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Personality Traits in Patients With Cirrhosis Are Different From Those of the General Population and Impact Likelihood of Liver Transplantation

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Abstract

Background: Personality traits influence clinical outcomes in chronic diseases, but their impact in cirrhosis is unknown. We studied the personality of patients with cirrhosis undergoing liver transplant (LT) evaluation and determined their correlation to clinical outcomes.

Methods: A multicenter prospective study of adult patients undergoing LT evaluation was performed from 1/2018 to 10/2019. The "Big Five" personality traits of conscientiousness, extraversion, openness, neuroticism and agreeableness plus agency were assessed with the MIDI Personality Scale and compared to the general population. Frailty was assessed with the Liver Frailty Index.

Results: Two hundred sixty-three LT candidates were enrolled. Twenty-four percent had HCV, 25% NASH and 25% ETOH (mean MELD=15.7). Compared to the general population, LT

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AUTHOR CONTRIBUTIONS

D.P.L., O.S., and A.J.T. contributed to the concept; J.P. performed the statistical analysis; O.S., A.J.T., D.P.L., J.P., and D.M. wrote the manuscript; J.C.L., J.L., N.R.M., A.-M.F., A.D., D.B.-C., R.W., J.C.C., and C.L. reviewed the final manuscript.

candidates had higher openness (3.1 vs 2.9; p<0.001), extraversion (3.2 vs 3.1; p<0.001), agreeableness (3.5 vs 3.4; p=0.04), agency (2.9 vs 2.6; p<0.001) and neuroticism (2.2 vs 2.1; p = 0.001) and lower conscientiousness (3.3 vs 3.4; p=0.007). Patients with higher conscientiousness were more likely to receive a LT (HR=2.76; p=0.003).

Conclusions: Personality traits in LT candidates differ significantly from the general population, with higher conscientiousness associated with a higher likelihood of receiving a transplant.

1. INTRODUCTION

Cirrhosis is a chronic disease that affects millions of patients in the United States and often leads to severe complications and death.^{1,2} The only curative therapy is liver transplantation (LT), which requires complex self-care, strict medication adherence and longitudinal follow-up prior to and after transplantation.^{3,4} The ability to navigate such a complex medical path is likely influenced by inherent patient characteristics, such as personality traits, which are defined as enduring patterns of thoughts, feelings and actions.⁵ The field of personality psychology is particularly relevant today as personalized, precision medicine has emerged as a cornerstone of clinical practice.⁶ While the scope of precision medicine has largely focused on genetics and biomarkers to tailor individualized treatments, understanding patients' psychosocial characteristics is critical to optimizing patient care.⁶

Personality traits, often referred to under the framework of the "Big Five" personality domains, are known to influence health behaviors in a variety of chronic medical conditions.^{7–11} However, little is known about the impact of personality on patients with cirrhosis.^{12–15} An association between personality traits and cirrhosis is plausible given known relationships between personality traits and key health behaviors that are associated with the most common causes of cirrhosis. For example, low conscientiousness, one of the "Big Five" domains, is associated with maladaptive health behaviors such as alcohol use and obesity, two common causes of cirrhosis.^{7,16–20} A high level of neuroticism, another one of the "Big Five" domains, is associated with a sedentary lifestyle²⁰ and could denote a higher risk of frailty, which is a strong predictor of waitlist $^{21-26}$ and posttransplant mortality.²⁷⁻³⁰ Hence, it is likely that personality traits in patients with cirrhosis are different from those of the general population and may influence disease presentation, treatment, and clinical outcomes. Moreover, personality assessment could identify patients with intrinsic disadvantages who may benefit from targeted support to optimize their outcomes. To this end, we studied the personality traits of patients with cirrhosis undergoing transplant evaluation at two large transplant centers and compared them to those of the general population.

2. MATERIALS AND METHODS

2.1 Health Behavioral Model of Personality (HBM of Personality)

This study is grounded in a well-established theory of personality psychology known as the health behavioral model of personality (HBM). This theory suggests that personality traits impact overall health outcomes and thus mortality through their influence on specific behaviors that patients engage in throughout their lifetimes.^{31,32} For example, individuals

with high conscientiousness are more likely to follow a healthy diet, exercise regularly and attend regular doctor visits, which in turn leads to improved health outcomes.^{7,19,20}

Based on the HBM of Personality, healthcare interventions do not have the same efficacy for each individual. Therefore, personality-informed interventions, which appreciate personality traits as a major aspect of behavioral signatures, are more powerful than one-size-fits-all interventions. Moreover, greater clinical impact can be achieved if interventions are targeted towards certain personality traits.^{31,32} This study applies the theoretical framework of the HBM of Personality, with the working hypothesis that patients evaluated for liver transplantation have different personality traits than the general population and that these traits influence their ability to navigate the complex LT process (Conceptual Model, Figure 1).

2.1 Cohort definition:

A prospective study of adult (18 years of age), English-speaking patients with cirrhosis undergoing outpatient liver transplant evaluation was performed at two transplant centers (Northwestern Memorial Hospital [Center A] and University of California, San Francisco [Center B]) between January 2018 and October 2019. Patients with overt hepatic encephalopathy at the time of enrollment were excluded from the study. Those with a history of hepatic encephalopathy were included if they did not actively demonstrate evidence of confusion. Those with alcohol use disorder, opioid use disorder and psychiatric comorbidities were not excluded. All eligible patients who consented for the study were enrolled prior to waitlisting.

Institutional review board approval was obtained at each respective center (NMH IRB: STU00203181, UCSF IRB: STU00203582).

2.2 Personality Assessment:

Personality traits were assessed once by patients themselves at time of initial LT evaluation using a modified version of the Midlife Development Inventory (MIDI) personality scale (Table S1), a standardized and validated measure of the "Big Five" personality domains of agreeableness, neuroticism, openness, conscientiousness and extraversion, as well as agency (Definitions, Table 1).

The MIDI is a well-established personality measure, demonstrating excellent reliability and construct validity.^{33,34} The MIDI requires patients to rate themselves on each of 38 items (adjectives) using a four-point Likert scale (1: not at all, 2: a little, 3: some, 4: a lot). Global scores for each domain were calculated and compared to the general population using the Midlife in the United States (MIDUS) database which characterizes norms of personality from a general population cohort. A score difference of 0.1 is a clinically notable difference in personality.^{16,33,35} Although personality traits are not clinical entities and represent normal dimensions of human functioning such as verbal ability or executive function, there are wide individual differences in each trait. Differences of .1 on a four-point scale are meaningful, reflecting substantial difference among people and their behavioral patterns.³⁶

2.3 Frailty

Frailty was assessed using the Liver Frailty Index (LFI),²² which consists of three separate components: 1) Balance testing, 2) Repeat chair stands, and 3) Grip testing. LFI scores categorize patients into three categories of frailty: robust (LFI 0–3.2), prefrail (LFI 3.2–4.4) and frail (LFI >4.5).²²

2.4 Demographics & Clinical Data

Etiology of liver disease, presence of hepatocellular carcinoma (HCC) and cause of death were extracted from electronic medical records. Basic patient demographics (age, gender, ethnicity), clinical data (creatinine, total bilirubin, INR), as well as number and duration of hospitalizations since time of LT evaluation were obtained using the Northwestern Enterprise Data Warehouse (NEDW). Biologic Model for End Stage Liver Disease - Sodium (MELD-Na) scores were calculated at time of personality assessment.³⁷

2.5 Outcomes

The primary outcome in this study was the personality distribution of patients with cirrhosis. Secondary outcomes included likelihood of waitlisting, likelihood of transplantation, number of hospitalizations, length of hospital admissions and all-cause mortality.

2.6 Statistical Analysis

Since all statistical analyses were considered exploratory, no predetermined power analyses were conducted to determine appropriate sample sizes for testing specific hypotheses. All statistical analyses were conducted in SAS v9.4 and p-values of <0.05 were considered statistically significant.

To describe the sample, patients' demographics and clinical characteristics were summarized using means, SDs, and ranges for continuous variables and frequencies and percentages for categorical variables. Summaries of these characteristics were given for the overall sample and by study site. Statistical comparisons of each characteristic by site were made with chi-square tests or t-tests (or nonparametric equivalent), as appropriate.

Next, mean trait scores for each domain were compared to national normative values from the MIDUS national, longitudinal health study using one-sample t-tests. Mean MIDUS personality scores were also compared between etiologies of liver disease using two sample t-tests. We compared MIDUS scores between categories of frailty by estimating least squares means (LS means) within each group using ANOVA. We then calculated effect sizes for differences between each group as the difference between group means divided by the pooled SD, as well as p-values. Effect sizes are interpreted as: small = 0.20, <0.50; medium = 0.50, <0.80; large = >0.80. We compared the median number of hospitalizations and days hospitalized between groups of patients with mean or above mean MIDUS scores and patients with below mean MIDUS scores using Kruskal-Wallis tests. Mean personality scores between patients who did not die during the course of the study were compared using two sample t-tests. Finally, time to event analysis was conducted to estimate the likelihood of receiving a liver transplant. Personality scales were dichotomized as above mean or mean or below. We first used Kaplan Meier methods to generate product-limit

failure plots stratified by each level of the dichotomized personality scales (above mean or mean or below). The log-rank test was used to test whether the failure curves differed significantly. Next, we entered each dichotomized personality score into separate Cox proportional hazards models with the outcome as time to liver transplant adjusting for MELD.

3. RESULTS

We enrolled 263 liver transplant candidates at Center A (n=159) and Center B (n=104). The mean age of the transplant candidates was 59 (21–76) years, 101 (38%) were female, 189 (72%) were White, 32 (12%) were Hispanic and 16 (6%) were Black. The mean MELD score at the time of personality assessment was 15.7 (6.0–34.9) and the main etiologies for cirrhosis were hepatitis C (HCV) in 64 (24%), nonalcoholic steatohepatitis (NASH) in 67 (25%), and alcoholic cirrhosis in 66 (25%) patients (Table 2). Basic demographics and clinical characteristics of the study cohort at NMH were similar to all patients evaluated for liver transplantation at the center, with no significant differences in age (59 years vs 59 years; p = 0.16), gender (38% vs 45% female; p = 0.24) or mean MELD-Na (15.7 vs 15.6; p = 0.10). The main etiologies of cirrhosis in all patients evaluated at NMH were NASH (35%), alcoholic cirrhosis (38%), primary biliary cirrhosis/primary sclerosis cholangitis (10%) and HCV (8%). There were significantly more patients with HCC in the study cohort than in the entire candidate pool (28% vs 8%; p < 0.05).

Of the personality traits assessed (scale of 1–4), the average score for agency was 2.9 +/– 0.6, for agreeableness was 3.5 +/-0.6, for openness was 3.1 +/-0.5, for neuroticism was 2.2 +/-0.6, for extraversion was 3.2 +/-0.6, and for conscientiousness was 3.3 +/-0.5. Compared to the general population, those with cirrhosis had higher levels of openness (3.1 vs 2.9; p < 0.001), extraversion (3.2 vs 3.1; p < 0.001), agreeableness (3.5 vs 3.4; p = 0.04), agency (2.9 vs 2.6; p < 0.001), and neuroticism (2.2 vs 2.1; p = 0.001). However, conscientiousness (3.3 vs 3.4; p = 0.007) was significantly lower than the general population (Table 3). Differences of 0.1 are considered both clinically and statistically significant.^{16,33,35}

Patients with HCC (3.3 vs 3.1; p = 0.02) had higher levels of extraversion and higher levels of openness (3.2 vs 3.0, p=0.05) than those without HCC. Those with NASH and those with biliary disease (primary biliary cirrhosis or primary sclerosing cholangitis) were more agreeable than those without NASH (3.6 vs 3.4; p = 0.05) and those without biliary disease (3.7 vs 3.5; p = 0.03) (Table 4). No differences in personality distribution were found between the two centers.

In terms of frailty, robust patients (LFI 0–3.2) had higher agency (p < 0.001) and openness (p < 0.001) compared to frail patients, with a large effect size (effect size [ES] = 0.81 and 0.96, respectively). Compared to frail patients, robust patients also had significantly higher agreeableness (p = 0.005) and extraversion (p < 0.001), with a moderate effect size (ES = 0.73 and 0.71, respectively). Findings were similar when comparing robust patients to their prefrail counterparts, with the exception of agreeableness and consciousness. Robust patients had a similar level of agreeableness as prefrail patients, but significantly higher

conscientiousness (p=0.04), with a small effect size (ES = 0.38) (Table 5). Patients with a higher than average level of conscientiousness were significantly more likely to receive a liver transplantation (Figure 2). This significant association was retained even after adjusting for MELD [Hazard ratio (HR): 2.76, 95% CI 1.42–5.36, p = 0.003)] (Table 6). None of the other personality traits were associated with time to liver transplant. There was no association between personality traits and likelihood of being waitlisted, number of hospitalizations or mortality. However, higher conscientiousness was associated with a longer median length of hospital stay (p = 0.03) (Tables 7 and 8).

Fourteen subjects died during the study period. Five of these patients were on the waitlist, while the remainder were still undergoing transplant evaluation or determined to not be transplant candidates. No patients died after receiving a LT.

4. DISCUSSION

In this prospective multicenter study, we found that patients with cirrhosis evaluated for liver transplant have significantly lower levels of conscientiousness than the general population. Patients with cirrhosis who received a liver transplant have higher levels of conscientiousness compared to those who do not. This is the first study to comprehensively assess personality traits in patients with cirrhosis evaluated for liver transplantation.

The emergence of personalized, precision medicine over the past decade has led to the recognition that patient care can be optimized by targeting the needs of each individual or certain groups of individuals with similar qualities. In recent years, the focus of personalized medicine has largely centered on the use of epigenetics and proteomics to better define pathophysiology and subsequently improve prognostics and therapeutics.⁶ The role of personality traits in optimizing clinical care, however, has largely remained unexplored in the field of liver transplantation.

Personality traits have been studied extensively in patients with chronic medical conditions and certain traits have been linked to all-cause mortality as well as numerous healthenhancing and maladaptive behaviors. A high level of conscientiousness describes an individual who is diligent, reliable, self-disciplined and goal-oriented.^{38,39} While never studied in cirrhosis, conscientiousness has been studied in various other chronic diseases including type 2 diabetes mellitus, hypertension, dyslipidemia and obesity and higher conscientiousness is strongly associated with lower all-cause mortality and increased longevity.^{7–10,12–15} Lower conscientiousness, on the other hand, has been linked to faster disease progression¹¹ and higher mortality rates in patients with chronic renal disease.^{40,41} Higher levels of conscientiousness correlate with greater adherence to physicians' recommendations for lifestyle modifications, medication regimens, healthier eating habits and increased physical activity.^{7,18–20,42,43}

Our finding that conscientiousness is lower in patients with cirrhosis compared to the general population suggests that patients with cirrhosis, who require a complex treatment regimen, are additionally challenged by their intrinsic personality traits. This is particularly relevant in patients who are considered for liver transplantation, which involves adherence

to multi-drug therapy, frequent follow-up and regular physical activity to decrease frailty. Interestingly, we found that patients with higher conscientiousness were more likely to receive a liver transplant at both centers, suggesting that personality traits may influence which patients on the waiting list receive a transplant. It is unclear why more conscientious individuals have a higher likelihood of receiving a transplant. Given the known relationship between higher conscientiousness and positive health behaviors, however, it is possible that individuals with higher conscientiousness are more adept at navigating the healthcare system and the complex steps required prior to liver transplantation. Alternatively, it is possible that these patients are more likely to receive and accept opportunities such as 'dropped livers', which require a quick response and the ability to come to a transplant center on short notice. It is important to note that there was no correlation between conscientiousness and likelihood of being waitlisted. Therefore, our data do not suggest that healthcare providers are unwittingly selecting and advocating for patients with high conscientiousness. Regardless of the factors driving the correlation between conscientiousness and likelihood of LT, our study demonstrates that patients with lower conscientiousness are inherently vulnerable in the liver transplantation process and might require targeted support to optimize their outcomes and ensure an equal likelihood of receiving a LT. For example, although the primary onus is on patients themselves to follow physician recommendations, more frequent check-ins by the transplant coordinators or automatized reminders (ie, medication reminders) could improve pre- and posttransplant outcomes.44

Physical activity and nutrition are of particular importance to those with cirrhosis during pre- and posttransplant care. Due to the physiological sequelae of cirrhosis, patients are prone to deconditioning and malnutrition, with 17% of patients awaiting liver transplantation known to be frail.²¹ Frailty strongly predicts both waitlist,^{21–26} posttransplant mortality,^{27–30} and a higher frequency of hospitalizations,^{45–47} even after adjusting for severity of liver disease as measured by the MELD score. Our finding of lower conscientiousness and higher neuroticism in cirrhosis also denotes a tendency towards a sedentary lifestyle and thus, another barrier that needs to be overcome to reduce frailty in liver transplant candidates. Interestingly, we did not find that frail patients had a lower level of conscientiousness in our study. However, we did find that they had lower agency, a trait similar to conscientiousness and closely related to self-efficacy and independence.^{48,49}

The notable personality differences between patients with cirrhosis and the general population also suggests that inherent personality traits may predispose patients to the development of liver disease. For example, lower conscientiousness is associated with maladaptive health behaviors including tobacco use, excessive alcohol consumption, illicit drug use, risky sexual behaviors and unhealthy eating habits, which are known risk factors for cirrhosis.^{16–18} We also found that patients with cirrhosis had significantly higher levels of neuroticism than the general population. Neuroticism has been consistently associated with a sedentary lifestyle, obesity and substance abuse,^{7,16,17,50} which are risk factors for nonalcoholic fatty liver disease, alcohol-associated liver disease and hepatitis C. The implications of higher extraversion and agreeableness in cirrhosis are less clear as these personality traits have not been studied as extensively in other healthcare settings. However, higher levels of extraversion and agreeableness are likely contributors to the development

of liver disease, as they are associated with alcohol consumption, a risk factor for cirrhosis independent of primary etiology.⁵¹

Future studies on personality-informed interventions may prove to be impactful. For example, personality assessment could be used to screen for patients who are more likely to struggle with self-directed physical activity at home and to devise realistic, individualized interventions to prevent worsening frailty. Patients with particularly low conscientiousness (ie, lacking the discipline to exercise consistently) may benefit from regular reminders to exercise as part of a self-management program, which has been shown to improve self-efficacy and self-care behaviors in end-stage renal disease patients.⁴⁴ Moreover, those with low conscientiousness may benefit from frequent contact with nurses and pharmacy staff to increase medication compliance. If so, personality-informed interventions could prove invaluable to decreasing posttransplant complications such as acute or chronic cellular rejection and potentially graft failure.

Finally, it is critical to note that personality assessment is not intended to replace a comprehensive psychiatric and social assessment in the transplant evaluation process. A brief personality evaluation cannot diagnose complex psychiatric comorbidities or identify the appropriate social support necessary for transplantation. Rather, personality assessment could provide objective, unbiased data into a patient's overall disposition that would supplement the psychiatric and social assessment.

This study has several limitations. It is critical to note that our study specifically evaluated patients who were being considered for liver transplantation – a small subset of all patients with cirrhosis who have more advanced liver disease and access to a tertiary care center. Thus, our current findings cannot be applied to all individuals with cirrhosis. Although our study only included patients from two transplant centers, which could theoretically limit the generalizability of our findings, the transplant centers were in different geographical locations of the country. Despite significantly different patient populations, findings were similar. Although we excluded those with overt hepatic encephalopathy, our study did not evaluate the presence of covert hepatic encephalopathy at time of personality evaluation. This is the first study to evaluate personality traits in patients with cirrhosis and it is unclear how or if HE effects personality traits. It is possible that covert HE impacts an individual's ability to complete the personality assessment accurately.

Furthermore, we only assessed personality at one time point in this study, yet it is critical to note that most personality experts believe that personality traits are largely consistent throughout adult life.⁵² Finally, our study found an association rather than a causal relationship between personality traits and cirrhosis. Given the stability of personality over time, we hypothesize that certain personality traits predispose patients to cirrhosis rather than cirrhosis causing significant changes in personality. This study does not conclusively answer that question. Lastly, the differences in personality scores between our cohort and the general population were often small (ie, one-tenth of a point). However, as established in the personality psychology literature and agreed upon among experts in personality research (D.M.), this signifies a clinically relevant finding and can lead to notable differences in behavior.⁵⁰

Given the well-established association between personality traits and health outcomes, consistently measuring personality traits in patients with cirrhosis may provide a validated and objective tool – rather than a 'gestalt' - to assess patients' internal resources. More importantly, personality assessment could prove critical to the development of individualized interventions to improve clinical outcomes before and after liver transplantation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS:

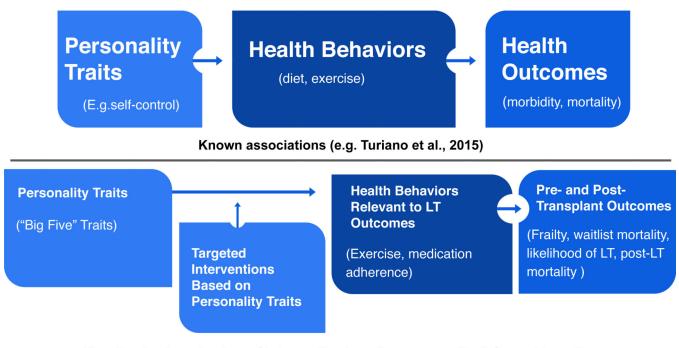
BMI	body mass index
COPD	chronic obstructive pulmonary disease
ES	effect size
GI	gastrointestinal
НСС	hepatocellular carcinoma
HCV	hepatitis C
LFI	Liver Frailty Index
MELD	Model of End Stage Liver Disease
MIDI	Midlife Development Inventory
MIDUS	Midlife in the U.S. Survey
NASH	Nonalcoholic Steatohepatitis
NEDW	Northwestern Enterprise Data Warehouse
PBC	Primary Biliary Cirrhosis
PSC	Primary Sclerosing Cholangitis

REFERENCES

- 1. Mazumder N, Atiemo K, Zhao L, et al. Unearthing the epidemiology of an insidious disease: using "big data" to examine cirrhosis in the population. Hepatology. 2019;70:393A–394A.
- 2. Heidelbaugh JJ, Bruderly M. Cirrhosis and chronic liver failure: part I. Diagnosis and evaluation. Am Fam Physician. 2006;74:756–762. [PubMed: 16970019]
- D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. J Hepatol. 2006;44:217–231. [PubMed: 16298014]
- 4. Jain A, Reyes J, Kashyap R, et al. Long-term survival after liver transplantation in 4,000 consecutive patients at a single center. Ann Surg. 2000;232:490–500. [PubMed: 10998647]
- 5. McCrae RR, Costa PT. The Five Factor theory of personality. In: John OP, Robins RW, Pervin LA, eds. Handbook of Personality. 3rd ed. The Guilford Press; 2008.
- Jameson JL, Longo DL. Precision medicine personalized, problematic, and promising. N Engl J Med. 2015;372:2229–2234. [PubMed: 26014593]
- 7. Goodwin RD, Friedman HS. Health status and the five-factor personality traits in a nationally representative sample. J Health Psychol. 2006;11:643–654. [PubMed: 16908463]
- Wilson RS, Schneider JA, Arnold SE, et al. Conscientiousness and the incidence of Alzheimer disease and mild cognitive impairment. Arch Gen Psychiatry. 2007;64:1204–1212. [PubMed: 17909133]
- Duchek JM, Balota DA, Storandt M, et al. The power of personality in discriminating between healthy aging and early-stage Alzheimer's disease. J Gerontol B Psychol Sci Soc Sci. 2007;62:P353–P361. [PubMed: 18079420]
- Sutin AR, Terracciano A, Deiana B, et al. Cholesterol, triglycerides, and the Five-Factor Model of personality. Biol Psychol. 2010;84:186–191. [PubMed: 20109519]
- Brickman AL, Yount SE, Blaney NT, et al. Personality traits and long-term health status: The influence of neuroticism and conscientiousness on renal deterioration in type-1 diabetes. Psychosomatics. 1996;37:459–468. [PubMed: 8824126]
- Kern ML, Friedman HS. Do conscientious individuals live longer? A quantitative review. Health Psychol. 2008;27:505–512. [PubMed: 18823176]
- Wilson RS, Mendes De Leon CF, Bienias JL, et al. Personality and mortality in old age. J Gerontol B Psychol Sci Soc Sci. 2004;59:P110–P116. [PubMed: 15118013]
- Friedman HS, Tucker JS, Tomlinson-Keasey C, et al. Does childhood personality predict longevity? J Pers Soc Psychol. 1993;65:176–185. [PubMed: 8355139]
- Iwasa H, Masui Y, Gondo Y, et al. Personality and all-cause mortality among older adults dwelling in a japanese community: a five-year population-based prospective cohort study. Am J Geriatr Psychiatry. 2008;16:399–405. [PubMed: 18403571]
- Turiano NA, Chapman BP, Gruenewald TL, et al. Personality and the leading behavioral contributors of mortality. Health Psychol. 2015;34:51–60. [PubMed: 24364374]
- Turiano NA, Hill PL, Roberts BW, et al. Smoking mediates the effect of conscientiousness on mortality: the Veterans Affairs Normative Aging Study. J Res Pers. 2012;46:719–724. [PubMed: 23504043]
- Bogg T, Roberts BW. Conscientiousness and health-related behaviors: a meta-analysis of the leading behavioral contributors to mortality. Psychol Bull. 2004;130:887–919. [PubMed: 15535742]
- 19. Sutin AR, Stephan Y, Luchetti M, et al. The five-factor model of personality and physical inactivity: a meta-analysis of 16 samples. J Res Pers. 2016;63:22–28. [PubMed: 29056783]
- Wilson KE, Das BM, Evans EM, et al. Personality correlates of physical activity in college women. Med Sci Sports Exerc. 2015;47:1691–1697. [PubMed: 25386714]
- Lai JC, Feng S, Terrault NA, et al. Frailty predicts waitlist mortality in liver transplant candidates. Am J Transplant. 2014;14:1870–1879. [PubMed: 24935609]
- 22. Lai JC, Covinsky KE, Dodge JL, et al. Development of a novel frailty index to predict mortality in patients with end-stage liver disease. Hepatology. 2017;66:564–574. [PubMed: 28422306]

- Lai JC, Covinsky KE, McCulloch CE, et al. The liver frailty index improves mortality prediction of the subjective clinician assessment in patients with cirrhosis. Am J Gastroenterol. 2018;113:235– 242. [PubMed: 29231189]
- 24. Carey EJ, Steidley DE, Aqel BA, et al. Six-minute walk distance predicts mortality in liver transplant candidates. Liver Transpl. 2010;16:1373–1378. [PubMed: 21117246]
- 25. Ney M, Haykowsky MJ, Vandermeer B, et al. Systematic review: pre- and post-operative prognostic value of cardiopulmonary exercise testing in liver transplant candidates. Aliment Pharmacol Ther. 2016;44:796–806. [PubMed: 27539029]
- 26. Orman ES, Ghabril M, Chalasani N. Poor performance status is associated with increased mortality in patients with cirrhosis. Clin Gastroenterol Hepatol. 2016;14:1189–1195.e1. [PubMed: 27046483]
- Sundaram V, Lim J, Tholey DM, et al. The Braden Scale, a standard tool for assessing pressure ulcer risk, predicts early outcomes after liver transplantation. Liver Transpl. 2017;23:1153–1160. [PubMed: 28512923]
- Pereira JLF, Galant LH, Rossi D, et al. Functional capacity, respiratory muscle strength, and oxygen consumption predict mortality in patients with cirrhosis. Can J Gastroenterol Hepatol. 2016;2016:6940374.
- Tapper EB, Finkelstein D, Mittleman MA, et al. Standard assessments of frailty are validated predictors of mortality in hospitalized patients with cirrhosis. Hepatology. 2015;62:584–590. [PubMed: 25846824]
- 30. Tandon P, Reddy KR, O'Leary JG, et al. ; North American Consortium for the Study of End-Stage Liver Disease. A Karnofsky performance status–based score predicts death after hospital discharge in patients with cirrhosis. Hepatology. 2017;65:217–224. [PubMed: 27775842]
- 31. Murray AL, Booth T. Personality and physical health. Curr Opin Psychol. 2015;5:50–55.
- Graham EK, Weston SJ, Turiano NA, et al. Is healthy neuroticism associated with health behaviors? A coordinated integrative data analysis. Collabra Psychol. 2020;6(1):32. [PubMed: 33354649]
- Turiano NA, Pitzer L, Armour C, et al. Personality trait level and change as predictors of health outcomes: findings from a national study of Americans (MIDUS). J Gerontol B Psychol Sci Soc Sci. 2012;67(1):4–12. [PubMed: 21765062]
- 34. Mroczek DK, Kolarz CM. The effect of age on positive and negative affect: a developmental perspective on happiness. J Pers Soc Psychol. 1998;75(5):1333–1349. [PubMed: 9866191]
- Turiano NA, Mroczek DK, Moynihan J, et al. Big 5 personality traits and interleukin-6: Evidence for "healthy Neuroticism" in a US population sample. Brain Behav Immun. 2013;28:83–89. [PubMed: 23123863]
- Funder DC, Ozer DJ. Evaluating effect size in psychological research: sense and nonsense. Adv Methods Pract Psychol Sci. 2019;2(2):156–168.
- 37. Kim WR, Biggins SW, Kremers WK, et al. Hyponatremia and mortality among patients on the liver-transplant waiting list. N Engl J Med. 2008;359:1018–1026. [PubMed: 18768945]
- Roberts BW, Chernyshenko OS, Stark S, et al. The structure of conscientiousness: an empirical investigation based on seven major personality questionnaires. Pers Psychol. 2005;58:103–139.
- Chapman BP, Roberts B, Duberstein P. Personality and longevity: knowns, unknowns, and implications for public health and personalized medicine. J Aging Res. 2011;2011:759170. [PubMed: 21766032]
- 40. Christensen AJ, Ehlers SL, Wiebe JS, et al. Patient personality and mortality: a 4-year prospective examination of chronic renal insufficiency. Heal Psychol. 2002;21:315–320.
- Christensen AJ, Moran PJ. Psychological aspects of end-stage renal disease. In: Johnston DW, Johnston M, Bellack AS, et al., eds. Comprehensive Clinical Psychology. Elsevier Science Publishers; 1998.
- 42. Hill PL, Roberts BW. The role of adherence in the relationship between conscientiousness and perceived health. Health Psychol. 2011;30:797–804. [PubMed: 21604876]
- 43. Rhodes RE, Courneya KS, Bobick TM. Personality and exercise participation across the breast cancer experience. Psychooncology. 2001;10:380–388. [PubMed: 11536416]

- 44. Karadag E. The effect of a self-management program on hand-washing/mask-wearing behaviours and self-efficacy level in peritoneal dialysis patients: a pilot study. J Ren Care. 2019;45(2):93–101. [PubMed: 30825408]
- 45. Tandon P, Tangri N, Thomas L, et al. A rapid bedside screen to predict unplanned hospitalization and death in outpatients with cirrhosis: a prospective evaluation of the Clinical Frailty Scale. Am J Gastroenterol. 2016;111:1759–1767. [PubMed: 27481305]
- Dunn MA, Josbeno DA, Tevar AD, et al. Frailty as tested by gait speed is an independent risk factor for cirrhosis complications that require hospitalization. Am J Gastroenterol. 2016;111:1768– 1775. [PubMed: 27575708]
- 47. Sinclair M, Poltavskiy E, Dodge JL, et al. Frailty is independently associated with increased hospitalisation days in patients on the liver transplant waitlist. World J Gastroenterol. 2017;23:899–905. [PubMed: 28223735]
- Bandura A. Self-efficacy: toward a unifying theory of behavioral change. Psychol Rev. 1977;84:191–215. [PubMed: 847061]
- Lopes AC, Xavier RF, AC Pereira AC, et al. Identifying COPD patients at risk for worse symptoms, HRQoL, and self-efficacy: a cluster analysis. Chronic Illn. 2019;15:138–148. [PubMed: 29343090]
- Mroczek DK, Spiro A, Turiano NA. Do health behaviors explain the effect of neuroticism on mortality? Longitudinal findings from the VA Normative Aging Study. J Res Pers. 2009;43:653– 659. [PubMed: 20161240]
- Roerecke M, Vafaei A, Hasan O, et al. Alcohol consumption and risk of liver cirrhosis: a systematic review and meta-analysis. Am J Gastroenterol. 2019;114(10):1574–1586. [PubMed: 31464740]
- Roberts BW, DelVecchio WF. The rank-order consistency of personality traits from childhood to old age: a quantitative review of longitudinal studies. Psychol Bull. 2000;126:3–25. [PubMed: 10668348]



Hypothesized mechanism of intervention based on personality-informed targeting

Figure 1.

Conceptual model of the health behavior model of personality applied to LT candidates. LT, liver transplant.

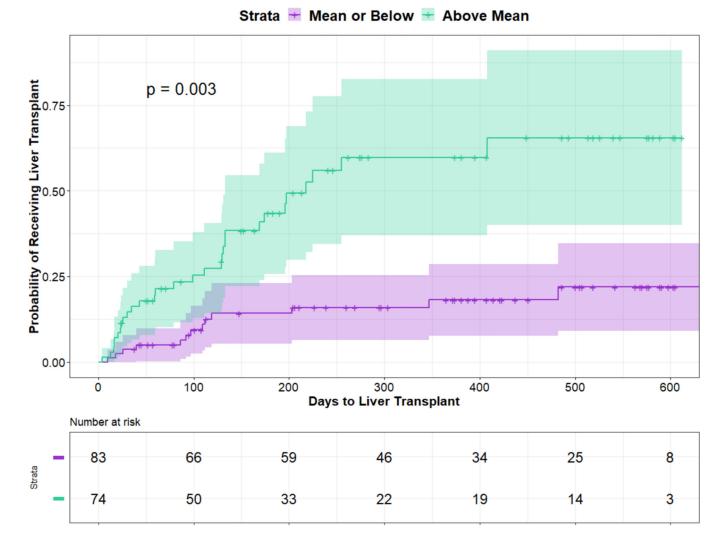


Figure 2.

Associations between time to transplant and conscientiousness unadjusted.

Table 1.

Personality domains and definitions.

Personality trait	Basic tendencies	Characteristic adaptions
Agreeableness	Willingness to defer to others during interpersonal conflict.	Forgiving attitude, belief in cooperation.
Neuroticism	Tendency to experience dysphoric effect, such as sadness, hopelessness, and guilt.	Low self-esteem, pessimistic attitudes.
Openness	Need for variety, novelty, and change.	Interest in travel, many different hobbies, diverse vocational interests.
Conscientiousness	Strong sense of purpose and high aspiration levels.	Long-term planning, leadership skills, technical expertise.
Extraversion	Preference for companionship and social stimulation.	Social skills, numerous friendships.
Agency ^a	Tendency towards self-efficacy and independence.	Self-confidence, inclined to take initiative.

^aNot one of the "Big Five" personality domains.

Table 2.

Patient characteristics.

	Overall (n = 263)	Center A (n = 159)	Center B (n = 104)	Р
Age, mean (range), years	59 (21–76)	58 (21–76)	61 (37–75)	0.09
Female gender, n (%)	101 (38)	62 (39)	39 (38)	0.81
Race/ethnicity, n (%)				0.01
Hispanic	32 (12)	15 (9)	17 (16)	
Non-Hispanic White	189 (72)	122 (77)	67 (64)	
Non-Hispanic Black	16 (6)	8 (5)	8 (8)	
Non-Hispanic Asian	10 (4)	2 (1)	8 (8)	
Non-Hispanic other	16 (6)	12 (8)	4 (4)	
Etiology (not mutually exclusive), n (%)				
HCV	64 (24)	25 (16)	39 (38)	< 0.001
NASH	67 (25)	55 (35)	12 (12)	< 0.001
PBC/PSC	34 (13)	21 (13)	13 (13)	0.87
ЕТОН	66 (25)	39 (25)	27 (26)	0.79
Other	26 (10)	14 (9)	12 (12)	0.47
HCC, n (%)	91 (36)	44 (29)	47 (45)	0.01
MELD, mean (range)	15.7 (6.0–34.9)	16.9 (6.4–34.9)	13.6 (6.0–25.0)	< 0.001
Creatinine, mean (range)	1.1 (0-6.3)	1.2 (0-6.3)	1.1 (0.4–5.8)	0.34
Bilirubin, mean (range)	3.2 (0-38.8)	3.6 (0-38.0)	2.4 (0.3–20.7)	0.007
INR, mean (range)	1.4 (0-6.9)	1.4 (0-6.9)	1.3 (0.2–2.5)	0.30
Liver Frailty Index, n (%)				0.23
Robust (0 to <3.2)	46 (22)	21 (20)	25 (25)	
Prefrail (3.2–4.4)	130 (63)	64 (61)	66 (65)	
Frail (4.5)	31 (15)	20 (19)	11 (11)	
Mortality, n (%)	25 (10)	15 (9)	10 (10)	0.93

ETOH, ethyl alcohol; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; INR, international normalized ratio; MELD, Model for End-Stage Liver Disease; NASH, nonalcoholic steatohepatitis; PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis.

Table 3.

Personality traits of patients with cirrhosis vs the general population.

	Cirrhosis, mean (95% CI)	General population mean	Р
Agency	2.9 (2.8, 3.0)	2.6	< 0.001
Agreeableness	3.5 (3.4, 3.6)	3.4	0.04
Conscientiousness	3.3 (3.2, 3.4)	3.4	0.007
Extraversion	3.2 (3.2, 3.3)	3.1	< 0.001
Neuroticism	2.2 (2.1, 2.3)	2.1	0.001
Openness	3.1 (3.0, 3.2)	2.9	< 0.001

CI, confidence interval.

Table 4.

Personality traits by etiology of cirrhosis and presence of HCC.

			_
Presence of HCC, mean	HCC	No HCC	P
Agency	3.0	2.8	0.06
Agreeableness	3.6	3.5	0.19
Conscientiousness	3.3	3.2	0.34
Extraversion	3.3	3.1	0.02
Neuroticism	2.1	2.2	0.08
Openness	3.2	3.0	0.05
Etiology, HCV, mean	HCV	No HCV	P
Agency	3.0	2.9	0.07
Agreeableness	3.5	3.5	0.89
Conscientiousness	3.3	3.4	0.83
Extraversion	3.3	3.2	0.25
Neuroticism	2.1	2.2	0.58
Openness	3.1	3.0	0.40
Etiology, NASH, mean	NASH	No NASH	P
Agency	2.9	2.9	0.73
Agreeableness	3.6	3.4	0.05
Conscientiousness	3.4	3.3	0.31
Extraversion	3.2	3.2	0.76
Neuroticism	2.3	2.1	0.11
Openness	3.0	3.1	0.15
Etiology, PBC/PSC, mean	BIL	No PBC/PSC	P
Agency	2.9	2.9	0.93
Agreeableness	3.7	3.5	0.03
Conscientiousness	3.3	3.3	0.99
Extraversion	3.2	3.2	0.93
Neuroticism	2.1	2.2	0.51
Openness	3.2	3.1	0.31
Etiology, ETOH, mean	ЕТОН	No ETOH	P
Agency	2.9	2.9	0.62
Agreeableness	3.4	3.5	0.09
Conscientiousness	3.3	3.3	0.53
Extraversion	3.2	3.2	0.61
Neuroticism	2.1	2.2	0.14
Openness	3.1	3.1	0.61

ETOH, ethyl alcohol; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; NASH, nonalcoholic steatohepatitis; PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis.

Table 5.

Comparison personality traits by degree of frailty.

	Robust (N = 46)	Prefrail (N = 130)	Frail (N = 31)	Difference: robust vs prefrail		Difference: prefrail vs frail			Difference: robust vs frail			
	Mean, SD	Mean, SD	Mean, SD	Mean diff	ES ^a	Р	Mean diff	ES a	Р	Mean diff	ES a	Р
Agency	3.1 (0.5)	2.9 (0.6)	2.6 (0.6)	0.3	0.43	0.01	0.2	0.38	0.04	0.5	0.81	< 0.001
Agreeableness	3.7 (0.4)	3.5 (0.5)	3.3 (0.6)	0.2	0.36	0.12	0.2	0.36	0.05	0.4	0.73	0.005
Conscientiousness	3.5 (0.4)	3.3 (0.6)	3.3 (0.6)	0.2	0.38	0.04	0	0	0.77	0.2	0.38	0.07
Extraversion	3.4 (0.5)	3.2 (0.5)	3.0 (0.6)	0.2	0.36	0.05	0.2	0.36	0.02	0.4	0.71	< 0.001
Neuroticism	2.1 (0.6)	2.2 (0.6)	2.2 (0.5)	-0.1	-0.17	0.78	0	0	0.82	-0.1	-0.17	0.69
Openness	3.3 (0.4)	3.1 (0.5)	2.8 (0.6)	0.2	0.38	0.03	0.3	0.58	0.004	0.5	0.96	< 0.001

^{*a*}ES: calculated as difference in group means divided by pooled SD for each personality domain. Effect sizes are interpreted as: small = 0.20, <0.50; medium = 0.50, <0.80; large = 0.80. SDs are as follows: Agency = 0.61; Agreeableness = 0.55; Conscientiousness = 0.53; Extraversion = 0.56; Neuroticism = 0.59; Openness = 0.52.

ES, effect size.

Table 6.

Model for End-Stage Liver Disease-adjusted hazard ratio of transplant associated with personality traits.

Dichotomized personality estimate: (above mean vs mean or below)	Hazard ratio (95% CI)	Р
Agency	1.16 (0.62, 2.18)	0.65
Agreeableness	1.29 (0.68, 2.44)	0.44
Conscientiousness	2.76 (1.42, 5.36)	0.003
Extraversion	0.80 (0.43, 1.50)	0.48
Neuroticism	0.77 (0.42, 1.40)	0.40
Openness	1.34 (0.71–2.54)	0.37

CI, confidence interval.

Table 7.

Comparison of personality traits between patients who died and those who remain alive.

	Died	Alive	Р
Agency, mean (range)	3.0 (1.2-4.0)	2.9 (1.2-4.0)	0.26
Agreeableness, mean (range)	3.4 (2.0-4.0)	3.5 (1.2-4.0)	0.43
Conscientiousness, mean (range)	3.4 (2.3-4.0)	3.3 (1.5-4.0)	0.41
Extraversion, mean (range)	3.2 (2.2-4.0)	3.2 (1.4-4.0)	0.73
Neuroticism, mean (range)	2.2 (1.0-3.3)	2.2 (1.0-4.0)	0.92
Openness, mean (range)	3.1 (2.0-4.0)	3.1 (1.0-4.0)	0.90

Table 8.

Association between personality and number of hospitalizations and days hospitalized.

	Number of hospitalizations, median (IQR)	P	Days hospitalized, median (IQR)	P
Agency		0.64		0.21
Above mean	1.0 (2)		1.5 (10)	
Mean or below	0.0 (2)		0.0 (7)	
Agreeableness		0.24		0.13
Above mean	1.0 (2)		1.0 (11)	
Mean or below	0.0 (2)		0.0 (7)	
Conscientiousness		0.08		0.03
Above mean	1.0 (2)		4.0 (13)	
Mean or below	0.0 (2)		0.0 (8)	
Extraversion		0.66		0.98
Above mean	0.0 (2)		0.0 (10)	
Mean or below	1.0 (2)		1.0 (8)	
Neuroticism		0.86		0.82
Above mean	0.0 (2)		0.0 (9)	
Mean or below	1.0 (2)		1.0 (8)	
Openness		0.36		0.48
Above mean	0 (2)		0 (8)	
Mean or below	0.5 (1)		4.5 (9)	

IQR, interquartile range.