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Personality and EQ-5D scores among individuals with chronic conditions

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Abstract
Background Personality is associated with self-rated health, but prior studies have not examined associations with preference-based measures. We hypothesized similar associations would exist with preference-based health.
Methods We analyzed baseline data from chronically ill individuals enrolled in a self-management intervention. We conducted regression analyses with the EQ-5D summary index score and dimension scores (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) as dependent variables, The key independent variables were NEO-Five Factor Inventory (NEO-FFI) personality factors (Neuroticism, Conscientiousness, Extraversion, Openness, Agreeableness), adjusting for age, gender, educational level, minority status, and chronic conditions.
Results Of 415 participants, 245 (59%) had ≥2 chronic conditions, 384 (94%) completed the NEO-FFI and 397 (96%) the EQ-5D. After adjustment, Neuroticism was associated with EQ-5D summary index scores [−0.04 per 1 SD increase in Neuroticism (95% CI −0.06, −0.01)]. Neuroticism [AOR 2.99 (95% CI 2.06, 4.35; $P < 0.001$)] and Openness [1.32 (95% CI 1.00, 1.75; $P = 0.05$)] were associated with worse anxiety/depression scores, while Conscientiousness was associated with better usual activities scores [0.66 (95% CI 0.49, 0.89; $P = 0.01$)].
Conclusions The associations between personality factors and self-rated health appear to extend to preference-based measures. Future studies should explore whether personality affects preference-based health estimates in cost-effectiveness analyses.

Keywords Bias · Chronic disease · Health status · Personality · Quality of life

Abbreviations

CDSMP	Chronic Disease Self-Management Program
CEA	Cost-effectiveness analysis
CES-D	Center for Epidemiologic Studies Depression Scale
CI	Confidence interval
CLAD	Censored least absolute deviations
COPD	Chronic obstructive pulmonary disease
FFM	Five Factor Model
HAQ	Health Assessment Questionnaire
HIOH	Homing in on Health
MCID	Minimal clinically important difference
NEO-FFI	Neo-Five Factor Inventory
OLS	Ordinary least squares
QALY	Quality-adjusted life-year
RCT	Randomized controlled trial
SD	Standard deviation

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Self-rated health is an increasingly important health outcome as people live longer with chronic disabling conditions [1]. A number of studies have demonstrated significant associations between personality characteristics and self-rated health [2–18]. Most have employed the Five Factor Model (FFM), a personality framework that has resulted from over seven decades of research [19]. The personality factors in the FFM are Neuroticism, which reflects distress-proneness, chronic negative emotions, and stress reactivity; Extraversion, or positive mood, sociability, and vigor; Openness to Experience (Openness), entailing interest in novel ideas and experiences, and aesthetic/intellectual sensibilities; Agreeableness, reflecting trust, altruism, and amicability; and Conscientiousness, which involves reliability, diligence, and achievement-orientation. These five personality factors capture the major axes of psychological and behavioral variation in humans, and each has been independently associated with a number of important health behaviors and outcomes [20–27], including self-rated health. Specifically, lower levels of self-reported health have been noted in individuals with higher levels of Neuroticism[4–8, 10–18] and/or lower levels of Conscientiousness [8, 10, 11, 13], Agreeableness [8, 13, 15, 16], Extraversion [2–6, 8, 10, 13, 16, 18], and/or Openness [6, 8, 9, 11, 16].

Previous studies demonstrating FFM factor/self-rated health associations have employed non-preference-based self-rated health measures. While one might hypothesize similar associations would exist between FFM personality factors and preference-based health, this remains unexamined. It is also not clear whether any associations between self-rated health and personality would remain significant after adjusting for other patient characteristics known to influence preference-based health scores, such as socio-demographic factors [28–31] and medical conditions/diagnoses [29, 30, 32].

Elucidating the interrelationships among patient FFM personality factors, socio-demographic and disease-related factors, and preference-based health assessments is important because preference-based health measures are increasingly being used as primary outcome measures in both observational studies [33, 34] and randomized controlled trials (RCTs) [35, 36]. Additionally, utility scores derived from preference-based health measures are used to derive quality-adjusted life-years (QALYs), the denominator in cost-effectiveness ratios used in cost-effectiveness analyses (CEA) [37]. If significant FFM factor/preference-based health associations persisted after adjusting for other characteristics known to influence preference-based health, it would suggest a heretofore unrecognized yet potentially important source of bias. In other words, QALYs and the CEAs that employ them may be affected by variance in psychological characteristics beyond the individual variation in specific health preferences they are intended to capture. Such bias might reduce the external validity of RCTs and the CEAs that rely on their findings if, for example, the status of one or more personality factors differed in a trial sample as compared with the general population of patients to which one would like to generalize the findings of the trial. Prior research demonstrates enrollment and/or attrition bias driven by psychological variables [38–41], including FFM personality factors [42], may indeed affect at least some RCTs. Personality bias could similarly threaten the external validity of observational studies, and is also likely to limit their *internal* validity since group assignment is non-random.

To further address these issues, we examined associations between FFM personality factors and preference-based health at baseline among participants in a RCT of the Homing in on Health (HIOH) self-efficacy enhancing intervention, a home delivery variant of the Stanford Chronic Disease Self-Management Program (CDSMP) [43]. The study sample included primary care patients aged 40 and older suffering from one or more chronic diseases, a sample with enough active medical illness to permit meaningful study of personality influences on patient self-rated health. Whereas the CDSMP is provided to small groups of individuals in centralized locations, our one-to-one, home-delivered adaptation was designed to make the CDSMP content available to those less able to participate in the original program, due to functional limitations, transportation problems, or discomfort with group settings. The overall goals of the project were to determine whether in-home and/or telephone versions of HIOH would enhance self-efficacy and thereby improve health outcomes, including self-rated health, for people with chronic conditions.

We employed an extensively validated measure of personality, the NEO Five Factor Inventory (NEO-FFI) [44], and the widely employed and well-validated EQ-5D preference-based self-rated health measure [45]. We used baseline data from our RCT participants to determine whether significant associations existed among FFM personality factors and EQ-5D scores, after adjusting for participant socio-demographic factors and medical conditions. Based on the prior FFM and self-rated health literature, we hypothesized higher levels of Neuroticism, and lower levels of Extraversion, Conscientiousness, Agreeableness, and Openness, would each independently be associated with less favorable EQ-5D summary index scores. We also explored associations between FFM factor and EQ-5D dimension scores (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression).

Methods

Study setting, sample recruitment, and randomization

Study activities described were conducted from July 2004 through February 2008. The local Institutional Review Board approved the study protocol. A convenience sample of subjects was recruited from the 12 offices and 70 family physician and general internist practices in a university-affiliated primary care network located in Northern California. The study coordinator obtained permission from participating physicians to contact their patients. Billing code information was used to identify those aged 40 or older with one or more of the following chronic illnesses: arthritis, asthma, chronic obstructive pulmonary disease, congestive heart failure, depression, and/or diabetes mellitus. Mass-mailed study announcements, direct telephone calls, and announcement flyers posted in participating offices were also employed to recruit patients who met these criteria.

The study coordinator used a standard script to screen interested patients for further eligibility criteria: ability to speak and read English; residence in a private home with an active telephone; adequate eyesight and hearing to participate via telephone and read study materials; and at least one basic activity impairment, as assessed by the Health Assessment Questionnaire [46], *and/or* a score of 4 points or greater, suggestive of clinically significant depressive symptoms, on the 10-item version of the Center for Epidemiologic Studies Depression Scale [47]. The requirement for participants to have some basic activity impairment and/or active depression symptoms was based on findings of pre-study focus groups [48] and discussions with the developers of the CDSMP, which indicated such individuals would be least likely to participate in the original CDSMP but might still be willing and able to participate in a one-to-one, home-delivered variant of the program.

A study nurse visited eligible individuals in their homes, using a standardized interview checklist, augmented by clinical judgment, to assure they were medically stable for participation in the study (all were). During the home visit, the nurse also obtained informed consent and administered the baseline study questionnaire (see "Measures"). Subjects were randomly assigned to one of two HIOH intervention groups or a usual care control group. The study methods and interventions have been described in detail elsewhere [49].

Measures

Big 5 personality factors

At baseline, subjects completed the 60-item NEO-FFI [44], an extensively validated abbreviated version of the NEO Personality Inventory-Revised. The five 12-item scales in this measure tap the central Big 5 factors: Neuroticism, Extraversion, Openness to Experience, Agreeableness, and Conscientiousness. In the regression analyses, scores were standardized [mean = 0, standard deviation (SD) = 1] to facilitate interpretation. Cronbach's α for the five scales ranged from 0.70 to 0.87 in this sample.

Self-rated health

At baseline, subjects also completed the five-item EQ-5D descriptive system [45]. Subjects rated their problems along five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) as of the day of assessment, using a three-category scale (no problems, some problems, extreme problems) for each dimension. In addition to the separate dimension scores, each subject's responses were converted into a summary index (EQ-5D index) by applying scores from a population-based United States (U.S.) valuation set [50]. Though the minimal clinically important difference (MCID) for the EQ-5D summary index score remains somewhat controversial, various investigators have suggested values ranging from 0.03 [51] to 0.07 points [52, 53].

Covariates

Other patient characteristics also measured at baseline via self-report were: age (in years); gender; race/ethnicity; marital status; and education level (less than high school graduate, high school diploma or equivalent, some college, college degree, any graduate school). Subjects also self-reported whether or not they had any of the study chronic conditions (arthritis, asthma, chronic obstructive pulmonary disease, congestive heart failure, depression, and/or diabetes mellitus), as well as the number of daily medications they were taking.

Analyses

All analyses were conducted using Stata, version 10.0 (StataCorp, College Station, TX). Ordinary least squares (OLS) regression analyses were conducted with the EQ-5D summary index as dependent variable. The key independent variables were the five FFM factors, age, gender, educational status, minority status (minority or non-Hispanic White), and the presence of each of the study chronic conditions (as a series of dummy variables). Because of the highly skewed and truncated distributions of EQ-5D summary index and dimension scores, OLS likely produces biased parameter estimates. However, this analytic approach is the one most commonly used for analyzing these self-rated health measures, and, in general, OLS is

robust to violation of the assumption of normality for the dependent variable. Alternative analytic techniques have been explored [54], and each has its limitations. We also examined the use of censored least absolute deviations (CLAD) regression [29], and this produced results consistent with OLS (results available from the authors).

We used five sets of ordinal logistic regression analyses to examine the relationship of each EQ-5D dimension with the independent variables as described above. We tested the proportional odds assumption, and found no evidence of non-proportionality going from one dimension level to another for any of the independent variables in any of the five sets of analyses. Thus, we report adjusted odds ratios, reflecting the average adjusted odds ratios for each independent variable associated with a change in level for a given dimension.

Results

There were 415 participants enrolled in the trial. Of these, 94 (23%) were male and 321 (77%) female, with a mean age of 60 years (range 41–95). Most participants (59%) reported two or more chronic conditions. Table 1 provides a summary of subjects' baseline characteristics; 384 (94%) completed the NEO-FFI and 397 (96%) completed the EQ-5D at baseline.

Table 2 summarizes the regression analysis of EQ-5D summary index score on the patient characteristics. Better self-rated health was significantly associated with having diabetes, whereas worse self-rated health was significantly associated with reporting arthritis, depression, and greater Neuroticism. There were no significant associations of Agreeableness, Conscientiousness, Extraversion, and/or Openness with EQ-5D summary index scores. In analyses conducted sequentially adding the socio-demographic, medical conditions, and FFM factors, the adjusted variances explained in the EQ-5D analyses were 4.0, 13.6, and 19.6%.

Table 3 summarizes the findings of ordinal regression analyses of the EQ-5D domains on patient characteristics. Worse mobility and self-care scores were each associated with increasing age and having heart failure or arthritis. Worse usual activities and pain scores were each associated with diabetes and arthritis, while better usual activities and pain scores were each associated with greater Conscientiousness. Finally, better anxiety/depression scores were associated with increasing age, more education, and having diabetes, while worse anxiety/depression scores were associated with greater Neuroticism and/or Openness. There were no significant associations of Agreeableness or Extraversion with any EQ-5D dimension scores.

Discussion

Our study findings add to the growing body of literature demonstrating that patient personality factors are associated with patients' self-ratings of their health, and demonstrate the association extends to a preference-based health measure. They also suggest complex interrelationships exist among patient personality factors, socio-demographics, medical conditions, and preference-based health assessments, raising important questions regarding the external validity of clinical research studies including CEAs.

Table 1 Characteristics of participants

Characteristic	$n = 415$
Age, years, mean (*SD*)	60.4 (11.5)
Female, *n* (%)	321 (77.4)
Minority, *n* (%)	81 (19.8)
Years of education, *n* (%)	
<12	7 (1.7)
12	54 (13.2)
13–15	161 (39.3)
16	122 (29.8)
>16	66 (16.1)
Illnesses, *n* (%)[a]	
Diabetes	172 (41.4)
Heart failure	48 (11.6)
Chronic obstructive pulmonary disease	43 (10.4)
Asthma	98 (23.6)
Arthritis	233 (56.1)
Depression	193 (46.5)
Uninsured, *n* (%)	10 (2.4)
Personality factors, mean (*SD*)	
Neuroticism	21.3 (9.4)
Extraversion	25.9 (7.5)
Conscientiousness	31.8 (6.9)
Agreeableness	33.6 (5.4)
Openness	28.6 (6.4)
EQ-5D	
Summary index, mean (SD)	0.74 (0.17)
Dimensions, *n* (%) at levels 1, 2, and 3[b]	
Mobility	176 (44.3), 219 (55.2), 2 (0.5)
Self-care	292 (73.6), 105 (26.4), 0 (0)
Usual activities	168 (42.3), 219 (55.2), 10 (2.5)
Pain/discomfort	102 (25.7), 256 (64.5), 39 (9.8)
Anxiety/depression	231 (58.2), 153 (38.5), 13 (3.3)

SD Standard deviation

[a] Percentages exceed 100 because many participants had more than one condition

[b] 1, No problem; 2, some problem/limitation; 3, severe problem/unable

Table 2 Adjusted relationships between baseline patient characteristics and EQ-5D summary index score

Characteristic	Coefficient	95% CI	*P*
Age, years	0	(−0.00 to 0.00)	0.289
Female	−0.02	(−0.06 to 0.02)	0.289
Minority	−0.02	(−0.06 to 0.03)	0.444
Years of education[a]			
12	0.11	(−0.02 to 0.24)	0.088
13–15	0.09	(−0.04 to 0.21)	0.160
16	0.12	(−0.00 to 0.25)	0.051
>16	0.11	(−0.02 to 0.24)	0.098
Illnesses			
Diabetes	0.04	(0.00 to 0.07)	0.039
Heart failure	−0.04	(−0.09 to 0.02)	0.203
Chronic obstructive pulmonary disease	−0.03	(−0.09 to 0.03)	0.285
Asthma	−0.02	(−0.06 to 0.02)	0.435
Arthritis	−0.09	(−0.13 to −0.06)	<0.001
Depression	−0.06	(−0.10 to −0.02)	0.005
Personality factors[b]			
Neuroticism	−0.04	(−0.06 to −0.01)	0.002
Extraversion	0	(−0.03 to 0.02)	0.66
Conscientiousness	0.02	(−0.00 to 0.04)	0.078
Agreeableness	−0.01	(−0.03 to 0.01)	0.355
Openness	0	(−0.02 to 0.02)	0.971

CI Confidence interval

[a] Reference, <12 years

[b] Personality factors were standardized with a mean of 0 and a standard deviation of 1. Analyses also adjusted for group assignment

Consistent with a number of prior studies exploring associations between FFM factors and self-rated health as assessed using non-preference-based measures [4–8, 10–18], we found higher Neuroticism was associated with worse preference-based health, as measured by the EQ-5D summary index, in our sample of chronically ill RCT participants. The association appeared robust, persisting after adjustment for socio-demographic factors [17–20] and medical conditions/diagnoses [18, 19, 21] that are recognized powerful correlates of self-rated health.

The effect of a 1 SD change in Neuroticism on EQ-5D summary index scores was comparable to that of having depression or arthritis, greater than the effect of having diabetes, heart failure, or chronic lung disease, and much greater than the effects of socio-demographic variables that are currently almost universally measured and adjusted for in clinical studies. Neuroticism also accounted for more variance in EQ-5D summary index scores than these traditionally measured variables. For a 1 SD increase in Neuroticism, the summary index score was decreased by 0.04, which falls within the MCID range for the EQ-5D of 0.03 [51] to 0.07 [52, 53]. Across an entire population, which encompasses in excess of 4 standard deviations in personality scores, the effect of Neuroticism on EQ-5D summary index scores would therefore be around 0.16. Thus, the association between Neuroticism and EQ-5D summary index scores we observed appears to have importance from a population health perspective.

Regarding individual EQ-5D dimensions, higher Neuroticism was associated with worse anxiety/depression scores, a finding consistent with a large body of prior research. We also noted higher Openness was associated with worse anxiety/depression scores, a finding that may seem more puzzling at first glance. However, predicting the effects of relatively high levels of FFM personality factors is not always a straightforward matter, and beyond its potential benefits, high Openness may have some downsides [55]. For example, a prior study found higher Openness was associated with worse scores on the Social Functioning scale of the non-preference-based SF-36 self-rated health measure [21], and has also been associated with mood disorders [56]. Several attributes of high Openness individuals might help to explain such findings. These include a tendency toward high sensitivity to feelings and emotions, as well as a proclivity for unconventional or esoteric interests that might make it difficult for individuals to relate to others who do not share such interests [57]. Thus, interrelationships between FFM personality factors and self-rated health can be complex, underscoring the need for additional empirical research in this area. Finally, higher Conscientiousness was associated with better usual activities scores, consistent with prior literature concerning

Table 3 Adjusted relationships between baseline patient characteristics and EQ-5D dimension scores

Characteristic	Mobility			Self-care			Usual activities			Pain/discomfort			Anxiety/depression		
	AOR	95% CI	*P*	AOR	95% CI	*P*	AOR	95% CI	*P*	AOR	95% CI	*P*	AOR	95% CI	*P*
Age[a]	1.03	1.01, 1.05	0.01	1.35	1.07, 1.69	0.01	0.90	0.70, 1.17	0.45	0.94	0.75, 1.17	0.56	0.70	0.55, 0.91	0.01
Female	1.02	0.58, 1.78	0.95	1.02	0.58, 1.78	0.95	1.74	0.86, 3.52	0.13	1.15	0.66, 2.02	0.62	0.75	0.40, 1.41	0.37
Minority	1.13	0.64, 1.99	0.68	1.13	0.64, 1.99	0.68	1.35	0.70, 2.58	0.37	1.24	0.70, 2.22	0.46	1.22	0.65, 2.32	0.54
Education[b]															
13–15 years	1.14	0.57, 2.32	0.71	1.14	0.57, 2.32	0.71	1.39	0.61, 3.19	0.43	1.90	0.95, 3.81	0.07	0.49	0.23, 1.02	0.06
>15 years	0.83	0.40, 1.69	0.60	0.83	0.40, 1.69	0.60	0.88	0.37, 2.08	0.77	1.29	0.64, 2.62	0.47	0.29	0.13, 0.64	0.00
Illnesses															
Diabetes	0.83	0.51, 1.34	0.44	0.83	0.51. 1.34	0.44	0.42	0.24, 0.76	0.00	0.46	0.28, 0.74	0.00	0.58	0.34, 1.01	0.05
CHF	2.30	1.00, 5.27	0.05	2.30	1.00, 5.27	0.05	1.61	0.68, 3.82	0.28	0.89	0.42, 1.88	0.75	1.22	0.53, 2.81	0.64
COPD	1.04	0.48, 2.25	0.91	1.04	0.48, 2.25	0.91	1.24	0.52, 2.93	0.63	1.48	0.70, 3.16	0.31	0.96	0.41, 2.25	0.92
Asthma	1.36	0.78, 2.37	0.28	1.36	0.78, 2.37	0.28	1.23	0.66, 2.28	0.52	1.04	0.60, 1.80	0.90	1.10	0.60, 2.03	0.75
Arthritis	3.15	1.96, 5.06	0.00	3.15	1.96, 5.06	0.00	3.23	1.81, 5.77	0.00	3.18	1.97, 5.14	0.00	0.90	0.53, 1.52	0.70
Depression	1.33	0.76, 2.33	0.31	1.33	0.76, 2.33	0.31	1.86	1.00, 3.49	0.05	1.46	0.84, 2.56	0.18	2.70	1.53, 4.76	0.00
Personality[c]															
N	0.95	0.69, 1.32	0.77	0.95	0.69, 1.32	0.77	0.96	0.66, 1.38	0.82	1.00	0.72, 1.38	0.99	2.99	2.06, 4.35	0.00
E	0.87	0.65, 1.17	0.35	0.87	0.65, 1.17	0.35	0.95	0.68, 1.34	0.79	0.92	0.69, 1.23	0.59	0.94	0.68, 1.30	0.70
C	0.82	0.63, 1.06	0.12	0.82	0.63, 1.06	0.12	0.66	0.49, 0.89	0.01	0.70	0.54, 0.92	0.01	1.28	0.96, 1.70	0.09
A	1.08	0.84, 1.37	0.55	1.08	0.84, 1.37	0.55	1.07	0.82, 1.41	0.61	1.00	0.78, 1.27	0.99	1.32	1.00, 1.75	0.05
O	0.96	0.76, 1.21	0.73	0.96	0.76, 1.21	0.73	1.10	0.85, 1.43	0.46	1.17	0.92, 1.47	0.19	0.98	0.76, 1.26	0.88

AOR Adjusted odds ratio for a decline in one dimension level, *CI* confidence interval, *CHF* congestive heart failure, *COPD* chronic obstructive pulmonary disease

[a] In 10-year increments

[b] Reference <13 years

[c] Personality factors (standardized): *N* Neuroticism, *E* Extraversion, *C* Conscientiousness, *A* Agreeableness, *O* Openness

non-preference-based self-rated health measures [21]. These findings again all appeared robust, persisting after full adjustment for covariates.

We found no associations between Agreeableness and Extraversion and any EQ-5D dimension scores, consistent with the findings of a single prior study examining the relationship of personality factors with sub-facets of self-rated health, measured via SF-36 subscales [21]. We also found no associations of Agreeableness, Conscientiousness, Extraversion, or Openness with EQ-5D summary index scores. The results of prior studies concerning associations between these personality factors and self-rated health assessed via non-preference-based measures have been mixed, with some but not all finding associations, and the specific personality factors considered and/or found to be associated with self-rated health varying among "positive" studies [2–6, 8, 10, 11, 13, 16, 18].

The reasons for the differences in specific associations between FFM personality factors and self-rated health in our study compared with previous studies remain unclear. However, considerable variation among studies in regard to participant and design characteristics is likely to be one important contributor. For example, our analyses employed baseline data from RCT participants, whereas all prior studies exploring personality/self-rated health associations employed data from observational studies. This is salient because accumulating evidence suggests that RCT participants may differ from others, including observational study participants, in ways that may influence their self-assessments of health [58].

It also seems likely that different self-rated health measures may tap distinct and/or only partially overlapping facets of the broad subjective health construct. Indeed, a number of prior studies that compared the performance of different preference-based and non-preference-based self-rated health measures found important differences among measures in terms of baseline scores and responsiveness to change [33, 36, 59–62]. Thus, different self-rated health measures should not necessarily be expected to yield uniform results. There are also significant correlations among the FFM factors, so that the effects of the less salient factors may have been obscured in this sample. In analyses (not presented) that examined only one of the FFM factors at a time, three of the factors (Neuroticism, Conscientiousness, and Extraversion) exhibited strong adjusted associations in the direction predicted. Finally, all self-rated health measures have specific limitations in their performance that might influence the findings of analyses exploring personality factor/self-rated health associations. For example, the EQ-5D is susceptible to ceiling effects [53, 62, 63], and its scores tend to be skewed toward better health [64]. The possibility that different self-rated health measures may be differentially susceptible to contamination by different personality factors warrants further study.

Regardless of the specific connections between different FFM personality factors and self-rated health measures, our findings have potential ramifications for clinical research studies. For example, since it appears individuals with relatively high levels of Neuroticism have worse self-rated health as assessed by both preference-based and non-preference-based measures, one might hypothesize such individuals may have (and/or perceive they have) "more to gain" from interventions aimed at improving self-rated health than those with lower Neuroticism. Personality factors might also moderate the effects of interventions on preference-based health [65]. For example, one might hypothesize individuals higher in Neuroticism might be more (or less) responsive to a given intervention than those lower in Neuroticism. Indeed, in prior analyses, we found that the self-efficacy enhancing effects of our study experimental intervention were confined to participants who were higher in Neuroticism and/or lower in Conscientiousness, Agreeableness, and Extraversion [66].

Such personality-driven effects on intervention receptiveness and/or response may reduce the external validity or applicability of RCTs as well as observational studies if, as some research evidence suggests [38–42], the status of psychological variables such as FFM personality factors is different in those who enroll and remain in clinical studies than for the general population. Personality effects may additionally threaten internal validity in observational studies. Subjects are not randomly assigned to groups in such studies, so it is unlikely the status of various personality factors is equally distributed among groups.

Finally, it follows from these examples that unmeasured personality effects might bias the findings of CEAs, since preference-based health assessments are used to calculate QALYs for use in cost-effectiveness ratios. The key point is that routinely assessing the status of personality factors in clinical studies, along with the usual socio-demographic variables, would permit detection and, when indicated, statistical control for such effects. These examples, provided here for illustrative purposes, remain somewhat speculative given the relative paucity of supporting empirical research. Clearly, additional studies examining what are likely to be complex interrelationships among patient personality, changes in preference-based health in response to interventions, and intervention cost-effectiveness estimates appear warranted.

Our study had some limitations. As noted previously, we examined a sample of chronically ill outpatients who volunteered for a RCT, which may limit the generalizability of our findings to other groups and settings. For example, mean EQ-5D summary index and dimension scores were somewhat lower than in the general population [29, 30].

Likewise, mean Neuroticism scores were somewhat higher and mean scores for the other four FFM factors somewhat lower than reported in the general population [44]. Additionally, because our analyses were cross-sectional, causality cannot be inferred from the personality/preference-based health associations we observed. In other words, while it seems likely that the status of certain personality factors contributed to poorer health in some subjects, it may also be true that subjects' overall health and/or specific medical conditions helped shape the status of their personality factors over time. Indeed, recent research indicates that, rather than being viewed as intransigent "traits," FFM factors may best be conceptualized as general tendencies that are subject to significant change over time within some individuals [67]. It is also unclear to what extent differences in self-rated health among persons with varying levels of the FFM personality traits reflect differences in their reporting of subjective health and/or differences in "actual" underlying health. On the other hand, the apparently robust relationship between personality and mortality in a number of prior longitudinal studies strongly suggests a more fundamental relationship also exists [27].

In conclusion, our study demonstrated that personality factors in the FFM were associated with preference-based self-rated scores in a sample of outpatients participating in a RCT of a chronic illness self-management intervention. These associations remained significant even after adjusting for socio-demographic factors and medical conditions, which are known to influence preference-based health ratings. Furthermore, among these variables, FFM personality factors were the most powerful correlates of preference-based health. Our findings underscore the need for additional studies conducted with a wide array of samples, at least some of which are followed longitudinally, to further explore the potential for unmeasured effects due to patient personality factors in clinical research.

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