Personality pathways to mortality: Interleukin-6 links conscientiousness to mortality risk

Páraic S. O’Súilleabháin a,b,*, Nicholas A. Turiano c, Denis Gerstorf d, Martina Luchetti e, Stephen Gallagher a,b, Amanda A. Sesker c, Antonio Terracciano f, Angelina R. Sutin e

a Department of Psychology, University of Limerick, Limerick, Ireland
b Health Research Institute, University of Limerick, Limerick, Ireland
c Department of Psychology, West Virginia University, WV, United States
d Department of Psychology, Humboldt University Berlin, Germany
e Department of Behavioral Sciences and Social Medicine, Florida State University, Tallahassee, United States
f Department of Geriatrics, Florida State University, Tallahassee, United States

* Corresponding author at: Department of Psychology, University of Limerick, Limerick, Ireland.
E-mail address: paraic.osuilleabha@ul.ie (P.S. O’Súilleabháin).

https://doi.org/10.1016/j.bbi.2021.01.032
Received 13 October 2020; Received in revised form 21 December 2020; Accepted 28 January 2021
Available online 9 February 2021
0889-1591/© 2021 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

ABSTRACT

Personality is associated consistently with mortality hazards, but the physiological pathways are not yet clear. Immune system dysregulation may be one such pathway due to its role in age-related morbidity and mortality. In this preregistered study, we tested whether interleukin-6 (IL-6) and C-reactive protein (CRP) mediated the associations between personality traits and mortality hazards. The sample included 957 participants (M = 58.65 ± 11.51 years; range = 35–86 years) from the Midlife in the United States Survey that had 14 years of follow-up. Higher conscientiousness was associated with lower mortality hazards, with each one standard deviation higher conscientiousness associated with a 35% lower mortality risk. IL-6, but not CRP, partially mediated this association, with IL-6 accounting for 18% of this association in the fully adjusted model. While there was initial evidence that the biomarkers mediated both neuroticism and agreeableness and mortality risk, the indirect effects were not significant when controlling for the sociodemographic variables. Taken together, higher conscientiousness may lead to a longer life partially as a result of lower IL-6. This work highlights the importance of biological pathways that link personality to future mortality risk.

1. Introduction

Personality traits, as operationalized by the Five Factor Model (FFM; also referred to as the “Big Five”), have been linked consistently to long-term health outcomes, including mortality (Roberts et al., 2007). Robust evidence indicates higher conscientiousness—a tendency to be responsible, organized, and capable of self-control—is associated with lower risk of mortality (Graham et al., 2017; Jokela et al., 2013). Low scores of this trait, for example, are associated with an approximately 40% increased risk of mortality over an average of six years of follow-up (Jokela et al., 2013). In contrast, neuroticism—a tendency to experience more negative emotions such as fear and sadness—tends to be associated with elevated mortality risk (Graham et al., 2017), also across long follow-up periods in very old age (O’Súilleabháin and Hughes, 2018). However, protective effects for neuroticism and mortality risk have also been reported (Weiss and Costa, 2005). The evidence has been more mixed for the remaining personality traits within the FFM (e.g. Mroczek and Spiro, 2007; Ferguson and Bibby, 2012; O’Súilleabháin and Hughes, 2018). The consistent evidence that personality, particularly conscientiousness, is associated with mortality has led to great interest in identifying the pathways that explain this association.

Stemming from developmental psychology (Baltes and Goulet, 1970), the lifespan perspective is one that provides considerable avenues to view the possible ways that personality may impact mortality risk across the life course. As discussed by Hampson and Friedman (2008), both the critical period models (whereby exposure to risk during critical periods have longer-lasting effects than at other times) and accumulation models (impact of exposures to risk accumulates across the lifespan) have been well suited to examine personality and health associations. Most work on the possible pathways that contribute to the relation between personality and long-term mortality risk has focused on health-related behaviors (Friedman et al., 1995; Mroczek et al., 2009;
Risk Factors Collaboration, 2010). These biomarkers outperform traditional health risk prediction methods such as the Framingham Risk Score (DeFilippis et al., 2015) and are linked to the onset and development of chronic illnesses (Neta et al., 2017; Vasto et al., 2007).

Over the last decade, the idea that personality traits are associated with both IL-6 and CRP has received growing interest (Sutin et al., 2010; Luchetti et al., 2014). Evidence suggests that conscientiousness may have a protective role in inflammatory-related biomarkers (Luchetti et al., 2014; see also Allen and Laborde, 2017; Sutin et al., 2018; Elliot et al., 2017; Turiano et al., 2013; Wagner et al., 2019). For example, Luchetti and colleagues (2014) found higher conscientiousness to be associated with lower CRP across three large, US samples (N > 26,000): For each 1SD higher conscientiousness, the risk of exceeding the clinical threshold of CRP (>3 mg/l) was lowered by 10–15% across the samples. These results were also supported by a meta-analysis of published studies on both CRP (7 studies) and IL-6 (6 studies) where conscientiousness was negatively associated with both of the biomarkers (estimated r was −0.05 for CRP and −0.08 for IL-6; Luchetti et al., 2014). In addition to conscientiousness, the meta-analysis found a negative correlation between openness and CRP and no significant associations for extraversion or agreeableness (Luchetti et al., 2014). Higher neuroticism has been associated with higher levels of IL-6 (Sutin et al., 2010), but this association did not replicate in the findings for the other traits (Van der Linden et al., 2015; Allen and Laborde, 2017; Sutin et al., 2018; Elliot et al., 2017). Later studies have mostly supported the association between conscientiousness and lower inflammation; the findings for the other traits remain mixed (see Allen and Laborde, 2017; Wagner et al., 2019; Hengartner et al., 2016; Israel et al., 2014; Graham et al., 2018).

Much of the literature to date on the mechanisms between personality and mortality has examined behavioural pathways, with little research examining potential physiological pathways. Some literature has also examined the associations between personality and indices of biomarkers, including allostatic load, and have speculated that physiological dysregulation is one pathway that links personality to poor health outcomes (Stephan et al., 2016). The research that has considered the physiological pathways are either theoretical or solely examine the association between personality and specific biomarkers, not whether these biomarkers mediate the relation between personality and mortality. In this preregistered study, we addressed whether circulating levels of biomarkers could be an underlying mechanism through which personality is associated with mortality risk. Specifically, this research investigated if IL-6 and CRP provide a pathway linking personality and mortality risk over a period of 14 years. This study focused on IL-6 and CRP due to their role in age-related morbidity and mortality and their reported associations within the existing literature on personality and biomarkers. It was hypothesised that both biomarkers would mediate associations of both conscientiousness and neuroticism with mortality risks. For extraversion, openness, and agreeableness, we hypothesized that both IL-6 and CRP would not be a pathway linking them to mortality risk.

2. Method

2.1. Preregistration

Preregistration and related documents for this study are available at https://osf.io/263sf. The data used within this study are publicly available through the Inter-University Consortium for Political and Social Research (ICPSR). All analyses were conducted in accordance with the preregistration.

2.2. Participants

Data for this study were from the Midlife in the United States (MIDUS) study that had started in 1995 with 7,108 institutionalized adults between the ages of 25 and 75 years (Brim et al., 2019). The first follow-up (MIDUS 2) was between 2004 and 2006 with 4,963 participants (Ryff et al., 2017). A subset of these participants took part in a biomarker study (N = 1255; Ryff et al., 2019). Each participant was invited to attend a clinical research center for a comprehensive examination by trained medical staff that included the collection of biological specimens, a thorough physical exam, and the recording of medical history data (Ryff et al., 2019). Of the available sample with IL-6 and CRP data (n = 1,235), some participants did not complete the personality assessment (n = 199) or provide medication data (n = 79). As such, the present sample included 957 adults (M ± SD = 58.62 ± 11.50 years, range: 35 – 86; females, M ± SD = 57.87 ± 11.27 years, range: 35 – 86; males, M ± SD = 59.58 ± 11.74 years, range: 36–85). All protocols reported within this study were granted full ethical approval as part of the MIDUS 2 Biomarker Project, in accordance with the Declaration of Helsinki.

An attrition analysis previously reported by Graham and colleagues (2018) found that those who did not complete the biomarker project were higher in neuroticism, lower in openness to experience, less educated, less healthy, and more likely to be white.

Compared to participants deceased during the follow-up, participants who were alive on the final update were younger (t = −2.43, p < 0.001, 95% CI [−15.52, −11.29]), more likely to be female (χ² = 10.81, p = 0.001), higher in conscientiousness (t = 2.99, p = 0.003, 95% CI [0.045, 0.22]), had lower levels of difficulty in completing activities of daily living (t = −3.20, p = 0.002, 95% CI [−0.36, −0.09]), lower levels of logIL-6 (t = −6.03, p < 0.001, 95% CI [−0.25, −0.13]), and did not use oral non-steroidal anti-inflammatory medication (χ² = 13.01, p < 0.001) at baseline (see Table 1).

2.3. Measures

2.3.1. Mortality

Vital status was determined and collated through several methods (National Death Index (NDI), closeout interviews, and during longitudinal sample maintenance), with the most recent update in October 2018. Because only month and year of death were available for each deceased participant, they were assigned the 15th day of the month as their exact date of death (Turiano et al., 2015). There were 111 deaths across the follow-up (M ± SD = 137.15 ± 26.66 months; range = 6–171); 846 participants were reported as alive on their most recent update. Time was defined as the number of months between the date of the MIDUS 2 Biomarker assessment and date of death.

2.3.2. Personality

Personality traits were assessed using the Midlife Development Inventory (MDI) Personality Scales (Lachman and Weaver, 1997). Participants indicated the extent to which 26 adjectives described them on a 4-point Likert scale ranging from 1 “not at all” to 4 “a lot”. Items for each personality traits are as follows: Neuroticism (moody, worrying, nervous, calm [reverse]), Extraversion (outgoing, friendly, lively, active, talkative), Openness to Experience (creative, imaginative, intellect,
of ADL refer to greater difficulty in performing activities. *Note

Table 1

| Deceased (n = 111) | Alive (n = 846) | Complete Sample (n = 957) |
|-------------------|---------------|-------------------------|
| Mean (SD)/%       | Mean (SD)/%   | Mean (SD)/%             |
| IL-6 (pg/mL)*     | 4.23 (4.18)   | 2.63 (2.57)             | 2.82 (2.85)            |
| CRP (ug/mL)*      | 3.73 (7.37)   | 2.63 (3.79)             | 2.76 (4.37)            |
| Neuroticism       | 1.95 (0.61)   | 2.05 (0.63)             | 2.04 (0.63)            |
| Extraversion      | 3.11 (0.60)   | 3.13 (0.57)             | 3.13 (0.57)            |
| Openness to Experience | 2.97 (0.52)   | 2.96 (0.52)             | 2.96 (0.52)            |
| Agreeableness     | 3.41 (0.48)   | 3.44 (0.50)             | 3.44 (0.50)            |
| Conscientiousness | 3.35 (0.47)   | 3.49 (0.43)             | 3.47 (0.44)            |
| Age (years)       | 70.61 (11.44) | 57.09                   | 58.65 (11.51)          |
| Sex (Female)      | 41.4%         | 57.9%                   | 56%                    |
| Race (White)      | 96.4%         | 92.9%                   | 93.3%                  |
| Education         | 7.63 (2.49)   | 7.78 (2.46)             | 7.76 (2.46)            |
| Chronic Conditions| 1.18 (1.26)   | 0.99 (1.29)             | 1.01 (1.29)            |
| ADL               | 1.41 (0.71)   | 1.18 (0.49)             | 1.21 (0.53)            |
| Smoking (no)      | 42.3%         | 57.7%                   | 55.9%                  |
| Corticosteroid    | 82%           | 87.9%                   | 87.3%                  |
| Medication (no)   | 33.3%         | 51.5%                   | 49.4%                  |
| NSAID Oral (no)   | 88.3%         | 86.6%                   | 86.8%                  |

Note: *= prior to transformation, ADL = activities of daily living, higher values of ADL refer to greater difficulty in performing activities.

Curious, broad-minded, sophisticated, adventurous), Conscientiousness (organized, responsible, hardworking, thorough, careless (reverse)), and Agreeableness (helpful, warm, caring, soft-hearted, sympathetic). McDonald omegas for each personality trait are as follows (McDonald, 1999): Neuroticism (ω = 0.74), Extraversion (ω = 0.79), Openness to Experience (ω = 0.77), Conscientiousness (ω = 0.73), Agreeableness (ω = 0.82). Cronbach’s α levels were all greater than 0.68.

2.3.3. Inflammatory markers

Blood samples were collected at three examination sites (University of California, Los Angeles (UCLA); Georgetown University; University of Wisconsin). Serum IL-6 was measured using a high-sensitivity enzyme-linked immunosorbent assay (ELISA; R & D Systems). High-sensitivity CRP was assessed via plasma with a particle enhanced immunonephelometric assay (BNII nephelometer from Dade Behring). IL-6 was assayed in the MIDUS Biocore Laboratory (University of Wisconsin, Madison). CRP was assayed at the Laboratory for Clinical Biochemistry Research (University of Vermont). Intra and inter-assay coefficients of variance were in the acceptable range for both inflammatory markers; IL-6 (3.25, 12.31%), and CRP (4.4%, 5.7%). See Ryff and colleagues (2019) for more details about the biomarker assessment.

2.3.4. Confounding variables

The following variables were included as covariates (each measured at the biomarker clinic visit): age; sex (male, female); race (white, other); education (highest level of education “attained ranging from no schooling or some grade school” to “professional degrees such as PhD or MD”); smoking (ever smoker versus non-smoker); chronic conditions (total number of doctor-diagnosed medical conditions; e.g., hypertension, heart disease, diabetes, cancer, stroke); and activities of daily living (ADL); the extent to which health impacts their ability to perform ten activities (e.g. bathing, dressing) ranging from “not at all” to “a lot”). Comprehensive information on medication use was also collated as part of the biomarker project. Each participant was required to bring all their medications to the clinic visit in the original containers, such that medication names and dosages were accurately recorded. Information pertaining to medications were then linked to generic names and corresponding drug IDs via linkage to the Lexi-Data database, which were then linked to their therapeutic and pharmacologic class codes. For this study, any form of corticosteroid (encompassing inhalant, nasal, ophthalmic, otic, rectal, systemic, and topical) medications were dummy coded (no, yes). Both oral and parenteral non-steroidal anti-inflammatory medication (NSAID) were also included as further covariates (no, yes).

The full correlation table of all variables is available in the supplementary materials. Each covariate was selected given they have been repeatedly implicated as critically important in the context of the variables under direct examination within this present study (e.g. National Institutes of Health, 2020; Cutler and Lleras-Muney, 2006; O’Súilleabháin et al., 2019, 2020; Levine et al., 1993).

2.4. Analyses

Statistical analyses were conducted using Mplus Version 8 (Muthén and Muthén, 2020). Cox Proportional Hazards Model was used to estimate the risk of death to consider time-to-event including those reported as alive (censored). While allowing for direct and indirect effects on survival time, a structural equation model framework was utilised to estimate mediation in Cox proportional hazards (Asparouhov et al., 2006). All confidence intervals (CI) are reporting 95% thresholds. To statistically test inflammation as an indirect pathway in the predictive effect of personality for mortality hazards, models included IL-6 and CRP simultaneously as mediators. As outlined previously (Turiano et al., 2015), this approach is critical as it allows for the assessment of both mediators together as their combined indirect effect may significantly explain the association between personality and mortality. This approach also incorporates the correlations between indirect effects (Preacher and Hayes, 2008; Turiano et al., 2015).

A base-10 logarithm transformation was performed on both IL-6 and CRP variables to reduce skewed distributions. CRP levels above 10 mg/L may reflect current infection. These observations (n = 29) were retained in the present analysis to provide superior estimates of associations (Moriarity et al., 2021), in addition to the retention of outcome variance that is meaningful (O’Connor et al., 2009). Main analyses were conducted both with and without those observations to determine if estimates changed. Results did not differ. Examination of chronic conditions revealed a number of extreme outlier observations (n = 6). Winsorizing was employed to limit the number of chronic conditions to 6 which was deemed to represent the closest observation not deemed suspect (Tukey, 1962). To ensure winsorization did not alter estimates significantly, main analyses were conducted with chronic conditions winsorized at both 5 and 7. Results did not differ. To determine if lag in time (defined as the length of time between when the psychometric and biological data were collected; M ± SD = 25.94 ± 14.67 months; range = 0–61) could be an important confounding factor, analyses were conducted both with and without controlling for it. Results did not differ. As such, and in line with this variable not being formally included within the preregistration of this study, it was not included as a possible confounding variable. Personality traits were standardized for ease of interpretation, such that associations with personality reflected a difference of one standard deviation. Assessment of Schoenfeld residuals for IL-6 revealed a potential violation of the assumption of proportionality. In accordance with the interaction method when a potential violation of the assumption occurs (Allison, 2010), we included an interaction term of IL-6 and months to death as a covariate for IL-6.

Prior to examining mediation, each variable was assessed as a predictor of mortality. Model 1 tested the effects of personality traits collectively for mortality. Model 2 included sociodemographic factors (age, sex, race, education). Model 3 included health-related confounders (smoking, chronic conditions, activity of daily living, corticosteroid medication, oral NSAID, and parenteral NSAID). Model 4 included both IL-6 and CRP. Following these initial models, a series of models then tested whether the biomarkers mediated this pathway. Specifically, Model 5 examined both biomarker mediation pathways for each personality trait on mortality, with mortality, IL-6, and CRP adjusted for the remaining personality traits not under direct examination. Similar to the
first set of analyses, Model 6 adjusted for age, sex, race, and education and Model 7 further adjusted for smoking, chronic conditions, activity of daily living, corticosteroid medication, oral NSAID, and parenteral NSAID.

3. Results

Several baseline variables had a direct effect on mortality (see Table 2). Consistent with previous analyses of earlier follow-up periods in MIDUS (Graham et al., 2017), Conscientiousness was associated lower mortality risk (HR 0.74; p 0.001; 95% CI, 0.61–0.87), such that each 1 SD increase in conscientiousness was associated with a 35% reduced mortality. This effect was attenuated with the introduction of demographic controls (HR 0.80; p 0.028; 95% CI, 0.64–0.96) and the health-related factors (HR 0.81; p 0.038; 95% CI, 0.65–0.97). The association, however, was reduced to non-significance when adjusted for IL-6 and CRP in Model 4 (HR 0.66; p 0.73). No other personality trait was associated with mortality. In the fully adjusted baseline model, IL-6 was associated with greater mortality risk (HR 2.99; p 0.001; 95% CI, 0.49–5.49). There was no significant association for CRP (HR 0.91; p = 0.733; 95% CI, 0.42–1.40). Of the remaining predictors within the fully adjusted baseline model, age (HR 1.10; p < 0.001; 95% CI, 1.08–1.13) and ADLs (HR 1.33; p = 0.043; 95% CI, 0.96–1.70) were associated with greater mortality risk.

Each personality trait was examined for the potential that IL-6 and CRP may mediate between it and mortality because mediation does not require a direct effect from the predictor to outcome variable (Preacher et al., 2007). The combined indirect effects of both biomarkers were a significant indirect pathway between conscientiousness and mortality risk (Table 3). IL-6 emerged as a robust mediator of the association between conscientiousness and mortality in each model: Model 5 (p = 0.001), Model 6 (p = 0.028), and Model 7 (p = 0.032). These significant mediation results assessed models accounted for an estimated 23.46%, 18.47%, and 17.65% of the effect of conscientiousness on mortality through IL-6, respectively (see Table 3). No significant indirect effect for CRP was observed. There was some evidence of an indirect pathway from neuroticism and agreeableness to mortality through IL-6 in Model 5, but neither indirect effect remained significant with the sociodemographic adjustments. There was no significant effect for extraversion or openness. See supplementary tables for all mediation results for extra- version, openness, and agreeableness. While it was not included in the preregistration of this manuscript, we also did an exploratory test for an interaction between neuroticism and conscientiousness on its association with IL-6 and mortality. No significant association emerged.

4. Discussion

We found support for our preregistered hypotheses: Both IL-6 and CRP were an indirect path that partially linked conscientiousness to mortality risk. Examination of both IL-6 and CRP revealed that IL-6 was the significant contributor to this mediating effect. As such, higher conscientiousness was found to be associated with a longer life partially as a result of lower IL-6. Contrary to our preregistered hypothesis, we did not find that CRP itself was a significant mediator. Although there was some initial evidence that the biomarkers mediated both neuroticism and agreeableness and mortality, the indirect effects were not significant when controlling for the sociodemographic variables. Finally, as expected, the biomarkers did not mediate either extraversion or openness and mortality risk.

The conscientiousness findings are critically important because they

---

1 This fully adjusted significant finding remained virtually unchanged for conscientiousness whether or not the remaining personality traits were adjusted for within the model.
Model 7 in addition to confounding variables in Model 5 and 6, adjusts for personality traits not under direct examination.

* indicates that the HR is presented.
^ indicates that the estimate is presented.

Table 3

|                | Conscientiousness | Neuroticism |
|----------------|-------------------|-------------|
|                | IL-6 Estimate/HR [95% CI], p | CRP Estimate/HR [95% CI], p | IL-6 Estimate/HR [95% CI], p | CRP Estimate/HR [95% CI], p |
| Model 5        |                   |             |                   |             |
| Indirect effect | -0.080, 0.009     | -0.058, -0.002 | -0.080, 0.009     | -0.058, -0.002 |
| effect^        | [-0.126, -0.007]  | [-0.100, -0.014] | [-0.126, -0.007]  | [-0.100, -0.014] |
| Direct effect   | -0.035, 0.026     | -0.015, 0.011  | 0.001, 0.009      | 0.001, 0.009  |
| Total effect    | -0.341, -0.251    | -0.192, -0.136 | -0.341, -0.251    | -0.192, -0.136 |
| Full indirect effect^ | -0.015, 0.006 | -0.059, -0.020 | -0.015, 0.006 | -0.059, -0.020 |
| Direct effect   | 0.771, [0.633, 0.908], 0.004 | 0.874, [0.684, 1.064], 0.225 |
| AIC            | 3472.824          | 3472.824      | 3579.689          | 3579.689      |
| BIC            | 3579.689          | 3579.689      |                    |               |
| Model 6        |                   |             |                   |             |
| Indirect effect | -0.041, 0.001     | -0.016, 0.000 | -0.041, 0.001     | -0.016, 0.000 |
| effect^        | [-0.078, -0.016]  | [-0.094, -0.004] | [-0.078, -0.016]  | [-0.094, -0.004] |
| Direct effect   | 0.016, 0.026     | 0.033, 0.026  | 0.016, 0.026      | 0.033, 0.026  |
| Total effect    | -0.222, -0.180    | 0.135, 0.151  | -0.222, -0.180    | 0.135, 0.151  |
| Full indirect effect^ | -0.016, 0.016 | -0.040, 0.008, 0.16 | -0.016, 0.016 | -0.040, 0.008, 0.16 |
| Direct effect   | 0.835, [0.663, 1.006], 0.084 | 1.163, [0.910, 1.416], 0.173 |
| AIC            | 5962.820          | 5891.291      | 6156.910          | 6085.381      |
| BIC            | 6156.910          | 6085.381      |                    |               |
| Model 7        |                   |             |                   |             |
| Indirect effect | -0.039, 0.003     | -0.028, 0.002 | -0.039, 0.003     | -0.028, 0.002 |
| effect^        | [-0.074, -0.013]  | [-0.060, -0.008] | [-0.074, -0.013]  | [-0.060, -0.008] |
| Direct effect   | -0.015, 0.024, 0.048 | 0.222, 0.407, 0.355 | 0.222, 0.407, 0.355 | 0.222, 0.407, 0.355 |
| Total effect    | -0.221, -0.180    | 0.096, 0.126  | -0.221, -0.180    | 0.096, 0.126  |
| Full indirect effect^ | -0.036, -0.068, -0.004, 0.028 | -0.027, -0.056, 0.002, 0.069 | -0.036, -0.068, -0.004, 0.028 | -0.027, -0.056, 0.002, 0.069 |
| Direct effect   | 0.833, [0.663, 1.003], 0.080 | 1.133, [0.973, 1.392], 0.287 |
| AIC            | 5888.771          | 5815.731      | 6169.708          | 6096.668      |
| BIC            | 6169.708          | 6096.668      |                    |               |

Note: HR = Hazard Ratio, AIC = Akaike Information Criterion, BIC = Bayesian Information Criterion.

Model 5 adjusts for the remaining personality traits not under direct examination.

Model 6 in addition to the previous adjustment, Model 5 adjusts for age, sex, race, education.

Model 7 in addition to confounding variables in Model 5 and 6, adjusts for chronic conditions, ADL, smoking, corticosteroid medication, oral NSAID, and parental NSAID.

* indicates that the estimate is presented.
^ indicates that the HR is presented.
^ Effect of personality on mortality through the indirect inflammation path.
2 Effect of the indirect inflammation path and direct path of the personality trait on mortality.
3 Sum of the indirect paths.
4 Direct effect of the personality trait on mortality.
These results provide a critical insight into biological mechanisms that underlie personality associations, which may be particularly important in the context of conscientiousness and biological health indices (Sutin et al., 2018). Given number of events is a critical component in terms of statistical power when computing a Cox regression, a limitation with the present study design is that <12% of the sample had died. While there are challenges with inferring cause of death due to complexity with comorbidities at the end of life, it may be worthwhile to examine cause-specific mortality within larger samples to determine if specific causes are responsible for the association within the present study.

To conclude, our results indicate that individuals higher in conscientiousness live longer in part because of lower circulating levels of IL-6. These results provide a critical insight into biological mechanisms that link this personality trait to longevity. In doing so, we highlight the importance and need to identify biological pathways that bridge this link from personality to future mortality risk for future work. This study provides a crucial piece to the personality-health puzzle in suggesting that the biomarker IL-6, which is at the core of inflammatory and aging processes, provides a pathway which partly explains why conscientiousness is associated with long-term mortality risk.

Author contributions

P. S. O’Sullivanbheart conceptualized this study. P. S. O’Sulliabheart performed the statistical analyses with assistance from N. A. Turiano, and D. Gerstorf. P. S. O’Sulliabheart, N. A. Turiano, D. Gerstorf, A. Terracciano and A. R. Sutin performed data interpretations. P. S. O’Sulliabheart completed the initial draft of the manuscript with contributions from M. Luchetti, S. Gallagher, and A. A. Sesker. All authors provided critical revisions to the manuscript. All authors approved the final version of the manuscript for submission.

Funding

Funding stemmed from John D. and Catherine T. MacArthur Foundation, Research Network on Successful Midlife Development. United States Department of Health and Human Services. National Institutes of Health. National Institute on Aging (5-PO1-AG20166-04; PO1-AG020166). In addition, the Biomarker Project was supported by the National Institutes of Health National Center for Advancing Translational Sciences, Clinical and Translational Science Award program; UL1TR001409 (Georgetown), UL1TR001881 (UCLA), 1UL1RR025011 (UW).

PSO was supported by the Royal Irish Academy (Charlemont Grant). NAT acknowledges support from the West Virginia Prevention Research Center supported by Cooperative Agreement Number 1-U48-DP-005004 from the Centers for Disease Control and Prevention. MI, AAS, AT, and ARS were supported by the National Institute on Aging of the National Institutes of Health under Award Numbers R01AG053297 and R01AG068093. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Royal Irish Academy, the National Institutes of Health, or the Centers for Disease Control and Prevention. The funders had no role in the study design, collection, analysis, interpretation of the data, writing this manuscript, and decision to submit for publication.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.
Brain Behavior and Immunity 93 (2021) 238–244

O’Süilleabháin, P.S., Hughes, B.M., 2018. Neuroticism predicts all-cause mortality over 19-years: The moderating effects on functional status, and the angiotensin-converting enzyme. J. Psychosom. Res. 110, 52–57. https://doi.org/10.1016/j.jpsychosomres.2018.04.013.

O’Süilleabháin, P.S., Hughes, B.M., Oomen, A.M., Joshi, L., Cunningham, S. 2019. Vulnerability to stress: Personality facet of vulnerability is associated with cardiovascular adaptation to recurring stress. J. Psychosom. Res. 144, 34–39. https://doi.org/10.1016/j.jpsychores.2019.06.013.

O’Süilleabháin, P.S., Satin, A., Gerstorf, D., 2020. Body mass index, waist circumference, and mortality risks over 27 years of follow-up in old age. Am. Epidemiol. 46, 20–23. https://doi.org/10.1093/aje/kwa046.012.

Preacher, K.J., Hayes, A.F., 2008. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. Behavior Res. Methods 40 (4), 879–891. https://doi.org/10.3758/brm.40.4.879.

Preacher, K.J., Rucker, D.D., Hayes, A.F., 2007. Addressing Moderated Mediation Hypotheses: Theory, Methods, and Prescriptions. Multivar. Behav. Res. 42 (1), 185–227. https://doi.org/10.1080/002731710701341316.

Proctor, M.J., McMillan, D.C., Horgan, P.G., Fletcher, C.D., Talwar, D., Morrison, D.S., 2015. Systemic inflammation predicts all-cause mortality: A Glasgow inflammation outcome study. PLoS One, 10(3), e0116206. https://doi.org/10.1371/journal. pone.0116206.

Robert, B.W., Kucnel, N.R., Shiner, R., Caspi, A., Goldberg, L.R., 2007. The Power of Personality: The Comparative Validity of Personality Traits, Socioeconomic Status, and Cognitive Ability for Predicting Important Life Outcomes. Perspect. Psychol. Sci. 2 (4), 313–345. https://doi.org/10.1111/j.1745-6916.2007.00047.x.

Ryff, C.D., Seeman, T., Weinstein, M., 2019. Midlife in the United States (MIDUS II): Biomarker Project, 2004–2009 (ICPSR 29282; Version V9). ICPSR. https://doi.org/10.3886/ICPSR29282.v9.

Ryff, C., Almeida, D.M., Ayamian, J., Carr, D.S., Cleary, P.D., Coo, C., Davidow, R., Rubinow, C.H., Lachman, M.E., Marks, N.F., Mróczek, D.K., Seeman, T., Selzer, M.M., Singer, B.H., Sloan, R.P., Tun, P.A., Weinstein, M., Williams, D., 2017. Midlife in the United States (MIDUS II), 2004–2006 (ICPSR 4652; Version V7). ICPSR. https://doi.org/10.3886/ICPSR04652.v7.

Süilleabháin, P.S., Mróczek, D.K., Howard, S., Hughes, B.M., 2016. Conscientiousness and mindfulness in midlife coping: An assessment based on MIDUS II: Anxiety stress and coping. Personality and Mental Health 10 (1), 29–42. https://doi.org/10.1002/pmh.1323.

Süilleabháin, P.S., Satin, A.R., Luchetti, M., Terracciano, A., 2016. Allostatic Load and Personality: A 4-Year Longitudinal Study. Psychosom. Med. 78 (3), 302–310. https://doi.org/10.1016/j.psymed.2016.01.020.

Süilleabháin, P.S., Howard, S., Hughes, B.M., 2017. Conscientiousness and mindfulness in midlife coping: Evidence from a cross-sectional and a prospective longitudinal epidemiologic study in a Swiss community. J. Psychosom. Res. 84, 44–51. https://doi.org/10.1016/j.jpsychores.2016.03.012.

Weiss, A., Costa Jr, P.T., 2005. Domain and Facet Personality Predictors of All-Cause Mortality in the Elderly Population: A 27-Year Follow-Up. Psychol. Med. 35 (3), 467–477. https://doi.org/10.1017/S003329170426524X.

Listi, F., Nuzzo, D., Lio, D., Caruso, C., 2007. Inflammatory networks in ageing, age-related diseases and longevity. Mech. Ageing Dev. 128 (1), 83–92. https://doi.org/10.1016/j.mado.2006.11.015.

Listi, F., Nuzzo, D., Lio, D., Caruso, C., 2016. Inflammatory networks in ageing, age-related diseases and longevity. Mech. Ageing Dev. 149, 5–12. https://doi.org/10.1016/j.mado.2015.10.004.