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## **The impact of personality traits on the course of frailty**

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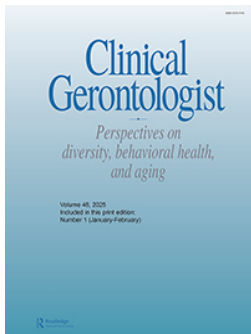
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## The impact of personality traits on the course of frailty

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### ABSTRACT

**Objectives:** Determinants of frailty are generally explored within context of somatic healthcare and/or lifestyle characteristics. To examine the impact of personality traits on change in frailty and the potential role of depression.

**Methods:** A 2-year follow-up study including 285 patients with a depressive disorder and 116 never-depressed controls. Multiple linear regression analyses were conducted to regress the Big Five personality traits (independent variables) on different frailty measures (dependent variables), including the Frailty Index, Frailty phenotype, gait speed, and handgrip strength. Analyses were adjusted for confounders (with and without depressive disorder) and baseline frailty severity. Interactions between personality traits and depressive disorder were examined.

**Results:** All personality traits were associated with change in at least one frailty marker over time. Over time, a higher level of neuroticism was associated with an accelerated increase of frailty, whereas a higher level of extraversion, agreeableness, conscientiousness and openness were associated with an attenuated increase of frailty. None of the associations were moderated by depression. Additional adjustment for depression decreased the strength of the association of neuroticism, extraversion and conscientiousness with frailty.

**Conclusions:** Personality traits have impact on frailty trajectories in later life.

**Clinical implications:** Underlying pathways and potential modification by psychotherapy merit further study.

### KEYWORDS

Frailty; depression; big five; personality traits; older patients

## Introduction

Understanding the diversity in biological aging between people is a major goal in geroscience (Kennedy et al., 2014). Biomedical frailty has been introduced to identify older persons at risk of adverse health outcomes (Fried et al., 2001) and is increasingly recognized as a clinical marker of a patient's biological age on top of chronological age (Bartley et al., 2016; Kojima, 2017). While personality traits shape a person's behavior and stress-responses throughout their lives (Damian et al., 2019), these traits have hardly been examined as a determinant of the biological aging process.

To our knowledge, one cross-sectional and four prospective studies have addressed the association between personality traits and biomedical frailty (Dánielsdóttir et al., 2019; Gale et al., 2017; McHugh et al., 2016; Stephan et al., 2017; Tolea

et al., 2012). All prospective studies have identified a high level of neuroticism as a risk factor for the progression of frailty over time. Within three cross-sectional cohorts a higher level of neuroticism was associated with higher Frailty Index scores. This association remained after excluding all mental health items (i.e. depressed mood). Results within a longitudinal cohort suggest a causal relationship between neuroticism and frailty (Dánielsdóttir et al., 2019). Individual studies, albeit chance findings, have also pointed to a protective effect of a higher level of conscientiousness (Gale et al., 2017; Tolea et al., 2012), and of a higher level of extraversion (Gale et al., 2017) on the progression of frailty over time. Openness and agreeableness have only been cross-sectionally associated with frailty (McHugh et al., 2016), but not with a change in frailty over time in any of the

prospective studies (Gale et al., 2017; Stephan et al., 2017; Tolea et al., 2012).

Thus far, depression has barely been considered in these studies. As a depressive disorder is associated with accelerated biological aging itself (Mezuk et al., 2012), it might be an exploratory factor in the association between personality traits and frailty. Moreover, a moderating role for depression by accelerating the impact of personality traits on aging, cannot be excluded yet.

The aim of the present study was to examine prospectively the association of the Big Five personality traits and two-year change in frailty. A second objective was to examine a potentially moderating of explanatory role of depression in this association.

## Methods

### Design and population

The present study was embedded in the Netherlands Study of Depression in Older persons (NESDO), a clinical cohort study (Comijs et al., 2011). NESDO included 378 depressed and 132 non-depressed participants aged 60–93 years. Depressed patients aged  $\geq 60$  years were included when the Composite International Diagnostic Interview (CIDI, version 2.1; Smitten et al., 1998; Wittchen et al., 1991) confirmed the diagnosis of a past six-month major depressive disorder and/or dysthymia, or a minor depression according to DSM-IV-TR (Comijs et al., 2011). Inclusion criteria were also an available NEO Five-Factor Inventory (NEO-FFI; Hoekstra & De Fruyt, 2014), at least one frailty measure, and two-year follow-up data through site visits (Comijs et al., 2015). Exclusion criteria were a clinically suspected or established diagnosis of dementia, a Mini-Mental State Examination (MMSE) score under 18 points (Folstein et al., 1975) to avoid exclusion of severely depressed patients, or insufficient mastery of the Dutch language. A lifetime history of depression was an additional exclusion criterion for the non-depressed participants.

The NESDO study was approved by the Ethical Review Board of the VU University Medical Center. All participants provided written informed consent.

## Measures

*Personality* – The Big Five personality traits, i.e. neuroticism (emotional instability), extraversion (outwardly directed energy, attention and orientation), openness (to experience), conscientiousness (direction one's own behavior based on the dominant environment demands), and agreeableness (orientation on experiences, interests, and goals of others) were assessed with the NEO-FFI (Costa & McCrae, 1992; Hoekstra & De Fruyt, 2014).

### Biomedical frailty

*Frailty index* – The frailty index (FI) is the ratio of health deficits present to the total number of deficits measured (i.e. blood-based biomarkers, incontinence and signs of tremor) and better predicts adverse health outcomes than chronological age and other indices of biological age (Mitnitski et al., 2015). Because of its continuous nature, the FI is sensitive to change and enables to study trajectories of frailty over time (Clegg et al., 2013). Patients scoring  $\geq 0.25$  are considered frail. The NESDO-FI was constructed according to the guidelines by Searle et al. (Searle et al., 2008) and is based on 41 non-depression related health deficits concerning chronic somatic diseases, objective and subjective measures of physical performance and cognitive performance, blood-born biomarkers, sensory functioning, and subjective health measures (Oude Voshaar et al., 2021).

*The Frailty Phenotype* – The Frailty Phenotype is a syndromic approach considering people frail when three out of five criteria are met (Fried et al., 2001). In our study, frailty severity according to the Frailty Phenotype was defined as the number of criteria met (range 0–5). Weakness was based on maximum handgrip strength in kg assessed twice with a handgrip dynamometer with the dominant hand. Cutoff scores were stratified by gender and BMI quartiles (Fried et al., 2001). Low physical activity based on daily activities, presented in metabolic equivalent (MET) minutes, was calculated with the International Physical Activities Questionnaire (IPAQ; Craig et al., 2003). Unintentional weight loss was defined as a positive answer on the CIDI question about unwanted weight loss (World Health Organization, 1997) or a BMI  $< 18.5$  kg/m<sup>2</sup>. Gait speed was determined by measuring the time in

seconds needed to complete a six-meter walk (Guralnik et al., 2000). Exhaustion was based on a positive answer on either item 20 (energy level) or 30 (leaden paralysis/physical energy) of the Inventory of Depressive Symptoms (IDS; Rush et al., 1996).

*Frailty proxies* – gait speed as well as handgrip strength were also examined as dimensional performance-based proxies for frailty. The Big-Five personality traits have been identified as determinants of both proxies of frailty previously. Higher neuroticism was found to be cross-sectionally associated with diminished handgrip strength, whereas higher extraversion and conscientiousness were associated with higher handgrip strength (Stephan et al., 2022). Lower neuroticism and higher extraversion, conscientiousness, and openness were prospectively associated with a higher gait speed (Stephan et al., 2018)

### Covariates

Covariates included sociodemographic variables (age, sex, and years of education), presence of a DSM-IV depressive disorder, as well as somatic health status (number of chronic somatic diseases and number of prescribed medications (see, (Collard et al., 2017)).

### Statistical analyses

Study completers and study dropouts were compared using Students t-tests for normally distributed continuous variables, nonparametric Mann Whitney U tests for skewed continuous variables, and  $\chi^2$  tests for categorical variables. Gait speed and low physical activity were log-transformed before using them in multivariable analyses.

Personality traits (independent variable) were regressed on all frailty severity measures at two-year follow-up (dependent variable) using multiple linear regression analyses. In model 1, we only adjusted for baseline frailty severity, whereas in model 2 we also adjusted for potential confounders (age, sex, years of education, number of chronic diseases and number of prescribed medications). No multicollinearity was found according to the correlation matrix and variance inflation factors. Separate models were built for each personality trait, as well as the individual frailty markers, i.e.

the frailty index, number of components met of the Frailty Phenotype (range 0–5), gait speed (time in seconds needed to walk 6 meter), and handgrip strength (kg).

Because depression generally amplifies the impact of maladaptive personality functioning on mental health outcomes, first we analyzed whether group status (depressed versus non-depressed) interacts with any of the personality traits in their association with change of frailty. In case of a significant interaction term, we present stratified results. In the absence of interaction, we will additionally adjust model 2 for the presence of a baseline depressive disorder (model 3) to examine whether depression can explain the association (possibly mediating factor). For each significant association between a personality trait and a frailty change marker, the relative change of the beta between model 2 and 3 is calculated; a change >10% is suggestive of clinically relevant mediation.

As the number of missing values was less than 5% on all covariates, missing covariates were substituted with their means. P-values < 0.05 were considered statistically significant. Statistical analyses were performed with IBM SPSS version 25.0 (SPSS, Inc., Chicago, IL).

## Results

### Study participants

Of the 510 NESDO-participants, 93/378 (24.6%) patients with a depressive disorder and 16/132 (12.1%) non-depressed persons had dropped out at 2-year follow-up ( $\chi^2 = 9.07$ ,  $df = 1$ ,  $p = .003$ ; Comijs et al., 2015). Those who dropped out were more often depressed, used more medication, and were more frail. Of the non-respondents, 28/109 (25.7%) were deceased (Comijs et al., 2015). Table 1 presents all baseline characteristics of the study population compared to those who dropped out. Of the eligible study participants ( $n = 401$ ), none had missing data with respect to the frailty index. Due to missing values regarding some components of the frailty phenotype, the longitudinal analyses of these parameters were based on 364 (frailty phenotype severity), 376 (gait speed) or 379 (handgrip strength) participants.

**Table 1.** Baseline characteristics of the study population.

| Characteristics:                        |              | Study sample<br>(n = 401) | Dropouts<br>(n = 109) | Statistics <sup>†</sup>                   |
|-----------------------------------------|--------------|---------------------------|-----------------------|-------------------------------------------|
| <i>Socio-demographics:</i>              |              |                           |                       |                                           |
| • Age (years)                           | mean (SD)    | 70.2 (7.3)                | 71.8 (7.4)            | t = -1.9; df = 508, p = .054              |
| • Female sex                            | n (%)        | 260 (64.8%)               | 71 (65.1%)            | Chi <sup>2</sup> < 0.1; df = 1, p = .954  |
| • Level of education (years)            | mean (SD)    | 11.1 (3.5)                | 10.3 (3.6)            | t = 2.3; df = 508; p = .012               |
| <i>Level of functioning parameters:</i> |              |                           |                       |                                           |
| • Global cognition (MMSE)               | mean (SD)    | 28.0 (1.7)                | 27.2 (2.5)            | t = 3.9; df = 507; p < .001               |
| • Number of chronic diseases            | mean (SD)    | 1.4 (1.2)                 | 1.5 (1.2)             | t = -0.8; df = 507; p = .407              |
| • Number of prescribed medication       | mean (SD)    | 3.9 (2.8)                 | 4.9 (3.1)             | t = -3.0; df = 505; p = .003              |
| <i>Personality (NEO-FFI):</i>           |              |                           |                       |                                           |
| • Neuroticism                           | mean (SD)    | 34.8 (9.3)                | 37.2 (9.3)            | t = -2.3; df = 474; p = .022              |
| • Extraversion                          | mean (SD)    | 36.5 (7.1)                | 33.5 (7.1)            | t = 3.7; df = 473; p < .001               |
| • Openness                              | mean (SD)    | 29.8 (5.3)                | 28.5 (5.4)            | t = 2.2; df = 470; p = .029               |
| • Agreeableness                         | mean (SD)    | 44.7 (5.3)                | 43.8 (5.7)            | t = 1.5; df = 471; p = .131               |
| • Conscientiousness                     | mean (SD)    | 38.2 (5.8)                | 37.2 (6.3)            | t = 1.6; df = 473; p = .116               |
| <i>Frailty:</i>                         |              |                           |                       |                                           |
| • Presence frailty phenotype            | n (%)        | 78 (20.1%)                | 37 (35.2%)            | Chi <sup>2</sup> = 10.6; df = 1, p = .001 |
| • Frailty (no. of components)           | median (IQR) | 1.0 (0.0–2.0)             | 2.0 (1.0–3.0)         | U = 8.8; p < .001                         |
| • Gait speed (seconds)                  | median (IQR) | 6.0 (5.0–7.0)             | 7.0 (6.0–9.0)         | U = 2.2; p = .025                         |
| • Handgrip strength (kg)                | mean (SD)    | 29.0 (11.4)               | 27.0 (21.2)           | t = 1.3; df = 504; p = .210               |
| • Presence frailty according to FI      | n (%)        | 125 (31.5%)               | 66 (60.6%)            | Chi <sup>2</sup> = 31.4; df = 1, p < .001 |
| • Frailty severity (FI)                 | mean (SD)    | 0.21 (0.10)               | 0.27 (0.11)           | t = -5.0; df = 508; p < .001              |
| <i>Psychopathology:</i>                 |              |                           |                       |                                           |
| • Depressive disorder                   | n (%)        | 285 (71.1%)               | 93 (85.3%)            | Chi <sup>2</sup> = 9.1; df = 1, p = .003  |

<sup>†</sup>Comparison using analyses of variance (continuous variables), Chi<sup>2</sup> statistics (categorical variables) and U standardized Test Statistic (continuous, skewed variables).

Abbreviations: SD, standard deviations; MMSE, Mini Mental State Examination; NEO-FFI, NEO Five Factor Inventory; IQR, interquartile ranges; kg, kilogram; FI, Frailty Index.

### Course of frailty

Since none of the interaction terms between any personality trait and depression status were significant when regressed on any frailty change marker, all results are presented in Table 2 for the whole sample.

Adjusted for confounders (model 2), all personality traits were associated with the change in at least one frailty marker, but none with a change in handgrip strength. A higher level of neuroticism was significantly associated with an increase of frailty components based on the frailty phenotype type and gait speed. For all other personality traits, a higher level was associated with significantly less increase of frailty over time. Extraversion and agreeableness were significantly associated with change in frailty based on the frailty index, frailty phenotype and gait speed; conscientiousness with the frailty phenotype and gait speed; and finally openness with the frailty index.

The impact of neuroticism, extraversion and conscientiousness, but not of agreeableness and openness were attenuated by >10% when additionally adjusted for the presence of depression (model 3).

None of the personality traits were associated with a significant change in handgrip strength over a two-year follow-up.

### Post-hoc sensitivity analyses

Post-hoc we repeated all analyses excluding the comparison group of non-depressed persons. None of the results reported in Table 2 changed significantly.

### Discussion

This study showed that all Big Five personality traits are significantly associated with change in at least one of the frailty markers examined in this study (albeit none with handgrip strength). The impact of these personality traits was not conditional upon the presence of a depressive disorder. Nonetheless, the impact of neuroticism, extraversion and conscientiousness might be partly explained by depression in contrast to the impact of agreeableness and openness. Altogether, these results show that personality traits may be an important determinant of biological aging.

**Table 2.** Regression models of personality traits with two-year change in frailty by linear regression.

| Personality traits<br>(NEO-FFI)             | Model 1 <sup>†</sup> |                 | Model 2 <sup>‡</sup> |                 | Model 3 <sup>§</sup> |                 | Delta $\beta$ (%)<br>Model 2–3 |
|---------------------------------------------|----------------------|-----------------|----------------------|-----------------|----------------------|-----------------|--------------------------------|
|                                             | $\beta$              | p               |                      |                 | $\beta$              | p               |                                |
| <b>Frailty Index (n = 401)</b>              |                      |                 |                      |                 |                      |                 |                                |
| • Neuroticism                               | 0.01                 | .793            | 0.03                 | .376            | −0.02                | .627            | n.a.                           |
| • Extraversion                              | <b>−0.07</b>         | <b>.025</b>     | <b>−0.07</b>         | <b>.022</b>     | −0.05                | .118            | 23.9%                          |
| • Agreeableness                             | <b>−0.08</b>         | <b>.015</b>     | <b>−0.10</b>         | <b>.001</b>     | <b>−0.10</b>         | <b>.002</b>     | 5.0%                           |
| • Conscientiousness                         | −0.05                | .146            | −0.06                | .070            | −0.04                | .236            | n.a.                           |
| • Openness                                  | <b>−0.09</b>         | <b>.004</b>     | <b>−0.07</b>         | <b>.034</b>     | <b>−0.07</b>         | <b>.028</b>     | 4.3%                           |
| <b>Frailty Phenotype severity (n = 364)</b> |                      |                 |                      |                 |                      |                 |                                |
| • Neuroticism                               | <b>0.15</b>          | <b>&lt;.001</b> | <b>0.15</b>          | <b>&lt;.001</b> | <b>0.11</b>          | <b>.034</b>     | 22.8%                          |
| • Extraversion                              | <b>−0.09</b>         | <b>.026</b>     | <b>−0.10</b>         | <b>.013</b>     | −0.06                | .180            | 40.4%                          |
| • Agreeableness                             | −0.08                | .060            | <b>−0.12</b>         | <b>.003</b>     | <b>−0.11</b>         | <b>.004</b>     | 5.1%                           |
| • Conscientiousness                         | <b>−0.12</b>         | <b>.005</b>     | <b>−0.12</b>         | <b>.003</b>     | <b>−0.09</b>         | <b>.029</b>     | 24.1%                          |
| • Openness                                  | −0.07                | .101            | −0.02                | .721            | −0.02                | .643            | n.a.                           |
| <b>Gait speed (s) (n = 376)</b>             |                      |                 |                      |                 |                      |                 |                                |
| • Neuroticism                               | <b>0.11</b>          | <b>.006</b>     | <b>0.10</b>          | <b>.007</b>     | 0.08                 | .110            | 21.6%                          |
| • Extraversion                              | <b>−0.10</b>         | <b>.010</b>     | <b>−0.11</b>         | <b>.004</b>     | <b>−0.09</b>         | <b>.038</b>     | 18.9%                          |
| • Agreeableness                             | <b>−0.06</b>         | <b>.097</b>     | <b>−0.14</b>         | <b>&lt;.001</b> | <b>−0.13</b>         | <b>&lt;.001</b> | 5.9%                           |
| • Conscientiousness                         | <b>−0.09</b>         | <b>.016</b>     | <b>−0.09</b>         | <b>.012</b>     | −0.07                | .074            | 23.3%                          |
| • Openness                                  | −0.06                | .134            | −0.01                | .911            | −0.01                | .863            | n.a.                           |
| <b>Handgrip strength (kg) (n = 379)</b>     |                      |                 |                      |                 |                      |                 |                                |
| • Neuroticism                               | −0.06                | .079            | −0.05                | .116            | −0.01                | .959            | n.a.                           |
| • Extraversion                              | 0.02                 | .548            | 0.02                 | .538            | −0.02                | .563            | n.a.                           |
| • Agreeableness                             | −0.04                | .242            | 0.00                 | .937            | −0.01                | .854            | n.a.                           |
| • Conscientiousness                         | 0.03                 | .415            | 0.02                 | .462            | −0.00                | .890            | n.a.                           |
| • Openness                                  | 0.01                 | .827            | −0.01                | .774            | −0.01                | .815            | n.a.                           |

<sup>†</sup>Model 1, only adjusted for baseline value of either number of frailty components, gait speed or handgrip strength in addition to the personality trait under study.

<sup>‡</sup>Model 2, additionally adjusted for age, sex, years of education, number of chronic diseases and number of prescribed medications.

<sup>§</sup>Model 3, additionally adjusted for the presence of a depressive disorder at baseline.

Abbreviations:  $\beta$ , standardized beta; s, seconds; NEO-FFI, NEO Five Factor Inventory.

Neuroticism was associated with accelerated biological aging as indexed by the frailty phenotype and gait speed, but in contrast with the ELSA study not with the frailty index (Gale et al., 2017). The absence of an association with the frailty index can be explained by our study population of primarily depressed patients. Depressive symptoms may amplify the neuroticism score and when depression would also confound frailty, it may dampen the increase of frailty over time as depressive symptom severity improved over time. Previously, the frailty index was shown to be partly confounded by self-reported depressive symptom severity (Oude Voshaar et al., 2021). The differential findings regarding the frailty phenotype and frailty index is interesting, as particularly the frailty phenotype is criticized for its overlapping criteria with depressive disorder (Lohman et al., 2016). Interestingly, a recent meta-analysis of four population-based samples (Stephan et al. (2022) showed that in the only study with sufficient prospective data, neuroticism was associated with increased levels of frailty over time (albeit

these analyses were not controlled for depression).

In contrast to the ELSA in which a higher level of agreeableness was associated with an increase of the frailty index (Gale et al., 2017), we found agreeableness associated with less increase of frailty over time. These opposing effects may also be explained by our study population. ELSA is a population study with a small minority of depressed participants, where a higher level of agreeableness, thus more adaptation to others, may increase frailty (infringing one's own rights, not setting boundaries), but when depressed as the majority in our study population, and therefore probably more frail and dependent on others, adapting to others can be supporting and leading to an attenuated increase of frailty over time.

### Methodological considerations

A strength of our study is the use of different frailty markers, especially as this is the first study among predominantly depressed patients. The predictive impact of three personality traits was partly explained by the presence of a depressive

disorder. Whether this is a real mediating effect or the result of inflated personality scores remains to be examined since depressive symptoms inflates self-reported personality trait scores (2018). Secondly, attrition of the overall sample was 21.4%. Since attrition was related to frailty and death, the identified associations might even be stronger. On the other hand, attrition in the NESDO study is relatively less compared with attrition within population-based aging studies (Chatfield et al., 2005). Finally, the statistical power to detect significant interaction terms is limited. This may have masked differential findings between depressed and non-depressed participants as results certainly holds true for the depressed subgroup based on the sensitivity analyses.

### Conclusions

The results described above are of clinical importance because they suggest that the Big Five personality traits are important and determining factors in biological aging. A meta-analysis found personality traits are associated with treatment course of psychiatric disorders. Higher agreeableness is associated with higher working alliance and thus more treatment success, and higher extraversion is associated with positive outcomes regarding symptomatology and improvement (Bucher et al., 2019). This implies a higher level of extraversion will result in shorter treatment duration. Future studies should examine how personality traits interfere with frailty progression over time. While depressive disorder may be one pathway as suggested by our results, also lifestyle, psychological resilience, and genetic predispositions should be examined. And one step further, it should be examined whether for example, higher agreeableness and extraversion are also associated with positive outcomes regarding interventions aimed at improving frailty (such as, for example, treatment by a dietician (Ni Lochlainn et al., 2021) or exercise training (Merchant et al., 2021)).

### Clinical implications

- Personality traits should be considered in older persons because of their impact on biological

aging irrespective of the presence of a depressive disorder.

- In older psychiatric patients, personality traits deserve attention because of their influence on treatment duration of psychiatric disorders.

### Disclosure statement

No potential conflict of interest was reported by the author(s).

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### Data availability statement

Data available on request due to privacy/ethical restrictions.

### Author contributions

All authors satisfy the four conditions of the ICMJE for an authorship by having substantially contributed to the concept of the study, interpretation of the data, critical revision of the article, approval of the final version, and agreed to be accountable for all aspects of the work. EGTB has analysed the data. EGTB and JD drafted the first version. RMK and ROV supervised data-analyses and writing.

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