistent with a community-dwelling sample (Yoshida et al., 2022). This lack of association also contrasts with the association between openness and better overall health (Strickhouser et al., 2017), which does not seem to manifest into a lower likelihood of polypharmacy. Finally, the lack of association between agreeableness and polypharmacy is consistent with prior research (Sachs et al., 2014; Yoshida et al., 2022).

The present study extends the current literature in several ways. First, it contributes to knowledge on the predictors of polypharmacy and excessive polypharmacy by identifying a replicable association with specific personality traits. Second, this study extends existing models and research on personality and health (Friedman & Kern, 2014; Strickhouser et al., 2017) by providing replicable evidence that neuroticism, extraversion, and conscientiousness is associated with the simultaneous use of multiple medicines. Third, polypharmacy could be a potential pathway linking higher neuroticism and lower conscientiousness to the risk of frailty, dementia, and mortality. That is, the consistent association between neuroticism and conscientiousness and frailty (Gale et al., 2017; Stephan et al., 2017), dementia (Aschwanden et al., 2021), and mortality (Graham et al., 2017), may be due, in part, to polypharmacy, which is implicated in a higher risk of frailty (Saum et al., 2017), cognitive impairment (Rawle et al., 2018), and mortality (Huang et al., 2022).

4.1. Limitations and perspectives

The strengths of the present study include the use of five large samples of middle-aged and older adults, the prospective design with up to 20 years of follow-up, the synthesis of results using meta-analyses, the use of validated measures of all five personality traits, and the test of potential clinical and psychological mediators. This study also has several limitations. The observational design does not allow to establish causality. Although personality may be a predictor of polypharmacy, it is also likely that polypharmacy may lead to personality changes. Furthermore, such potential bidirectional relationships may occur between personality, clinical and psychological mediators, and number of medications. For some samples, the total number of medications used included over-the-counter medications as well as other medications that were not prescribed and all samples relied on self-reported medication use. Finally, the present study included samples from the US and Europe. More research on samples from other cultures and areas of the world are needed to further test the generalizability of the findings.

5. Conclusion

In sum, the present study found replicable associations between personality and polypharmacy. Higher neuroticism is related to a higher risk of polypharmacy and excessive polypharmacy, whereas higher extraversion and conscientiousness are related to lower risk of polypharmacy. From a clinical perspective, personality assessment may improve the identification of individuals at risk of polypharmacy and help guide their medication prescription. Furthermore, these findings suggest that interventions directed toward changing personality traits, such as reducing neuroticism and improving conscientiousness (Stieger et al., 2021), may result in a lower number of conditions and associated polypharmacy.

Disclosure statement

The authors report no conflict of interest.

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Data availability statement

ELSA data are publicly available from the UK Data Service (UKDS, https://www.ukdataservice.ac.uk/); MIDUS data are available at http://midus.wisc.edu/index.php; HRS data are available at https://hrs.isr.umich.edu/data-products; WLS data are available at http://www.ssc.wisc.edu/wlsresearch/data/; LISS data are available at: www.lissdata.nl

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