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Prevention, use of health services, and genes: Implications of genetics for policy formation

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Abstract

We evaluate the hypothesis that genetic factors influence use of health services and health prevention behaviors in a national sample of adult twins in the US. We find evidence of significant genetic influences on preferences toward prevention, overall prevention effort, routine check-ups, and prescription drug use. Use of curative services do not appear to be influenced by genes. Our findings offer several implications for policymakers and researchers and suggest that genetics could be informative for health services and policy research.

I. Introduction

There is extensive debate about the extent to which recent national healthcare reform will actually affect the use of health services. At the heart of this discussion are questions about how the Patient Protection and Affordable Care Act (PPACA) mandates for obtaining insurance coverage and for insurance plans to fully cover preventive services such as routine physician visits at no out-of-pocket cost to consumers will modify use of preventive care and medical services. However, an emerging concern is that genetic differences between individuals can moderate subsequent policy effects. Individuals respond very differently to the same policy changes and some of these differences may have genetic origins.

Fletcher (2012) has shown that the smoking behaviors of individuals carrying a specific genetic risk variant that may predispose to smoking were not affected by tobacco taxation, unlike those carrying the protective variant associated with reduced smoking. Similarly, there is concern that tying participation in employer-sponsored wellness programs such as weight-reduction initiatives to insurance premium rebates (expanded under the PPACA by up to 30% of total premiums) may penalize those with genetic predisposition for obesity or low physical activity (Downey, 2014). Along the same line, understanding if genes play a role in the demand for preventive and curative health services and the extent of genetic

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influences is relevant not only for describing the underlying mechanisms of health service use, a complex human behavior with major implications for individual wellbeing and societal resource allocation, but also for evaluating the possibility that health policies such as the PPACA could have heterogeneous effects on use of health services among individuals due to genetic background, which is of great interest to policymakers. The possibility that genes influence the use of health services is not slim. Genes play a role in disease risks, individual preferences, and information processing, which could all be related to personal decisions about preventing illness and seeking healthcare treatments.

There are multiple levels to understanding the role of genetics in the use of health services and implications for policy. The first level is understanding the degree to which differences in personal prevention effort and use of health services across a population can be explained by genetic variation between individuals. Answering this question sheds light in the short-run on the extent to which the existing policy environment has moderated the influence of genes on differences in prevention and use of health services (and consequently in health status) within the population. This work is interesting for policymakers as even though it does not evaluate the effectiveness of specific policies or what additional interventions may achieve, it provides an assessment of the extent to which heritable factors determine population differences in important outcomes such as use of health services despite existing policies aimed at reducing disparities. For example, increasing the use of preventive care is of interest given the potential to slow down healthcare costs by reducing disease incidence and improving early diagnosis of illnesses. If genes are found to explain an important fraction of differences in use of preventive services, this would suggest that the portfolio of existing policies has not substantially limited the role of genetic differences as a major source of disparities in prevention effort and (through that) in health. Another implication of this first-level assessment is shedding light on the potential of genetic background to mediate? policy effects as discussed above. If genes explain little of the variation in prevention and health services use, the potential for genes moderating policy effects becomes less relevant than when genes play a greater role in these outcomes.

If genes are found to have an important effect on prevention and health services use, the next level of research could begin to unravel the specific genes involved and then use this information to identify the most reasonable physiological pathway through which the set of identified genes may influence this complex phenotype (e.g. KEGG pathways).. Such work could ultimately assist in the long-run in developing more effective and targeted interventions and policies aimed at modifying healthcare demand by accounting for relevant individual level heterogeneity in polymorphisms associated with health care utilization. For example, if demand for preventive services is found to be influenced by genes that increase risk tolerance, this knowledge could inform the redesigning of private and public coverage plans to be more effective in increasing use of preventive care, such as by increasing individuals' contribution (through copays or coinsurance) to covering curative services (which would increase perceived risk for those who are more risk tolerant) if they fail to obtain some minimum recommended preventive services. Identifying genetic mechanisms would enable a study of their interactions with healthcare policies to evaluate if policy consequences vary by genetic background and if policies are exacerbating or muting disparities in health and health services use due to genes. Designing and testing behavioral

interventions could also incorporate genetic heterogeneity, such as through testing subgroups defined by genetic risks, in order to develop interventions and policies that could mute unwarranted disparities due to genetics. The potential for genetics to inform policymaking in this way does not require screening the population to measure genetic differences as gene-by-policy interactions can be evaluated in national samples. Ultimately, despite multiple short- and long-term challenges (discussed below), it is not out of the realm of possibilities that individuals could in the future be offered the opportunity of genetic screening by their employers or insurance programs (such as in exchange for insurance rebates). Such screening would not only assess disease risks but could also predict patterns of healthcare use in order to provide individualized interventions and counseling to optimize use of preventive services and subsequently improve health and wellbeing.

In this paper, we evaluate the extent to which genes influence a broad range of measures of prevention and health services use. We address the question of how much genes explain differences in these outcomes within the population by comparing identical and non-identical twins from a unique national sample of US twins in 1995-1996. In addition to use of preventive and curative health services, we evaluate measures of preferences towards prevention, other personal beliefs relevant for healthcare, and overall prevention effort, all of which are relevant for understanding the different aspects of behavior related to use of health services. The extant literature that has considered this question is rather sparse, consisting of less than a handful of published studies summarized below. These studies point to a potentially important role for genes in health service use. However, prior studies have focused on care seeking for specific health conditions and excluded more generic measures of health services use that are not disease specific as physician visits, hospitalizations, and emergency visits. Furthermore, these studies did not include measures of preferences for prevention and health services use or measures of overall prevention effort. We evaluate several of these outcomes and expand the literature by providing a comprehensive assessment of a wide array of measures of health services use and related preferences and outcomes. We find evidence that prevention preferences and effort, routine check-ups, and prescription drug use are influenced by genetic background. Use of other types of healthcare services including hospitalizations, outpatient treatment for physical illness, mental health visits, and urgent care appear to be much less related to genes. These findings indicate that genetic factors play an important role in preventive care use and that the pre-ACA policy environment (in 1995-1996) had not ameliorated genetic influences on a major outcome that several policies before the ACA aimed to improve for the entire population. These findings also raise the possibility of genetic differences modifying policy effects on use of preventive visits. The paper proceeds as follows: Section II provides a literature review; section III illustrates a conceptual framework for how genetic variation may relate to prevention and health services use; section IV describes the data; section V introduces the empirical models; section VI reports the results; section VII concludes with discussion and policy implications.

II. Literature Review

A relatively small body of work has examined whether genes may explain differences in healthcare use outcomes. This research has compared identical and non-identical twins, a commonly used approach in social and behavioral sciences to estimate how much of the

variation in an outcome could be explained by genes. Under certain assumptions discussed below, the difference in correlation of an outcome between identical twins reared together who share ~100% of their genes from that between non-identical twins (also reared together) who share ~50% of their genes can be easily shown to be half of the outcome variance explained by genetic variation.

The extant literature has produced important findings regarding a potential role for genes in influencing individuals' decisions to seek and use curative care and preventive services, despite its limitation of focusing on disease-specific measures. True et al. (1997) studied four health conditions including high blood pressure, mental health, joint problems, and hearing problems and seeking treatment for these conditions in a sample of about 3600 male twins from the Vietnam Era Twin study (VET) with survey data collected in 1987. They found a considerable fraction of the variation in the conditions (24%-52%) and even higher fraction for the treatment seeking behaviors (42-56%) to be explained by genetic differences. Another study on seeking treatment for alcoholism using the same data source and telephone survey data collected in 1992 for about 3350 male twin pairs estimated that 41% of the variance is explained by genetic differences (True et al., 1996). Both studies strongly suggest that genes influence healthcare seeking behaviors. Less work has been done on use of preventive care. To our knowledge, only one study has investigated the extent of genetic influences on a direct measure of preventive services. Treloar et al. (1999) studied women's participation in cancer screening programs using data from an Australian twin sample and reported that a sizeable fraction (between 37-66%) of the variation in seeking these services could be influenced by genes (lowest genetic influence on breast self-examination and highest for Pap smear). Other studies have evaluated genetic influences on specific prevention activities outside of the healthcare market. For example exercise, an important health enhancing activity, has been reported to be genetically influenced, possibly by up to 42%-71% of the variation (Moor et al., 2011; Stubbe et al., 2006).

A few other studies have evaluated related outcomes including general health status and wellbeing. Romeis et al. (2000) studied self-rated health (measured on a scale from poor to excellent) in the male twin sample from the 1987 VET study survey for over 4600 twin pairs and reported that close to 40% of the variation could be contributed to genes. When controlling for the presence of major health problems, the explained variation slightly declined to 32.5%, indicating that genetic factors influence self-reported health status beyond a direct effect on the health conditions accounted for. Similarly, Romeis et al. (2005) reported that genes explained 17-33% of the variation in the SF-36 – a commonly used measure of health status – in a sample of about 2900 male twin pairs from the VET registry with survey data from 1992 and 1995. These results are not limited to twin studies. Using genome wide data from the Health and Retirement Study, researchers demonstrate that 22% of the variance of self-rated health is due to additive genetic influences (Boardman et al. forthcoming).

This small literature suggests a role for genetic factors in an individual's decision to seek and use preventive and curative health services for specific health conditions. However, less is known about whether genes influence more generic measures of health services independently of having specific health conditions such as routine check-ups, emergency

room visits, hospitalizations, and prescription drug use. Also, not much is known from previous studies about how measures of preferences towards prevention and overall prevention effort are influenced by genes. Understanding the extent of genetic influences on preferences is important for beginning to unravel the behavioral mechanisms impacted by genes and explain how genes relate to more distal outcomes such as use of health services.

Our study is one of the first studies to examine the influence of genes on a broad range of measures of prevention preferences and effort and use of preventive and curative health services in a national sample of US adult twins. We take advantage of a unique study that contains rich information about prevention preferences and effort and use of health services and compare identical and non-identical twins to evaluate the extent to which genes versus the environment explain the variation in these outcomes.

III. A Conceptual Framework for Genetic Influences

Genes could theoretically contribute to differences in prevention effort and use of health services through multiple channels. Of particular significance are genetic influences on disease risk and health needs, preferences, and information, which are all well-recognized determinants of health behaviors and healthcare demand. These potential channels are highlighted in Figure 1 and discussed below. Our purpose here is not to develop a theoretical model to be tested in this paper but rather to conceptually illustrate how genes could relate to prevention effort and healthcare use in order to further motivate the case for studying genetic variation in these important outcomes.

There is ample evidence that genes influence health in many ways including by changing risks for disease (both prevalence and severity) especially for important chronic and complex conditions like cardiovascular disease, diabetes, cancer, and mental health problems. Several studies have shown that much of the variation in several health conditions and measures could be explained by genetic factors, including as much as 40% for self-reported health status, 30-40% for major depression, 30% for hypertension, 50-80% for obesity and body mass index, over 50% for type-2 diabetes, 40-90% for asthma, and 30% for strokes (Agarwal, Williams, & Fisher, 2005; Carlsson et al., 2013; Kendler et al., 2006; J. Romeis et al., 2000; Thomsen et al., 2010). Genes also affect physical and cognitive development and aging. Health needs due to disease, disability, or aging are important determinants of health services use and costs. Indeed, the distribution of total healthcare spending across the population has been heavily skewed, with more than half of expenditures incurred by the top 5% of users (Berk & Monheit, 2001), and expenditures significantly increasing with age, by up to 4 times at ages 65+ relative to younger adults (Hartman et al., 2008). Therefore, genetic variation may contribute to the differences in use of health services in the population simply through effects on health status and aging.

Another channel through which genes could influence prevention and use of health services is through their effects on health-related preferences and personality traits. There is evidence for genetic influence on a range of general behavior preferences including risk taking, future discounting, self-efficacy, and trust in others (Benjamin, Ebstein, & Belmaker, 2008). These preferences are conceptually relevant for personal investments in ???(Grossman, 1972). For

example, individuals who are more present-oriented and discount future utility at a greater rate may be less likely to invest in their health through use of preventive services since future returns from these investments are less valuable to them. As much as 20% of the variation in risk taking could be explained by genes (Cesarini et al., 2009). Risky behaviors such as smoking persistence and alcohol dependence have also been shown to have an important genetic component (some estimates of how much variation could be explained by genes exceeded 50%; Boardman, Blalock, & Pampel, 2010; Maes et al., 2004; Stacey, Clarke, & Schumann, 2009). Preferences over future discounting could also be partly explained by genes, by as much as 30-50% (Anokhin et al., 2011). Another personality trait that could link genes and use of health services is how much one trusts others. Trust in healthcare providers has been shown to enhance the patient-provider relationship and continuity of care (Mainous et al., 2001). Close to 10-30% of the variation in trust may be explained by genes (Cesarini et al., 2008, Oskarsson et al, 2012), although estimates as high as 60% have also been reported (Sturgis et al., 2010).

Personal beliefs and knowledge about one's own health needs and availability, quality/effectiveness, and cost of health services have important effects on health behaviors and healthcare demand. However, these beliefs and knowledge are also related to one's cognitive ability and human capital attainment, which in turn are partly influenced by genes. For example, close to half of the variation in educational attainment (40%-70%) could be explained by genes (Branigan, McCallum, & Freese, 2013). Therefore, genetic effects on prevention effort and use of health services could occur via another pathway related to personal efficiency in information gathering and processing.

In summary, genes could theoretically contribute to variation in prevention effort and use of health services through several channels including health needs, preferences, and information. Of course, environmental (economic and social) effects also play an important role in these pathways. Ultimately however, the extent to which genes influence prevention and use of health services is an empirical question.

IV. Data

Sample

As discussed earlier, our approach to evaluating genetic influences on prevention and use of health services involves comparing identical and non-identical twins. We use data on a national sample of twins from the National Survey of Midlife Development in the United States (MIDUS I) conducted in 1995-1996. The survey aimed at collecting data on physical health, psychological wellbeing, and social indicators of adults aged 25-74 and on several characteristics that may influence these outcomes. MIDUS provides a broad range of measures of prevention and health services use that are of interest for our study. The total MIDUS I sample included 957 twin pairs. From those, 907 pairs (total of 1814 individuals) had data on whether the twins are identical or non-identical and consistent birth year/age between twins. Of that sample, 349 pairs were identical, 321 same-sex non-identical, and 237 different-sex non-identical twins. The analytical sample for our analysis ranges from 742 to 795 twin pairs with both twins having complete data, depending on the evaluated outcome¹.

Measures

The primary contribution of our work over the previous studies is the evaluation of genetic effects on a broad range of measures related to prevention and use of health services, including preferences, related personality traits, and generic measures of multiple health services that are not disease-specific. Evaluating a wide set of measures of health services use and related individual characteristics such as preferences toward prevention and healthcare provides a more comprehensive assessment of the various ways through which genes can influence complex and distal outcomes such as routine check-ups, prescription drug use, and hospitalizations. The MIDUS self-administered questionnaire provides data on multiple such measures. These measures can be conceptually grouped into seven general areas: prevention preferences, overall prevention effort, self-efficacy, personal health knowledge, belief in healthcare effectiveness, preventive care use, and use of curative health services. We describe the measures below and include detailed definitions and summary statistics in Table 1.

Prevention preferences are represented by responses to questions about one's beliefs in the effectiveness of prevention and how much personal activities influence health. One question asks about the overall dependence of health on personal prevention and requires the respondent to express the extent of agreement or disagreement on a seven-category scale from "strongly disagree" to "strongly agree" with the following statement: "Keeping healthy depends on things that I can do." Two other questions using a similar scale ask about effects of personal prevention on reducing heart attack and cancer risks. For these questions and others measured on a similar scale, we generally categorize respondents into two groups: those who strongly agreed versus those who less than strongly agreed or disagreed with the statement. The purpose is to better characterize a strong preference for prevention. Another reason is that our models to evaluate genetic influence described below are best adapted for either dichotomous or continuous measures but not ordinal scales.²

In addition to separately analyzing each of the measures of one's beliefs about the effectiveness of prevention for staying healthy, we generate an index for prevention preferences by aggregating these measures using principal component analysis (PCA).³ PCA is generally more reliable for aggregating multiple variables than approaches that arbitrarily assign equal or different weights to the various variables being aggregated. Furthermore, using PCA is theoretically intuitive, as the first component captures the single most important source of variation shared between these variables. We estimated the principal components with the original ordinal scales in order to utilize as much of the variation in the variables as possible when generating the aggregate index.⁴ The first

¹The total MIDUS I sample including the twin sample was followed up between 2004 and 2006 under MIDUS II to collect updated data on the same measures as MIDUS I. The follow-up included 742 pairs; of those 604 had data on identical/non-identical twin status and consistent data on birth year/age between twins. The sample with complete data on the outcomes we analyze for both twins ranges from 362 to 410 pairs. In the largest sample with complete data, 170 twin pairs are identical, 143 are same-sex non-identical, and 97 are different-sex non-identical. We only use MIDUS I data in this paper because the MIDUS II sample is remarkably smaller and less powerful than MIDUS I.

²Considering these ordinal measures as continuous is not ideal given their skewed distributions and that they lack interval data properties.

³Weights from the first principal component, which explains the largest common variation among the aggregated measures (by design), are derived for each measure and index scores are generated multiplying the weights by the measures and summing the product terms.

principal component explains 72% of the variation in the aggregated variables. By design, the index has a mean around zero and includes both positive and negative values; an increase in positive values indicates stronger preference towards prevention, and a decrease away from 0 indicates a lower preference.

Overall prevention effort is measured by two questions related to personal effort on prevention. The first measure is from a question about respondent's agreement on a seven-category scale with a statement about working hard to stay healthy; the second is a rank measure on a 0-10 scale of extent of thought and effort put into health.

Health-related self-efficacy is captured by a measure of one's perception of personal control over health on a 0-10 scale. Knowledge about personal health needs is measured by a question on one's awareness of body changes; responses are on a four-category scale and are dichotomized to capture those who are highly aware of things happening in their body. Personal beliefs about healthcare effectiveness are captured by the extent of one's agreement with a statement that getting better when ill is in the doctor's hands.

Use of preventive care is measured by visiting healthcare providers for a routine physical check-up or gynecological exam in past 12 months. Several measures of health services use for curative care during the past 12 months are evaluated including visiting health providers for scheduled treatments (separately for physical and mental health care), an indicator for any hospitalization, and use of urgent/emergency care which we measure by any use as well as an indicator for two or more urgent visits to capture repetitive use. The question about scheduled treatments is limited by the survey design due to combining visits to different providers including doctors, hospitals, clinics, dentists, and ophthalmologists. Similarly, the survey question about urgent care does not distinguish between different care-delivery settings (physician's office, clinic, or emergency room). Nonetheless, these measures are useful for an exploratory look into potential genetic effects on their variation.

Finally even though our study focuses on measures of prevention and health services use, we also evaluate genetic influences on generic measures of health status that are commonly studied in conjunction with health services use and that are thought to have a strong genetic component. We measure health status by two variables, own rating of health on a 0-10 scale, and the total number of chronic conditions the individual has. Self-reported health is one of the most commonly used measures of health status and wellbeing in health services and policy research and is a strong predictor of multiple aspects of physical and cognitive functioning, limitations in daily activities, overall wellbeing, and mortality risk (Idler and Benyamini 1997). As mentioned above, previous work has reported that genes explain a sizeable fraction of the variation in a related measure (Romeis et al, 2000). Similarly, the number of chronic conditions is an important indicator for health and wellbeing and predictor of quality of life and functioning. We analyze these two health measures separately and then aggregated into a health status index using PCA and the scores of the first principal

⁴The correlations between the latent variables underlying the observed measures are estimated using maximum likelihood (Kolenikov and Angeles, 2004).

component, which explains 70% of the variation in these two variables. An increase in the index represents worsening health.

V. Empirical Models

The main goal of our empirical analysis is to assess how much of the variation in the measures of prevention and health services use described above could be explained by genetic variation between individuals. A common approach to answering this question involves comparing the correlation of each outcome between identical twins who share all of their genes to that between non-identical twins who share one-half of their genes.⁵ This approach decomposes the variance in an outcome into genetic influences, environmental factors that twins share with one another, and environmental factors that are unique to each twin.⁶ In its simplest form, the model requires several assumptions: identical twins do not share a more similar home environment than non-identical twins (equal environment assumption)⁷; parents are not genetically related (random mating); genetic effects can be modeled as additive (i.e. each copy of the genetic risk variant adds linearly to the outcome); and there are no gene-by-environment interactions. Some assumptions can be relaxed under certain extensions of the basic model but issues related to non-random mating (Domingue et al. 2014) and other aspects of traditional twin based models have found renewed criticism in recent years (Burt and Simons 2014; Charney and English 2013). We discuss these limits of the twin based model in the conclusion of the paper.

We focus on estimating the basic model under the above assumptions in order to minimize the number of tests and type-1 error and decompose the variance in each outcome into fractions accounted for by additive genetic effects, environment factors shared between twins, and unique environmental factors.⁸ We recognize that the different models may yield different estimates;⁹ however, the basic model is appropriate for the main goal of this paper which is to evaluate the extent to which genes could explain a broad range of measures related to prevention and health services use and implications for health policy.

As a secondary analysis, we explore the extent to which prevention preferences represented in the PCA-generated prevention index are correlated with the health status index

⁵The twin model has been employed in several studies to estimate the heritability of economic and social traits related to health such as income and economic preferences such as risk-aversion, time-discounting, and trust (see detailed references in Benjamin et al, 2012).

⁶This model is commonly referred to as the ACE model to decompose the outcome variance into additive genetic influences (A), environmental factors shared by twins (C), and unique environmental factors (E). The fraction of the variance explained by genes is referred to as heritability estimate.

⁷We estimated a logistic regression to predict whether twins are identical or non-identical based on race (white versus non-white), indicators for financial status of the family when child was growing up relative to other families, number of times the family moved to a new neighborhood during childhood, and indicators for mother's educational level. These variables were jointly insignificant ($p=0.53$). Detailed regression results are in Appendix Table A1. This analysis does not represent a full test of the equal environment assumption between identical and non-identical twins, but indicates that there are no differences in these specific indicators between the two twin groups in the study sample.

⁸We estimate a threshold model for the binary outcomes and a linear model for continuous outcomes using the OpenMx suite of behavioral genetic models that is available through the computational program R (Boker et al., 2010). Mx is a statistical software package for structural equation modeling that is akin to commercial packages such as LISREL, EQS, and Amos (Neale et al. 2006). Because of the flexibility of the modeling, Mx has been the most widely used software for analyzing pairs of siblings and twins to provide estimates of an outcome variance that is due to genetic and environmental factors. More recently, the Mx structure has been modified to work within the R programming environment through the package OpenMx (Boker et al. 2011).

⁹For example, one could test models that assume no effects from shared environmental factors or models that assume dominant or interactive genetic effects in addition to the additive effects.

(combining self-reported health status and number of chronic conditions) due to shared genetic effects. We focus on this pair to examine if genes underlie the association between these two outcomes. This would aid in our understanding about the behavioral mechanisms that are genetically influenced and that link preferences and health. Relying on similar assumptions as those described above, the approach examines the covariance across twins and across the two outcomes (prevention preferences and health status). Within twin pairs, the analysis evaluates the extent to one could predict the second outcome of the first twin as a function of the first outcome of the second twin, and how this varies between identical and non-identical twins (a stronger relationship between identical twins supports shared genetic influences). We provide the technical details of this model in Appendix B. We do not evaluate shared genetic influences between health and the other evaluated outcomes such as prevention effort or use of preventive and curative health services as these can be endogenous to health and reversely affected by health status.¹⁰

VI. Results

Sample Description

The study sample has extensive variation in the outcomes of interest (Table 1). About 60% strongly thought that keeping healthy depends on one's actions. On a scale from 0 (no thought or effort dedicated to health) to 10 (very much thought and effort), average rating was 7. About 28% strongly believed that getting better is in the doctor's hands when ill. There was also variation in preventive and curative care use. About 69% had at least one routine check-up, and 29% had an outpatient visit to treat a physical illness. Fewer individuals had a mental health visit (18%). Close to one-third had at least one urgent care episode (about 10% had two visits). Over one-third of the sample (43%) used prescription drugs. Most individuals rated themselves as healthy (average of 2.2 on a scale from 0 "best possible health" to 10 "worst possible health"); prevalence of chronic conditions was about 2 per person on average.

Genetic Effects on Prevention and Health Service Use Outcomes

The results of decomposing the outcome variance into fractions explained by genes, shared environment, and unique environment are shown in Table 2. Regarding the genetic effects, the estimates represent the proportion of variation in the outcome that is accounted for by genetic differences in a population. Of the seven categories of outcomes that we examine, four demonstrate evidence for genetic influences: prevention preferences, overall prevention effort, preventive care use, and health status. In contrast, we find no evidence for genetic influences on self-efficacy, personal health knowledge, belief in healthcare effectiveness, and use of curative care for physical or mental health problems, except prescription drug use. Variation in the common environment does not appear to explain variation in several outcomes including prevention preferences, preventive visits, and prescription use,

¹⁰Individuals may modify their use of preventive and curative care because of acute illness events or chronic health problems. Similarly, personal health knowledge, control over health, and belief in healthcare effectiveness may be influenced by health status. These relationships are depicted using the bidirectional arrows in Figure 1. In such cases, evaluating shared genetic influence in this framework would not be as meaningful unless the reverse effects from health are appropriately modeled. In contrast, the measured preferences towards prevention are likely more exogenous and less affected by health status compared to these other measures.

consistent with the general findings from related studies on economic preferences (Benjamin et al, 2012).

The three individual measures grouped under prevention preferences show strong genetic effects, with genes explaining between 29% and 40% of the outcome variances. The genetic estimates are statistically significant, except for the dichotomous indicator for strongly thinking that health depends on personal prevention. Over one-third of the variation in having strong beliefs that personal effort reduces heart attacks and cancer could be explained by genetic differences. Similarly, about one third of the variation in the PCA-generated prevention preference index that aggregates all three measures is accounted for by genes. The results are consistent for overall prevention effort which also shows strong genetic effects. Over one-half of the variance in working hard to stay healthy and about one third of the variance in how much thought and effort are put into health could be accounted for by genetic variation.

The strong genetic effects on prevention preferences and effort are also observed for use of preventive services measured by whether the person had a routine checkup in the past 12 months. Close to 40% of the variation in this outcome could be accounted for by genetic differences. Observing strong genetic effects across these three outcome categories of prevention preferences, prevention effort, and preventive care use shows a consistency in results across these conceptually related measures and supports the validity of the analytical model.

A much weaker evidence of genetic relevance emerges for use of curative services. Of all the measures for curative care, only prescription drug use (in the past 30 days) shows a strong genetic component; over 40% of this outcome variance could be possibly accounted for by genes. Other measures of curative services use including outpatient visits for physical health problems, hospitalizations, and urgent/emergency services show no evidence of genetic influence. The only noteworthy exception is having a mental health visit; close to one quarter of that outcome variance could be accounted for by genetic differences, consistent with the evidence of genetic effects on mental health problems in the medical literature, although the estimate was statistically insignificant.

Consistent with the literature, both health status indicators (self-reported health and number of chronic conditions) show important genetic influence. As much as one third of the variation in self-reported health status and close of half of the variation in the number of chronic conditions (as well as half of the variance of the health status index combining both measures) could be explained by genes.

Shared Genetic Effects between Prevention Preferences and Health

As mentioned above, we evaluate the possibility that the genes influencing prevention preferences may be the same as those that influence health status. That is, some of the association between these two outcomes may be due to common genetic influences. We use the aggregated measures of prevention preference and health status in this analysis. This analysis is further supported by the evidence for genetic influence on prevention preferences and health status described above, as well as the correlation (albeit relatively small) between

the prevention preference and health status indices ($r = -0.19$).¹¹ The findings are somewhat mixed on the existence of shared genetic influences between these two outcomes (details of this analysis are in Appendix B). On the one hand, there is a stronger cross-twin-cross-outcome correlation for identical than non-identical twins (-0.09 versus -0.05). On the other hand, the estimate of the shared genetic component contributing to the association between these two outcomes is insignificant. Therefore, this exploratory analysis only provides very weak evidence of the possibility of a shared genetic mechanism linking prevention preferences and health status.

VII. Conclusions

Our study explores the extent to which genes could explain variation in a broad range of measures related to prevention and use of health services by comparing identical and non-identical twins in a national US sample. Measures of prevention preferences, overall prevention effort, personal belief in healthcare effectiveness and knowledge about health, and use of preventive and curative health services were evaluated. The findings suggest important genetic effects on prevention preferences, overall prevention effort, use of routine check-ups, and prescription drug use. An important genetic influence is also found on self-reported health status and number of chronic conditions, which are commonly used health measures linked to prevention and use of health services. In contrast, we find no evidence of genetic influences on visits to health professionals to treat physical health problems, hospitalization, and urgent care use. The latter two associations being particularly important because hospitalizations or urgent care use may have a greater tendency to be characterized as random events that are less likely to be controlled by the individual and therefore less likely to be heritable phenotypes. However, there is some indication that genes could still be relevant for visits to health professionals for mental health problems. Interestingly, the shared environment between twins does not seem to matter in explaining most of the evaluated outcomes with a few exceptions (self-efficacy, belief in healthcare effectiveness, hospitalizations).

The study findings have interesting implications for policymaking despite the fact that studies examining genetic variation using twin designs such as ours cannot evaluate the effectiveness of future specific policies in reducing population outcome disparities due to genetics.¹² One interpretation of the results is that the healthcare policy environment in the mid-90s has left a large room for genetic factors to contribute to disparities in prevention effort and preventive care use, despite several healthcare reform initiatives to improve access to preventive care. This could suggest that reducing population disparities in use of preventive services may require additional interventions beyond slight modifications in contextual factors (e.g. very small changes in the supply of primary healthcare providers). It is also unclear if and how disparities in use of preventive services due to genetic factors would change after the PPACA despite the provisions to expand insurance coverage and

¹¹The negative correlation is due to the opposite directions of the indices given the loading coefficients on the first principal component: an increase in the prevention index reflects stronger preferences for prevention; an increase in the health status index represents worsening health.

¹²Even if a large percentage of the variation in an outcome is explained by genetic differences, such a finding does not imply that outcome variation is not amenable to policy interventions.

eliminate out-of-pocket cost for preventive care. This concern is strengthened by the fact that the majority of the population had coverage of preventive care and paid relatively low out-of-pocket cost for preventive visits prior to the PPACA. Another consideration from the strong evidence of genetic effects on prevention is the possibility that genes could modify the effects of the PPACA and other health policies on use of preventive services. Whether PPACA will mute or exacerbate population disparities in preventive care use due to genes is an open question for future work that could be explored with data from the post-PPACA when such data become available.

Another implication from our findings is that use of curative services is much more related to contextual factors than preventive care. This is consistent with the literature which shows strong relationships between inpatient care utilization or outpatient visits to specialists and contextual factors such as provider supply but not for preventive services (Fisher & Wennberg, 2003). Related to that, our results suggest that most of the variation in healthcare expenditures (mostly allocated to inpatient and outpatient treatments) in the US is potentially explained by contextual factors and not by genetic differences. Reining in the costs of the US healthcare system partly by reducing population variation in use of health services requires understanding the root-causes of this variation. Individual-level heterogeneity in unobservables is a major obstacle to causal inference on determinants of healthcare demand. Our findings indicate that genetic heterogeneity is less of a concern when studying demand for curative inpatient and outpatient services. In contrast, the results highlight the need to consider genetic heterogeneity when studying prevention and use of prescription drugs.¹³ Similarly, our study suggests that disparities in health status and prevalence of chronic conditions are strongly related to genetic heterogeneity.

Our results are generally consistent with those from previous studies reviewed above that investigated related outcomes, even though the specific measures investigated in these studies were not the same as ours. Our estimates for the extent of genetic influences on prevention preferences (including for preventing cancer) and effort are consistent with those for participation in cancer screening program reported in Treloar et al. (1999) based on an Australian sample of women. Similarly, our estimates for prescription drug use and mental health visits are in the range of those from True et al. (1997) for seeking treatment for selective chronic conditions (such as high blood pressure and mental health problems) and True et al. (1996) for seeking treatment for alcoholism using male twins from the VET registry. Also, the estimates of genetic influence on the health status measures are close to those reported in Romeis et al. (2000, 2005) based on the VET sample.¹⁴

Even though the MIDUS provides a national sample of twins, the generalizability of the findings to subpopulations of particular interest to policymakers such as the uninsured,

¹³Our analysis of the possibility of the same genes contributing to prevention preferences and health status suggests that genetic factors may be a source of confounding in observational studies of the association between prevention and health that do not account for individual-level unobservables such as genetic factors. However, this analysis deserves replication in future research using a larger twin sample with more power to detect shared genetic effects between these outcomes.

¹⁴Finding results that are generally consistent with those from the VET samples limited to male twins does necessarily mean that there is no heterogeneity in genetic influences by gender. Unfortunately, our sample is not large enough to evaluate heterogeneity by gender in any meaningful way. We would only have 163 identical male twins and 123 non-identical male twins, and 186 identical female twins and 198 non-identical female twins. Clearly, these sample sizes are very small for a useful comparison by gender. Exploring heterogeneity by gender in large-enough samples could be an important future research direction.

individuals of low socioeconomic status, and the elderly is unknown and may be limited. The majority of the sample had health insurance coverage (over 91%). Also, even though the twin sample covered a wide age range (25 to 75 years), the majority (91.4%) were younger than 65 years. Use of curative health services is substantially higher among older adults (Hartman et al., 2008). It is possible that genetic influences on use of health services intensify with age due to greater onset of chronic conditions. Evaluating heterogeneity in genetic influences by age is not ideal in our case given the small size of stratified samples and limited power to test differences.¹⁵ Organizational changes in the healthcare system over time may also modify the generalizability of the results.¹⁶ Another caveat in our work is that the survey questions that collected data on use of health services were limited by combining multiple provider specialties and healthcare delivery settings, a relatively short follow-up period (past 12 months), and potential report error/bias. These limitations could have contributed to observing small genetic effects on use of curative services.

Our work echoes the conclusions from previous studies that genetics can bring useful information and tools into health services and policy research. Genetic models can be used to explain and account for differences in demand for services and to identify relevant behavioral and health production mechanisms that can subsequently be targeted to improve health and wellbeing. Investigating genetic mechanisms for prevention and health services use has promises but also multiple challenges as described for other disciplines such as economics (Benjamin et al, 2012). Identifying the molecular genetic pathways underlying prevention preferences, prevention effort, and use of services that appear to be genetically influenced can be helpful for revealing the underlying biological effects and resulting behavioral mechanisms including subtleties and heterogeneities in behavior. In the long-term, such knowledge could help in designing more effective and targeted interventions. For example, if the genetic effects on prevention preferences mainly operate through influencing risk tolerance and fear of monetary loss, interventions could be designed to address such pathways more directly such as by requiring a minimum number of preventive services (such as at least one annual visit for routine checkups) with a financial penalty for failure to comply in the form of higher co-insurance for curative services. In terms of advancing research, since genetic variants can be relatively easily measured, they can serve as indicators for latent and difficult-to-measure variables such as preferences and personality traits and be included as control variables to improve explanatory power. There are also major challenges to be addressed before such work could yield useful information. The complexity of human behavior suggests that multiple genes could be at play, each having a very small effect. Identifying these effects requires very large samples and well measured outcomes.¹⁷ Furthermore, understanding how these genes function in shaping human behavior is complex. Therefore, the value of unravelling the molecular genetics of outcomes

¹⁵We generally observe close differences in correlations between identical and identical twins for most of the outcomes with a significant genetic component (from Table 2) when comparing the full sample (age range of 25-74 years) with two age subgroups: 25-64 and 25-44 years (Table C1 in Appendix C). These results indicate relatively stable genetic influences by age for the majority of the sample that is younger than 65 years but do not provide much information on the estimates for individuals 65 years and older.

¹⁶There have been multiple organizational changes in the healthcare system from 1995-1996, a period characterized by large HMO penetration, low insurance premium growth, gatekeeping, and extensive use of controls on healthcare utilization introduced by managed care plans. Since then, some of these controls have changed for the majority of the privately covered population, while other utilization management techniques such as care management programs for chronic conditions have been introduced. The healthcare workforce is also changing with a decline in supply of primary care physicians.

such as health services use will like take a long time before it can be well-realized. In the short term however, discovering genes that contribute to prevention and health service use outcomes could enable studying their interactions with health policies to evaluate potential heterogeneity in policy consequences for groups of different genetic risks.

Appendix A

Table A1

Coefficients of Logistic Regression of Identical vs. Non-Identical Twin Status on Family Background Indicators

Variable	Coefficient	Std. Err.	P-Value
White vs. non-White	-0.131	0.296	0.659
Family financial background ¹			
A lot better off	-0.192	0.434	0.657
Somewhat better off	-0.016	0.201	0.937
A little better off	0.426	0.173	0.014
A little worse off	-0.115	0.167	0.493
Somewhat worse off	-0.018	0.208	0.93
A lot worse off	-0.139	0.322	0.666
Number of times moved to new neighborhood	-0.001	0.021	0.96
Mother's educational level ²			
No School/some grade school	-0.003	0.271	0.992
Eight grade/junior high school	-0.240	0.208	0.25
Some high school	0.018	0.186	0.922
Some college	0.064	0.201	0.75
College graduate	-0.188	0.232	0.417
Intercept	-0.278	0.306	0.363

Notes: All covariates refer to childhood period.

¹ reference category=same as average family;

² =reference category is high school graduate. Model estimated at individual twin level (1548 twins with complete data on all variables); standard errors clustered at family level.

Appendix B

Evaluating Shared Genetic Effects

We employ a bivariate Cholesky model to estimate the shared genetic effects between prevention preferences and health status. This model relies on the same assumptions of equal environments and that non-identical twins share, on average, one-half of their genes but it

¹⁷A recent study of educational attainment combining data on over one million genetic variants and 100,000 individuals illustrates this challenge; only 3 variants explaining a very small fraction (0.02%) of the variation in educational attainment were statistically significant after correcting for multiple testing (Rietveld et al, 2013).

examines the covariance across twins and across traits as shown graphically in Figure B1. The Cholesky model estimates the parameters needed to describe the genetic correlation as detailed in Figure B1. This bivariate model estimates three latent factors (A, C, E as defined above) for each manifest variable. The important difference is the inclusion of a path between A_1 and prevention preference index and A_1 and the health status index. Evidence that trait 1 (prevention preferences) and trait 2 (health status) may be correlated because of common genetic influence is assessed based on path a_{21} which is the residual genetic influence from A_1 (genetic influence on trait 1) that is also affecting trait 2. The paths described in Figure B1 can be used with equation 1 to estimate the genetic correlation (r_g) coefficient as:

$$r_g = \frac{a_{21}a_{11}}{a_{11}^2}, \quad (1)$$

This correlation is characterized by the curved arrow at the top of Figure B1 describing the correlation between the two latent factors (A_1 and A_2). It is important to note, however, that the Cholesky model is best fit for large samples and strong correlations between the traits. Therefore, applying the Cholesky model is naturally limited in our case by the relatively small sample size and the small correlation between the prevention preference and health status indices (correlation coefficient = -0.19).

We first show in Table B1 descriptive analyses of the cross-twin, cross-outcome, and cross-twin cross-outcome correlations. The first entries echo those of the analyses exploring genetic effects on each outcome separately. Namely, the intra-pair correlation between identical twin pairs is stronger for prevention ($r = .2933$) and health ($r = .4428$) compared to non-identical twins ($r = .1560$ and $.2381$, respectively). These comparisons provide support for the notion that these two outcomes are partly explained by genetic variation. There is somewhat mixed evidence regarding the cross-outcome correlations when comparing identical and non-identical twins; the average correlation between the two outcomes ($r = -.19$) is fairly similar for identical and non-identical twins. The most important statistics in this table are the cross-twin cross-outcome correlations. These estimates describe the degree to which one is able to predict the second outcome of the first twin as a function of the value of the first outcome of the second twin. That is, does the prevention preference of the first twin correlate with the health status of the second twin. Most importantly, if these estimates are higher for identical twins, then there is evidence that shared genes may affect both outcomes. The output provides some (albeit fairly weak) evidence for this perspective. The average cross-twin cross-outcome correlation for identical twins is $-.09$ compared to an average of $-.05$ for non-identical twins.

The parameter estimates (paths) from the Cholesky model described above and standard errors are presented in Table B2. Based on these estimates, we calculate a genetic correlation (r_g) of $-.299$. The most important path in this specification is the a_{21} ($b = .248$, $se = .073$, $t = 3.388$) which provides some evidence that the relatively small correlation between prevention preferences and health is due, in part, to genes associated with both outcomes. All three additive genetic paths are statistically significant but gauging the statistical significance of genetic correlation is more complicated to assess. There are two approaches

to assess significance. First, one can compare the full saturated ACE model with one in which the r_g estimate is fixed to 0. This approach provided a likelihood ratio test of 2.34 with 1 degree of freedom which corresponds to a p-value of .126. Second, one can bootstrap these models and describe the bounds of the empirical confidence interval. Bootstrapping with 1000 replications yielded a 95% confidence interval of (−.999, .174) and a 90% confidence interval of (−.860, .048). The model fit and bootstrap methods do not provide enough evidence to reject the null hypothesis that the r_g estimate is equal to zero in the population. However, the direction and magnitude of these associations provides some evidence that these two outcomes may be influenced very weakly by common sets of genes. The lack of significance of the r_g estimate may be partly due to the small sample size and the relatively small correlation between the prevention preference and health status indices.

Table B1

Cross Twin, Cross Trait, and Cross-Twin Cross-Trait Correlations for Prevention Preference and Health Status Indices.

	Identical Twins (n=349)	Non-Identical Twins (n= 558)
Cross-twin		
r(prevention1, prevention2)	0.2933 [0.0000]	0.1560 [0.0007]
r(health1, health2)	0.4428 [0.0000]	0.2381 [0.0000]
Cross-outcome		
r(prevention1, health1)	−0.2055 [0.0002]	−0.1752 [0.0001]
r(prevention2, health2)	−0.1274 [0.0208]	−0.1901 [0.0000]
Cross-twin cross-outcome		
r(prevention1, health2)	−0.0858 [0.1315]	−0.0796 [0.0848]
r(prevention2, health1)	−0.1005 [0.0749]	−0.0199 [0.6669]

Notes: p values of correlations are in brackets.

Table B2

Bivariate Cholesky Parameter Estimates

	Estimate	s.e.	T	P-value
a11	−0.652	0.050	−12.976	0.000
a21	0.248	0.073	3.388	0.001
a22	0.796	0.044	17.957	0.000
c11	0.000	1.045	0.000	1.000
c21	0.000	1.114	0.000	1.000
c22	0.000	0.583	0.000	1.000
e11	−0.938	0.033	−28.780	0.000
e21	0.098	0.044	2.220	0.027
e22	0.855	0.031	27.291	0.000

Estimate	s.e.	T	P-value
-0.100	0.031	-3.201	0.001
0.016	0.034	0.462	0.644

Note: See Figure B1 for meaning of specific paths.

Figure B1.

Path Parameters from the Bivariate Cholesky Models: Genetic and Environmental Correlations for Prevention Preference and Health Status Indices

Appendix C

Table C1

Twin Correlations by Age

Outcome	25-74 years (n=907)		25-64 years (n=829)		25-44 years (n=47)
	Identical Twins (n=349)	Non-Identical Twins (n=558)	Identical Twins (n= 326)	Non-Identical Twins (n=503)	Identical Twins (n=189)
Heart risk prevention	0.232	0.056	0.239	0.056	0.280
Cancer risk prevention	0.264	0.094	0.234	0.085	0.288
Prevention preference index	0.293	0.156	0.305	0.170	0.290
Works hard	0.367	0.080	0.385	0.076	0.295
Thought/effort	0.330	0.182	0.316	0.199	0.351
Preventive care	0.262	0.102	0.259	0.090	0.337
Prescription drug use	0.282	0.133	0.268	0.161	0.221
Self-rated health	0.296	0.205	0.274	0.211	0.379
Number of chronic conditions	0.457	0.242	0.449	0.260	0.475

Outcome	25-74 years (n=907)		25-64 years (n=829)		25-44 years (n=47)
	Identical Twins (n=349)	Non-Identical Twins (n=558)	Identical Twins (n= 326)	Non-Identical Twins (n=503)	Identical Twins (n=189)
Health status index	0.443	0.238	0.423	0.255	0.514

Notes: Twin correlations on outcomes with significant genetic effects (Table 2) between identical and non-identical twins by age group. The total number of twin pairs (n) is in parentheses; the number of twin pairs with complete data varied by outcome.

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Figure 1. Conceptual Framework for Potential Pathways Linking Genes to Prevention, Use of Health Services, and Health

Notes: The figure shows a general conceptual model for various relationships through which genes can influence prevention effort, healthcare use and cost, and health status.

Bidirectional arrows reflect two-way relationship where two domains affect each other.

Table 1
Study Measures and Summary Statistics

Measure	MIDUS Question /Variable Description	% or Mean (SD)	# of Twin Pairs
<i>Prevention preferences</i>			
Responsible	Keeping healthy depends on things that I can do [†]	60.8	784
Heart risk prevention	There are certain things I can do for myself to reduce the risk of a heart attack [†]	76.5	785
Cancer risk prevention	There are certain things I can do for myself to reduce the risk of getting cancer. [†]	40.6	778
Prevention preference index	Scores from 1 st principal component from a PCA of above 3 measures	-0.10 (1.14)	775
<i>Overall prevention effort</i>			
Works hard	I work hard at trying to stay healthy [†]	23.1	769
Thought/effort	Using a 0 to 10 scale where 0 means “no thought or effort” and 10 means “very much thought and effort,” how much thought and effort do you put into your health these days?	7.3 (2.0)	790
<i>Health-related self-efficacy</i>			
	Using a 0 to 10 scale where 0 means “no control at all” and 10 means “very much control,” how would you rate the amount of control you have over your health these days?	7.9 (1.8)	789
<i>Knowledge about own health</i>			
	I am often aware of various things happening within my body [†]	23.5	784
<i>Belief in healthcare effectiveness</i>			
	When I am sick, getting better is in the doctor’s hands [†]	28.2	775
<i>Preventive care</i>			
	Any visit to doctor/hospital/clinic for a routine physical check-up or gynecological exam in past 12 months	69.1	757
<i>Use of healthcare treatments</i>			
Hospitalization	At least one hospitalization in past 12 months	10.6	761
Outpatient treatment for physical health	At least one visit to doctor/hospital/clinic/orthodontist/ophthalmologist for scheduled treatment/surgery in past 12 months	28.9	742
Mental healthcare	At least one visit to psychiatrist/general practitioner/other MD for emotional/mental/personal problem in past 12 months	17.9	767
Any urgent care	At least one visit to doctor/ER/clinic for urgent treatment in past 12 months	30.3	753
Two or more urgent visits	At least two visits to doctor/ER/clinic for urgent treatment in past 12 months	9.9	753
Prescription drug use	Used any prescription medicine in past 30 days	42.8	791
<i>Health status</i>			
Self-rated health	Using a scale from 0 to 10 where 0 means “the worst possible health” and 10 means “the best possible health,” how would you rate your health these days? (10 <i>minus</i> response on this scale)	2.3 (1.6)	792
Number of chronic conditions	Sum of chronic health conditions (based on a list of questions about 29 conditions)	2.2 (2.3)	795
Health status index	Scores from 1st principal component from a PCA of above 2 measures under health status	0.00 (1.19)	791

Notes: The Table reports the study variables, the exact question from MIDUS or description of variable construction, descriptive statistics (% for dichotomous variables and means and SD for continuous variables), and number of twin pairs with complete data on each variable. The summary statistics are based on the total number of twins (individuals) in the total analytical sample of 907 pairs with complete data.

[†] Question is on a 7-category scale from “strong disagree” to “strongly agree”. The dichotomous variable is constructed to indicate those who strongly agreed with the statement versus other responders.

¹ Question is on a 4-category scale from “not at all true” to “extremely true”. The dichotomous variable is constructed to indicate those who responded “extremely true” versus other responders.

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Table 2

Decomposition of Outcome Variance into Genetic and Environmental Components

Outcome	Proportion of Variance due to			P-value for genetic effects
	Genetic effects	Environmental effects shared by twins	Environmental effects unique to each twin	
<i>Prevention preferences</i>				
Responsible	0.286	0.0	0.714	0.157
Heart risk prevention	0.360	0.0	0.641	0.037
Cancer risk prevention	0.400	0.0	0.600	0.036
Prevention preference index	0.324	0.0	0.676	0.014
<i>Overall prevention effort</i>				
Works hard	0.540	0.0	0.460	0.002
Thought/effort	0.297	0.036	0.666	0.028
<i>Health-related self-efficacy</i>	0.053	0.134	0.813	0.729
<i>Knowledge about own health</i>	0.137	0.061	0.803	0.610
<i>Belief in healthcare effectiveness</i>	0.0	0.269	0.731	0.999
<i>Preventive care</i>	0.409	0.0	0.591	0.039
<i>Use of healthcare treatments</i>				
Hospitalization	0.0	0.128	0.873	0.999
Outpatient treatment for physical health	0.170	0.020	0.810	0.517
Mental healthcare	0.269	0.0	0.732	0.124
Any urgent care	0.047	0.017	0.936	0.862
Two or more urgent visits	0.0	0.0	1.0	0.999
Prescription drug use	0.439	0.0	0.561	0.038
<i>Health status</i>				
Self-rated health	0.290	0.047	0.663	0.038
Number of chronic conditions	0.495	0.0	0.505	<0.0001
Health status index	0.484	0.0	0.516	<0.0001

Notes: The p-values for the significance of the genetic effects (i.e. proportion of variance explained by genes) is based on likelihood ratio test comparing the model to one without genetic effects.