An Econometric Multi-state Model of Pathways to Disability and Mortality in Mid-ages.*

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2021-06-18

Abstract

This paper studies factors that affect enrollment onto a public insurance program such as the Social Security's DI (Disability Insurance) program and SSI (Supplemental Security Income) program, and the competing risk of death before disability enrollment by age 65. As individuals age, or misuse drugs, alcohols or intake less nutrient foods, the homeostatic regulatory mechanism that controls physiological body systems—such as respiratory, cardiovascular, neuroendocrine, immune, and metabolic—becomes more and more frail in its ability to face internal and external stressors. This leads to one-or-comorbid chronic diseases (such as diabetes, cancer, vascular, musculoskeletal, cognitive and mental disorders), DI-qualifying disabilities or death. The speed of progression through these health states depends on the rate of depletion of one's homeostatic health and frailty levels. Genetic and epigenetic factors comprised of internal and external environments, health care use, health related behavior and cognitive endowments modulate the depletion rate of homeostatic health over life cycle. These, in turn, determine the likelihood of various pathways through the health states. I use the Health and Retirement Study (HRS) data to estimate a multi-state time-to-event model of pathways through these health states. I use bio-markers such as BMI, CES-D, measures of cognitive health, and indicators of health related behaviors such as smoking, exercising and use of preventative care along the life-course as indicators of latent homeostatic health and frailty levels and how they affect the risks of following various pathways to disability or death before reaching age 65. **JEL Classifications:** I12, C41, C51.**Keywords:** Pathways to disability, OASDI, SSI, multistate time-to-event model, mortality, aging.

*This paper is dedicated in loving memory of my younger brother, Bishnu Pada Raut, who passed away in New Delhi on February 1, 2019, from lung cancer. He never smoked, never drank, and had normal BMI, CES-D and other standard biomarkers (personally observed) throughout his life. Why are there incidence of diseases and death at premature ages? Scientific community is actively exploring the answers to these questions and the ways to improve life. This paper is an inquiry in this vein. An earlier draft was presented at the 2019 Annual Conference of the Society for Government Economists, April 5, 2019, Washington, DC. I got many useful comments from the discussant, Elizabeth Bass at Congressional Budget Office, and from the audience. I had many insightful comments from Han Altae-Tran at MIT, John Phillips at NIH, and Javier Meseguer, David Pattison and Mark Sarney at SSA. David Pattison's detailed insightful comments on an earlier draft helped greatly the preparation of this draft. Thanks.

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1 Introduction

Identification of factors that determine disability and mortality incident rates is important for disability programs such as Social Security Disability Insurance (DI) and the Supplemental Security Income (SSI) programs. According to the biology of living organisms, all individuals succumb to aging, and experience diseases and disabilities of various kinds as they age. Diseases and disabilities can also be caused by injuries, genetic abnormalities and epigenetic reprogramming (epigenetic includes environmental factors and health-related individual behaviors). Some individuals stay in good health for a long period of time and then become disabled or die; some develop one or more chronic diseases such as diabetes, cancer, vascular, musculoskeletal, cognitive and mental disorders that expedite incidence of disability and death. I use the Health and Retirement Study (HRS) data to estimate a dynamic multi-state time-to-event econometric model of pathways to disability or to death before disability through various health states—specifically, normal health and one-or-more chronic diseases—before reaching age 65 for individuals in their early 50's. Genetic and environmental factors, health care use, health related behaviors and cognitive factors determine the progression of unobserved stock of internal health (also known as health-capital in economics, and frailty in gerontology). The state of internal health determines the risks of transitions to other health states and their transit times. I estimate the effects of these factors on the probabilities of transitions and the transit times along the pathways that individuals in their 50's follow before reaching age 65.

Before exploring pathways to disability, I must clarify the definition of disability that I study in this paper The definition of disability depends on the purpose of its use. Disability is a multidimensional concept and is defined in the literature using simple descriptions, conceptual models, classification schemes, and measurement methods (see for details, (Hahn, 1985; Marks, 1997; Altman, 2001; Albrecht and Verbrugge, 2003; Marks, 1997; Altman, 2001; Snyder et al., 2008)). I use the following statutory definition of disability that the Social Security Administration use for the DI and SSI programs (specified in the Social Security Act, Title II, § 223(d), paragraph (1)A):

> "inability to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment which can be expected to result in death or which has lasted or can be expected to last for a continuous period of not less than 12 months"

and with a vocational grid addendum stated in paragraph (2)A,

> "An individual shall be determined to be under a disability only if his physical or mental impairment or impairments are of such severity that he is not only unable to do his previous work but cannot, considering his age, education, and work experience, engage in any other kind of substantial gainful work which exists in the national economy, regardless of whether such work exists in the immediate area in which he lives, or whether a specific job vacancy exists for him, or whether he would be hired if he applied for work. For purposes of the preceding sentence (with respect to any individual), "work which exists in the national economy" means work which exists in significant numbers either in the region where such individual lives or in several regions of the country."

The definition of disability for the SSI program is almost identical.[1]

While a lot has been said about the definition of disability, very few papers provide a biological or a behavioral mechanism of disablement process from which policy implications for clinical practice and health care policy can be derived. The first disablement model was introduced by the sociologist Nagi (1965), which he further refined in (Nagi, 1976; Nagi, 1991). This model was extended by (Verbrugge and Jette, 1994; Verbrugge, Latham, et al., 2017) who added biological, environmental and behavioral risk factors affecting all four stages of the disablement process.[2] Disablement models are conceptual schemes that describe four distinct but related stages to arrive at a disability: starting from a pathology, leading to developments of impairments of body systems, then to functional limitations and finally to disability. I briefly describe these stages below.

Pathology is an interruption of the normal physiological process caused by developmental disorders (such as cerebral palsy, seizure disorders, mental retardation, hearing and vision impairments, autism, PKU, Huntington disease), infection, injury, trauma, metabolic imbalance (such as diabetes), degenerative disease processes (i.e., deterioration over time the functioning or the structure of tissues or organs leading to osteoarthritis, osteoporosis, cancer, Alzheimer or Parkinson's disease) or any other disease process. The impairments of body system involve loss or abnormality of an anatomical, physiological, mental, or emotional nature. Functional limitations include not being able to have one's ADL (activities of

[1] For details, see https://www.ssa.gov/OP_Home/ssact/title02/0223.htm section 223(d)(2) for the OASDI program, and https://www.ssa.gov/OP_Home/ssact/title16b/1614.htm paragraph 3(A) for the SSI program.

[2] Nagi model has been adapted by the World Health Organization in their classification scheme of disability, the latest one is World Health Organization (2001). See Üstün et al. (2010) for an application of the above disablement models in WHO's 2001 classification system, and see (Pope and Tarlov, 1991; Institute of Medicine, 2007) for more on this.

daily living) and IADL (instrumental activities of daily living), role activities (such as occupation, parenting, grand-parenting, and student roles), social activities (such as attending church and other group activities, and socializing with friends and relatives) and leisure activities (such as sports and physical recreations, reading, and distinct trips). The final stage is the disability, the definition of which depends on the purpose of the study and involves a combination of all the above models of disability.

The disablement models are useful for conceptualization, diagnosis and record keeping of disabilities but limited for the study of the causes of disability in epidemiological and policy research. The starting point of the above disablement models is an onset of a chronic disease or an injury causing a disability. For policy research on disability and mortality, it is important to study the biomedical processes modulated by genetic, epigenetic and behavioral factors in the manifestation and prognosis of disabling diseases and on the risk of disabling injuries. While an injury as the starting point of disablement process serves well for certain purpose such as for workers' compensation in sports, construction and factories, a large proportion of disabilities in the mid ages are caused by diseases–both physical and mental (see for instance, (Case and Deaton, 2015; The US Burden of Disease Collaborators, 2018)). Mechanism for non-accidental death is similar. Diseases, leading to disabilities — both developmental disabilities and late age disabilities — and to mortality are the result of modulated biomedical processes, which at the microbiology level are the outcomes of cellular aging. While aging, an individual succumbs to diseases and injuries leading to disability or death. Not all individuals experience the same deterministic aging process—some experience faster aging and aging related diseases than others. Why do people experience faster aging, diseases and mortality? At what stage of life, does it all begin—at mid-ages, at birth, or even earlier at conception? How do various genetic, epigenetic and behavioral factors modulate the aging process, culminating in diseases, disabilities and death? What biomarkers and epigenetic factors (including environmental factors and individual health related behaviors) predict better the process of aging and incidence of disease, disability and death over the lifespan?

I will not get into the details of the biomedical literature on these issues. Similar to the literature of behavioral genetics of personality and intelligence, the *nature-nurture* controversy exists in the health literature: Is it all nature (i.e., all genetics or genome) or is it all nurture (i.e., all epigenetics or epigenome modulated by the environment and health related individual behaviors) that determines the progression of health over the life span of an individual? The consensus so far is that it is neither the nature nor the nurture; it is a combi-

nation of the two that determines health developments over one's life span. The research so far found that certain genetic make-ups (i.e., certain sequences of DNA) predispose one to certain diseases, ((Barondes, 1999; Khoury et al., 2009; Bookman et al., 2011)), but the epigenetic inputs—especially at the very early stage of life, i.e. in the womb, but not the least at later stages of life—are also very important determinants of life expectancy and quality of life. The biomedical research so far has not found genes that are responsible for aging and age related diseases, leading to early disability and mortality. The twenty-first century biomedical research emphasizes more on the epigenetic factors than the genetic factors to explain the pattern of health developments over the life-span.

At the cellular level, aging means cellular senescence—i.e., after a certain number of cell divisions, it stops dividing or have defective replications, causing tissues or organs to increasingly deteriorate over time. Senescence leads to incidence of degenerative diseases. It is generally observed that women live longer than men and those with better life styles in terms of smoking, exercising and diets delay the aging process (for evidence, see (Blair et al., 1989; Vaupel, 2010; Austad and Fischer, 2016; Zarulli et al., 2018)). This line of biological inquiry led to explore the (cellular) molecular mechanism of aging process and to find biomarkers of aging that can be used to diagnose, monitor, and improve the age related physiological decline and disease. A good indicator of the aging process at the cellular level is the rate of decay in the telomere length. Telomeres are the caps at the end of chromosomes in a DNA sequence. They look like the plastic caps at the end of shoelaces. The main function of telomeres is to protect cells preserving the genetic content within each chromosome during cell divisions. Unfortunately, the telomere length shortens in the course of each cycle of chromosomal replication during cell division, reaching the Hayflick limit (about 40 to 60 cell divisions, Hayflick (1965)) with a critically short telomere length, after which the cells stop dividing or divide with chromosomal abnormalities. The rate of shortening of the telomere length is modulated by telomerase enzyme. Why the rate of decay in telomere length varies for individuals is an active area of biomedical research and the mechanism for it is not yet fully understood. Many studies find that higher stress of any kind— psychological, financial, social and chemical—is strongly associated with higher oxidative stress, lower level of telomerase enzyme, and shorter telomere length. Furthermore, shorter telomere length is associated with health related phenotypes of poorer health and higher risks for cardiovascular and immune diseases (see, (Epel et al., 2004; Shalev, Entringer, et al., 2013; DiLoreto and Murphy, 2015; Shalev and Belsky, 2016; Simons et al., 2016)).

More recently emerged second line of biomedical research on aging and aging related

diseases explores the epigenetic (which literally means on top of genetic) mechanism for these life-cycle processes. (See for instance, (Alisch et al., 2012; Barres and Zierath, 2011; Boks et al., 2009; Esteller, 2008; Hannum et al., 2013; Horvath, 2013)).

The above literature emphasizes that aging and age related diseases are associated with shortening of telomere length and changes in global methylation, and that stress, smoking, drinking, chemical misuse, and diet are important modulators for these changes. The question remains, what are the critical periods or the developmental milestones in life cycle that program the motions of health developments over the life span of an individual?

Research along this line began with the striking findings of (Barker, 1990; Barker, 1998) and later of Gluckman et al. (2008). They found strong associations between birth weight and many later life chronic diseases, including hypertension, coronary artery diseases, type 2 diabetes, and osteoporosis. Many other studies find that much of health developments in later life is determined very early in life—specifically during the prenatal period, right after conception, i.e. in the womb. Sometimes it is said in social sciences that inequality begins in the womb. The effect of an environmental stress in the womb on later life diseases and developmental outcomes is known as *programming*. Gluckman et al. (2008) observes that "like the long latency period between an environmental trigger and the onset of certain cancers, the etiology of many later life diseases such as cardiovascular disease, metabolic disease, or osteoporosis originate as early as in the intrauterine development and the influence of environments that created by the mother." For more empirical evidence on the developmental origin of later life diseases, see (Barker, 2007; Thornburg et al., 2010). The papers by (Kanherkar et al., 2014; Barbara et al., 2017) provide detailed descriptions of the biological process of development of life and health, starting from the conception. They explain how the global DNA demethylation of the fertilized egg right after conception creates an epigenetic "clean slate" to start a new life, followed by rapid remythylation to reprogram the maternal and paternal genomes to create epigenetic configurations in the fetus which rapidly produce specialized cells of the body with cell divisions. The environment provided in mother's womb during those times has long-term effects on the child's later cognitive and other health developments. While inputs at early milestone ages are important for later age health, healthy living and good healthcare are still important for maintaining health in mid ages.

Studies in social sciences find that low socio-economic status (SES) are associated with inflammation, metabolic dysregulation, and various chronic and age-related diseases such as type 2 diabetes, coronary heart disease, stroke, and dementia, and that low SES create

epigenetic changes in individuals that lead to faster biological aging even after controlling for health-related behaviors such as diet, exercise, smoking, alcohol consumption, or having health insurance, see for evidence, Simons et al. (2016). The study by Karakus and Patton (2011) uses the Health and Retirement Studies data and after controlling for education, race, income, health risk indicators like BMI and smoking, functional limitations like gross motor index, health limitations for work, and income, they find depression at baseline leads to significantly higher risk for developing diabetes, heart problems, and arthritis and no significant effect on developing cancer during the 12 years follow-up period. Renna (2008) uses National Longitudinal Survey of Youth data to find no significant effect of alchohol use on labor market outcomes such as on earnings or hours of work. Seib et al. (2014) collected data on a sample of older women in Australia and found that severe traumatic life events create strong stress levels that influence them to have unhealthy living and diet measured by BMI and develop stronger and earlier health problems. Conti et al. (2009) utilize the CES-D data in the Health and Retirement Survey dataset to construct a measure of depression, and find that depression of men and women have significant negative effect on employment status, early retirement, and application for DI/SSI benefits. More recently, Case and Deaton (2015) found a racial reversal in the mortality rates of the US mid-age population between 1993 and 2013. They found that all-cause mortality and morbidity of non-Hispanic white men and women of ages 45-55 have been increasing during the period, mainly due to increases in their incidence rates of drug and alcohol poisoning, suicide, chronic liver diseases and cirrhosis. Morbidity of the group culminate into serious disabilities and crowding into DI and SSI rolls and to lower labor force participation rates, especially among women. Such time reversals are confined to that age and racial group only, and the rates are higher for less educated than educated groups. They attribute such behavioral changes to increased (within and inter-generational) income inequality and rises in prescription of pain killer drugs and opioid, and falling price and easier availability of heroin.

I adopt all the above views and formulate a statistical model of disablement process. I postulate that as individuals age or misuse drugs, alcohols or intake less nutrient foods, the homeostatic regulatory mechanism that controls physiological systems — respiratory, cardiovascular, neuroendocrine, immune, and metabolic — becomes more and more fragile in its ability to face internal and external stressors, leading to early occurrence of disease, disability and the death. I draw from the microbiology literature that study the genetic and epigenetic mechanism for aging and timing and severity of aging related diseases, disability and death. I use available bio-markers (such as BMI, CES-D, cognition) and health related

behaviors such as smoking, exercising and using preventative care along the life-course to explain how they affect the risk of chronic diseases, disabilities and premature death. I use a multi-state time to event statistical framework to estimate the effects of these factors on the probabilities of following various pathways through normal health, diseases, disability or death before reaching age 65. The multi-state framework is more useful to study the effect of various covariates—the covariates that are specific to intermediate health states—on the risk of becoming disabled or being dead.

The rest of the paper is organized as follows. In Section 2, I provide an extended disablement model of this paper.In Section 3, I describe the subset of the Health and Retirement Survey dataset that I use for this study. In Section 4, I describe the econometric specification, estimation issues, present the estimates and discuss the results. Section 5 concludes the paper.

2 The Model

With insights from the disablement modeling literature of (Nagi, 1965; Verbrugge and Jette, 1994; Verbrugge, Latham, et al., 2017) and the biomedical literature on the aging process, I formulate and then estimate an econometric model of paths to enter disability rolls. An individual can be on the disability rolls if the individual has a qualifying disability before reaching age 65 and has not died before applying for disability benefits. I assume that an individual's getting on the disability rolls is a terminal event, i.e., the individual does not move to normal or diseased health states. After reaching this state, the individual is not followed any further. A competing risk for getting on the rolls is death before age 65. This is a competing risk because an individual cannot be at risk for disability enrollment if the individual is already dead and thus not at risk to get on the disability rolls. The individual is not followed after the event of enrollment onto the disability program as this is the event of interest in this paper and the assumption that once in disability, individual does does not recover. In the technical terms defined below, we treat the health states—disability and death—as absorbing states, i.e., once in that health state, an individual remains in that health state and removed from the sample for later considerations. An individual can be in normal health and then become disable or die before becoming disabled or may first become diseased with one or more diseases and again from that health state become disabled or die before becoming disabled. Various factors affect individual risks of various transitions of health states and the time they stay in each health state along the life-span. Both, in turn,

determine the timing of getting on to the disability rolls.

An individual at any time along the path to disability or to death before age 65 will be in the normal health state for a length of time, and then moves to another health state, say diseased health state, and remain there for some time, and then jump to the health state of disability or to death, or reach 65 and censored after that. There are many possible paths that an individual can follow. Even when the health states they pass through are the same, the duration of stay in each health state (also known as the *waiting time* in stochastic process literature) could vary. Each configuration of visited states and the waiting times in those states constitute one path. When time is continuous, the number of paths that one can follow is infinite. For an individual one path maybe more likely than another and may depend on the individual's genetic and prior health related behaviors. From the diagram below one can see various paths that an individual may follow during the study period. The focus of the paper is to study the probabilities of various transitions and the duration of stay in each health state.

I model the paths through various health states that individuals follow along their life-spans as a continuous-time finite-state Markov process $X(t), t \in T$, where at each time point t during the study period T, the random variable $X(t)$ takes a value from a finite set S of health states. In the present study, I take $T = [0, 14]$, treating age 51 as time period $t = 0$ and age 65 as time period $t = 14$. The state space S of the stochastic process contains health states $1 =$ "healthy or normal health", $2 =$ "ill with one or more chronic disease", $3 =$ "disabled with DI-or SSI-qualifying disability" and $4 =$ "Death". Sometimes I will use $S = \{h, i, d, D\}$ in place of $\{1, 2, 3, 4\}$.

Let the transition probabilities of our stochastic process $X(t)$ be given by

$$P_{hj}(s,t) = Prob(X(t) = j | X(s) = h), \tag{1}$$

for all $h, j \in S$, $s, t \in T$, $t \geq s$. Denote the matrix of transition probabilities by

$$P(s,t) \equiv \left(P_{hj}(s,t)\right)_{h,j=1\ldots4}. \tag{2}$$

An individual at time t may be in any of the health states in S, the probability of which, known as the *occupation probability*. The occupation probability at time t can be viewed as the proportion of population of age t who are in health state j. Let $\pi_j(t)$ be the occupation probability of an individual in health state j at time t. Denote all the occupation probabilities as a column vector $\pi(t) \equiv \left((\pi_j)(t), j \in S\right)$. Then the occupation probabilities move over

time recursively as follows,

$$\pi(t) = \pi'(s)P(s,t), 0 \leq s < t. \tag{3}$$

Note that given an initial distribution $\pi(0)$ and the transition probabilities $\left(P_{hj}(s,t), 0 \leq s < t, s, t \in T\right)$, we can calculate the occupation probabilities in all periods in T from the above recursive equation.

The following path diagram describes various pathways that individuals may go through in their mid-ages.

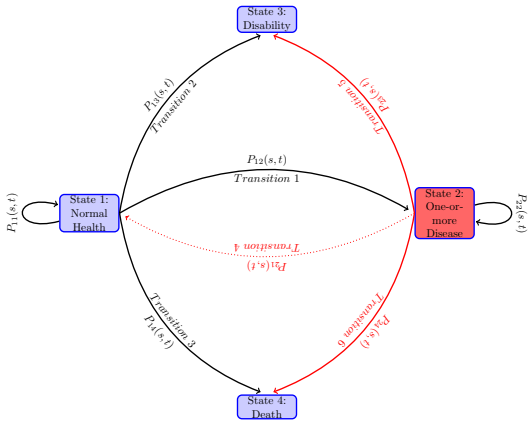

Figure 1: Path diagram of health trajectors.

It is known that the transition probability process of the stochastic process satisfies Chapman-Kolmogorov equation

$$P(s,t) = P(s,u) \cdot P(u,t), \text{ for all } s,u,t \in T \text{ with } s < u < t \tag{4}$$

I assume that the transition probabilities $P(s,t)$ are absolutely continuous in s and t. A *transition intensity*—also known as the *hazard rate* in the survival analysis literature when there is only one event of interest, and as the *cause-specific hazard rate* in the competing risk analysis[3]—of the health process X_t from health state h to health state j at time t is the

[3] See for instance, Raut (2017) for a competing risk analysis in a similar context using the SSA Administrative data and compare that with the present framework.

derivative

$$\begin{aligned}
\lambda_{hj}(t) &= \lim_{\Delta t \to 0} \frac{P_{hj}(t, t+\Delta t) - P_{hj}(t,t)}{\Delta t}, \text{ for } j \in S \\
&= \lim_{\Delta t \to 0} \frac{P_{hj}(t, t+\Delta t)}{\Delta t}, \text{ for } j \neq h \\
\lambda_{hh}(t) &= \lim_{\Delta t \to 0} \frac{P_{hh}(t, t+\Delta t) - 1}{\Delta t}, \text{ for } j = h, \\
&= -\lim_{\Delta t \to 0} \frac{\sum_{j \neq h} P_{hj}(t, t+\Delta t)}{\Delta t} \\
&= -\sum_{j \neq h} \lambda_{hj}(t)
\end{aligned} \tag{5}$$

For absorbing states $h = 3, 4$, the transition intensities $\lambda_{hj}(t) = 0$, for all $j, j \in S$. Denote the matrix of transition intensities by

$$\Gamma(t) = \begin{pmatrix} -(\lambda_{12}(t) + \lambda_{13}(t) + \lambda_{14}(t)) & \lambda_{12}(t) & \lambda_{13}(t) & \lambda_{14}(t) \\ 0 & -(\lambda_{23}(t) + \lambda_{24}(t)) & \lambda_{23}(t) & \lambda_{24}(t) \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}. \tag{6}$$

While $P_{hj}(s,t)$ is an unconditional probability, the transition intensity or the hazard rate $\lambda_{hj}(t)\Delta t$ is the conditional (instantaneous) probability of an individual experiencing the event j in the small time interval $[t, t+\Delta t)$ given that he has been in state h at time t. This conditional probability may depend on time t and other characteristics and the path through various health states that is followed by the individual to be in the health state h at time t. I am assuming that the process is Markovian, i.e., it depends only on the health state h that it is in at time s, and on the times s and t, but does not depend on the path that he followed to come to state h at time s. Or in other words, the future health condition depends on the current health condition but not how one came to the current health state.

It can be shown that the Chapman-Kolmogorov equation leads to the following Kolmogorov forward equation

$$\frac{\partial P(s,t)}{\partial t} = P(s,t) \cdot \Gamma(t) \tag{7}$$

and the initial condition $P(s,s) = I$ for all $s \in T$. Thus, given intensities $\Gamma(t)$, the solution $P(s,t)$ of the above differential equation defines a continuous time Markov chain and conversely, given absolutely continuous transition probabilities $P(s,t)$ for a continuous time Markov chain, one has the Kolmogorov forward equation Eq. (7). For the empirical work, I characterize the Markov chain of pathways through various health states with the

intensity matrix $\Gamma(t)$ and in our empirical specification, I parameterize $\Gamma(t)$ as function of covariates and estimate these using the HRS data set. I then use these estimates of the intensity matrix to estimate the transition probabilities and study their properties.

From the Fundamental Theorem of ordinary differential equations, we know that there exists a solution $P(s,t)$ to the system of ordinary differential equations in Eq. (7). In general, it is not possible to find analytical solution of the Kolmogorov forward equation. However, given the special structure for the intensity matrix and the assumption that there is no transition from the diseased health state to normal health state, and from the disability health state to diseased or normal health states, we can solve analytically the Kolmogorov forward equation Eq. (7). The solution derived in the Appendix is as follows:

$$P_{11}(s,t) = \exp\left(-\int_s^t \left(\lambda_{12}(u) + \lambda_{13}(u) + \lambda_{14}(u)\right) du\right) \tag{8}$$

$$P_{12}(s,t) = \int_s^t P_{11}(s,u)\,\lambda_{12}(u)\,P_{22}(u,t)\,du \tag{9}$$

$$P_{13}(s,t) = \int_s^t \lambda_{13}(u)\,P_{11}(s,u)\,du + \int_s^t \left[P_{11}(s,u)\lambda_{12}(u)\int_u^t P_{22}(u,\tau)\,\lambda_{23}(\tau)\,d\tau\right] du \tag{10}$$

$$P_{14}(s,t) = \int_s^t \lambda_{14}(u)\,P_{11}(s,u)\,du + \int_s^t \left[P_{11}(s,u)\lambda_{12}(u)\int_u^t P_{22}(u,\tau)\,\lambda_{24}(\tau)\,d\tau\right] du \tag{11}$$

$$P_{22}(s,t) = \exp\left(-\int_s^t \left(\lambda_{23}(u) + \lambda_{24}(u)\right) du\right) \tag{12}$$

$$P_{2h}(s,t) = \int_s^t \lambda_{2h}(u)\,P_{22}(s,u)\,du, h = 3,4 \tag{13}$$

The above formulas for the transition probabilities have interesting interpretations. If we view state 1 as "alive" and states 2, 3 and 4 (the states that an individual can move to from state 1) as the competing causes of death, then by the definition of transition probabilities in Eq. (1), $P_{11}(0,t)$ is the probability that the individual is alive at time t, i.e., did not die from any of the competing causes 2, 3 or 4 of death before age t. That is, $P_{11}(0,t)$, is nothing but the survival function of the competing risk literature. Denote by $\lambda_1(t) = \lambda_{12}(t) + \lambda_{13}(t) + \lambda_{14}(t)$, the combined risk or the hazard rate of exiting state 1 at time t. Then $\int_0^t \lambda_1(u)\,du$ is the cumulative hazard (also known as the cumulative risk or the integrated hazard) of dying by time t. Eq. (8) is nothing but the well-known formula in the survival analysis that survival function $S(t) = exp[-A(t)]$. In $P_{11}(s,t)$ the individual begins state 1 at time s

in stead of at time 0, and is more relevant in the multi-state models as the individual could be in some other health state before moving to health state at time s. In what follows, I will sometimes denote a transition $j \to h$ by a Greek letter or when the reference of the from state j and the to-state h is important, I will denote it by jh. Furthermore, I will often abbreviate a transition probability $P_{hj}(0,t)$ as $P_{hj}(t)$.

The interpretation of the other transition probabilities are slightly more complex in the multi-state context as there are multiple pathways to move from one state to another state and not all other states that one moves to are absorbing states. For instance, the transition probability $P_{12}(s,t)$ is by definition the probability of an individual being in health state 2 (i.e., have one-or-more diseases) at time t given that he was in health state 1 at time s. The formula for it in Eq. (9) means that for an individual in health state 1 at time s to be in health state 2 at time t, he has to be in health state 1 up to a time u, ($s < u < t$), the probability of which is $P_{11}(s,u)$, and make an instaneous transition at time u (i.e., during $[u, u+du)$ from state 1 to state 2, the probability of which is $\lambda_{12}(u)du$ and remain in state 2 during the remaining time u through t, the probability of which is $P_{22}(u,t)$). Moreover, this transition time u takes any of the mutually exclusive values between s to t and thus we need to integrate over these mutually exclusive values of u between s and t, which is represented in the formula in Eq. (9).

$P_{13}(s,t)$, the probability of a person who is in normal health, i.e. in state 1 at time s to be on the DI rolls, i.e., in state 3 at time t has two parts—corresponding to the two mutually exclusive paths that can lead to this: First, he can be in good health state until time u ($s < u < t$) (the probability of which is $P_{11}(s,u)$) and then transit to the disability health state 3 at time u with probability $\lambda_{13}(u)du$. Second, from state 1 at time s, he moves to state 2 at time u ($s < u < t$) (the probability of which is $P_{12}(s,u)$) and then transit to the disability health state 3 at time u with probability $\lambda_{13}(u)$. Once arrived on the on he stays there until t with probability 1 (as it is an absorbing state) Since this is true for any value of u, we integrate over u to get the probability. I denote the probability of the direct path $1 \to 3$ as $Q_{12}(s,t)$ and the probability of the path $1 \to 2 \to 3$ as $Q_{123}(s,t)$. Similar is the interpretation of the two components for $P_{14}(s,t)$ in Eq. (11).

There are various random variables of interest corresponding to the waiting times. Let T^1 denote the duration of time one is in health state 1, T^3 the time one takes to move to health state 3 starting in good health state 1 at time $t = 0$. Similarly T^4 be the time of death starting at health state 1 at time $t = 0$. What are the waiting time distributions and the expected values of these random variables for different covariate values?

Suppose one is at normal health at age 50, our base time period, 0, the probability of his becoming disabled by time s directly from normal health, (i.e., not first becoming diseased and then become disabled) will depend on the competing risks of leaving the normal health state by time s either because of death or because of acquiring one or more diseases. Also note that if he is in good health at time 0, the transition probability $P_{13}(0, s)$, i.e., the probability that he will be in disabled state at time s is the sum of likelihood of all different mutually exclusive time paths.One such path is that he is in good health til time $u, u < s$ the probability of which is $P_{11}(0, u)$, and then he instantaneously become disabled at time u, which has the instantaneous probability of $\lambda_{12}(u)$ (the intensity function) and then he remains in disability state from time u to time s which has probability $P_{33}(u, s)$. But given our assumption that the disability health state is an absorbing state, $P_{33}(u, s) = 1$. Thus, the probability of following this path is given by $P_{11}(0, u)\lambda_{12}(u)$. From this one can calculate the probability of directly becoming disabled by time s from the normal health at time 0 is $\int_0^s P_{11}(0, u)\lambda_{13}(u)du$, I will denote this direct probability as $Q_{13}(0, s)$. The other way he could be in the disability health state by time s from the normal health state at time 0 is that he stays in normal health until time $u, u < s$ (the probability of which is $P_{11}(0, u)$, then moves to a diseased state at time u with instantaneous probability given by the intensity rate $\lambda_{12}(u)$ and stays in diseased state until time $\tau, u < \tau < s$ the probability of which is $P_{22}(u, \tau)$ and become disabled at time τ with instantaneous probability given by the intensity function $\lambda_{23}(\tau)$ and then he remains in the disability state during the remainder of the time $s - \tau$ whose probability is 1 as disability is an absorbing state. Thus starting from the normal health, the probability $Q_{123}(0, s)$ of his being in disability state at time s via the disease state is $Q_{123}(0, s) = \int_0^s P_{11}(0, u)\lambda_{12}(u) \int_u^s P_{22}(u, \tau)\lambda_{23}(\tau)d\tau du$. Finally, $P_{13}(0, s) = Q_{13}(0, s) + Q_{123}(0, s)$. The analytical solution that we will get also will have this property for the transition probabilities.

These qualitative properties of our disablement model can be studied from analytical solutions of these transition probabilities. In general, it is not possible to get analytical solutions. In the next subsection, I derive it under the assumption that the intensity matrix $\alpha(t)$ is time constant, i.e., independent of time t.

$$
\begin{aligned}
P_{13}(0,t) &= \int_0^t \lambda_{23}(u)\, P_{12}(0,u)\, du \\
&= \int_0^t \lambda_{13}(u)\, P_{11}(0,u) + \int_0^t \int_0^u P_{11}(0,x)\, \lambda_{12}(x) P_{22}(x,u)\, \lambda_{23}(u)\, dxdu \\
&= Q_{13}(0,t) + Q_{123}(0,t)
\end{aligned}
$$

2.1 Time constant intensity and explicit solution of the transition probabilities

Also see Cube et al. (2017).

For the time homogeneous case, we can derive explicit formula for the probabilities of getting on to the disability roll by following paths like $1 \to 3$ and $1 \to 2 \to 3$ as follows,

$$
\begin{aligned}
Q_{13}(0,t) &= \frac{\lambda_{13}}{\lambda_1}\left[1 - \exp(-\lambda_1 t)\right] \\
Q_{123}(0,t) &= \frac{\lambda_{12}\lambda_{23}}{\lambda_2}\left[\frac{\exp(-\lambda_2 t) - \exp(-\lambda_1 t)}{\lambda_2 - \lambda_1} + \frac{1 - \exp(-\lambda_1 t)}{\lambda_1}\right]
\end{aligned}
$$

To get more insight about the interdependence of the transition probabilities and their effects on each other, I consider the time constant case for which the transition probabilities can be solved analytically. Assume that $\lambda_{hj}(t)$ is constant over time, i.e., independent of t, and denote it by λ_{hj}. Denote by $\lambda_1 \equiv \lambda_{12} + \lambda_{13} + \lambda_{14}$, which is the intensity of exiting state 1 from any of the three competing risks of exit. Similarly, denote the transition intensity of state 2 by $\lambda_2 \equiv \lambda_{23} + \lambda_{24}$.

For the time homogeneous case, it is straightforward to calculate all the transition probabilities from Eq. (8) - Eq. (13) as follows.

$$P_{11}(t) = \exp(-\lambda_1 t), \tag{14}$$

$$P_{22}(s,t) = \exp(-\lambda_2 (t-s)), \tag{15}$$

$$P_{12}(t) = \frac{\lambda_{12}}{\lambda_2 - \lambda_1}\left[\exp(-\lambda_1 t) - \exp(-\lambda_2 t)\right] \tag{16}$$

$$P_{13}(t) = \frac{\lambda_{13}}{\lambda_1}\left[1 - \exp(-\lambda_1 t)\right] + \frac{\lambda_{12}\lambda_{23}}{\lambda_2}\left[\frac{\exp(-\lambda_2 t) - \exp(-\lambda_1 t)}{\lambda_2 - \lambda_1} + \frac{1 - \exp(-\lambda_1 t)}{\lambda_1}\right] \tag{17}$$

$$P_{14}(t) = \frac{\lambda_{14}}{\lambda_1}\left[1 - \exp(-\lambda_1 t)\right] + \frac{\lambda_{12}\lambda_{24}}{\lambda_2}\left[\frac{\exp(-\lambda_2 t) - \exp(-\lambda_1 t)}{\lambda_2 - \lambda_1} + \frac{1 - \exp(-\lambda_1 t)}{\lambda_1}\right] \tag{18}$$

$$P_{2h}(t) = \frac{\lambda_{2h}}{\lambda_2}\left(1 - \exp(-\lambda_2 t)\right), h = 3, 4. \tag{19}$$

In Eq. (19), the first term on the right hand side of $P_{13}(t)$ is the probability of directly transiting to state 3 from 1, i.e. $Q_{13}(t)$ and the second term is the probability of the indirect path $1 \to 2 \to 3$, i.e., $Q_{123}(t)$ in the notation of the previous section. Similar is the case for $P_{14}(t)$. It is possible to caluclulate these probabilities separately for our time homogeneous case.

Notice how the transition probabilities are interdependent. For instance, note that how $P_{13}(t)$ changes when there is a reduction in λ_{24}. A reduction in λ_{24} could be due to discoveries of medical technology that reduces the probability of death from the diseased state.

In the next section, I estimate the constant transition intensities from our data set using maximum likelihood procedure and study dynamics of the transition probabilities for various groups.

3 The data set and the variables

I use the Health and Retirement Study (HRS) dataset for empirical analysis. A lot has been reported on the family of HRS datasets—about its structure, purpose, and various modules collecting data on genetics, biomarkers, cognitive functioning, and more, see for instance (Juster and Suzman, 1995; Sonnega et al., 2014; Fisher and Ryan, 2017). The first survey was conducted in 1992 on a representative sample of individuals living in households i.e., in non-institutionalized, community dwelling, in the United States from the population of cohort born during 1931 to 1941 and their spouses of any age. "The sample was drawn at the household financial unit level using a multistage, national area-clustered probability sample

frame. An oversample of Blacks, Hispanics (primarily Mexican Americans), and Florida residents was drawn to increase the sample size of Blacks and Hispanics as well as those who reside in the state of Florida", Fisher and Ryan (2017). The number of respondents were 13,593. Since 1992, the survey were repeated every two years, each is referred to as a wave of survey. New cohorts were added in 1993, 1998, 2004 and 2010, ending the survey up with the sample size of 37,495 from around 23,000 households in wave 12 in 2014. RAND created many variables from the original HRS data for ease of use. I create all the variables (with a few exceptions mentioned below) from the RAND HRS dataset version P. The details of the Rand HRS version P can be found in Bugliari et al. (2016).

As mentioned in the introduction, I define the disability health state to be one that qualifies one to be on the disability programs OASDI or SSI. The data on disability is self-reported. Later I plan to use the Social Security Administration's matched administrative data on this variable and earnings variables not included here. The matched data will, however, reduce the sample size to half, as only 50 percent of the respondents are used for matching HRS with SSA Administrative data. The HRS data collected information on if and when the doctor diagnosed that the respondent has any of the severe diseases such as high blood pressure, diabetes, cancer, lung disease, heart attack, stroke, psychiatric disorder and severe arthritis. I drop respondents who received disability before the first survey year 1992 and I also drop the spouses in the sample who were not born between 1931 to 1941, that is the respondents in our sample are between age 51 to 61 and not disabled or dead in 1992. I ended up with the final sample size of 9,493 for this analysis.

Table 1 provides a few characteristics of the data.

Table 1: Distribution of the sample by health status in various survey rounds

		Percentage distriubtion of health status			
Survey year	**Total**	**Normal**	**With Diseases**	**Disabled**	**Died in period**
1992	9,493	39.65	60.35	0.00	0.00
1994	9,493	34.16	62.73	1.75	1.36
1996	9,198	30.17	66.72	1.52	1.59
1998	7,461	27.48	69.09	1.81	1.62
2000	5,791	25.38	71.14	1.49	1.99
2002	4,106	22.80	74.35	1.32	1.53
2004	2,437	20.68	75.91	1.40	2.01
2006	785	17.83	79.75	0.38	2.04

3.1 Variables

The demographic variables **White** and **Female** have the standard definition. The variable **College** is a binary variable taking value 1 if the respondent has education level of college and above (does not include some college), i.e., has a college degree and more and taking value 0 otherwise.

cesd: I used a score on the Center for Epidemiologic Studies Depression (CESD) measure in various waves that is created by RAND release of the HRS data. RAND creates the score as the sum of five negative indicators minus two positive indicators. "The negative indicators measure whether the Respondent experienced the following sentiments all or most of the time: depression, everything is an effort, sleep is restless, felt alone, felt sad, and could not get going. The positive indicators measure whether the Respondent felt happy and enjoyed life, all or most of the time." I standardize this score by subtracting 4 and dividing 8 to the RAND measure. The wave 1 had different set of questions so it was not reported in RAND HRS. I imputed it to be the first non-missing future CESD score. In the paper, I refer the variable as cesd. Steffick (2000) discusses its validity as a measure of stress and depression.

cogtot: This variable is a measure of cognitive functioning. RAND combined the original HRS scores on cognitive function measure which includes "immediate and delayed word recall, the serial 7s test, counting backwards, naming tasks (e.g., date-naming), and vocabulary questions". Three of the original HRS cognition summary indices—two indices of scores on 20 and 40 words recall and third is score on the mental status index which is sum of scores "from counting, naming, and vocabulary tasks"—are added together to create this variable. Again, due to non-compatibility with the rest of the waves, the score in the first wave was not reported in the RAND HRS. I have imputed it by taking the first future non-missing value of this variable.

bmi: The variable body-mass-index (BMI) is the standard measure used in the medical field and HRS collected data on this for all individuals. If it is missing in 1992, I impute it with the first future non-missing value for the variable.

Now I describe the construction of the behavioral variables.

behav_prev: The original HRS surveys starting in 1998 contain responses to a set of questions to capture the respondent's behavior towards preventive care. I used the dynamic IRT (item response theory) on these responses and used the first dominant factor's loadings for each individual, and define the variable behav_prev to take value 1 if the factor loading of the variable in a survey year is above the mean of the factor loading score and 0 otherwise.

This makes the measure to be on the same footing for all individuals and time periods. For the years 1992 and other years with missing values, I imputed it as the first future non-missing value.

behav_smoke: This variable is constructed to be a binary variable taking value 1 if the respondent has reported yes to ever smoked question during any of the waves as reported in the RAND HRS data and then repeated the value for all the years.

behav_drink: This variable created using the dynamic IRT on the categorical variables in the RAND HRS reporting the number of days per week the respondent drinks. The data is available from wave 3 (i.e., 1996) onward. Using the same methodology as for the behav_prev described above, I create this binary variable for all the years.

behav_vigex: The RAND HRS has data on whether the respondent did vigorous exercise three or more days per week. I created a variable to take value 1 in each period if the respondent did vigorous exercise three or more days per week in any of the waves, and value 0 otherwise. I then assign that variable to behav_vigex for all the years.

4 Econometric parameterization and Estimation

In statistical models, the dependence of transition probabilities on individual characteristics is generally done through parametric or semi-parametric specification of the transition intensity functions $\Gamma(t)$. One then estimates the transition probabilities from the non-parametric or semi-parametric estimates of the integrated transition functions. An *integrated transition intensity function* $\Lambda_{hj}(t)$ for a transition $h \to j$ is defined by $\Lambda_{hj}(t) = \int_0^t \lambda_{hj}(u)\, du$. Just like for a continuous random variable, it is easier to estimate its cumulative density function nonparametrically than its density function, for the time-to-event data with censoring, it is easier to estimate the integrated hazard function than the intensity function. While for the discrete case this problem does not arise, estimation of transition probabilities via nonparametric estimates of the integrated hazard function is an unified approach encompassing both discrete time and continuous time data. I follow this strategy.

To explain and gain insights into this estimation strategy, denote the matrix of all the cumulative hazard functions as $\Lambda(t) = \left(\Lambda_{hj}(t)\right)_{h,j=1,2,3,4}$, and the matrix of the derivatives of the component functions by $d\Lambda(t)$. Let the time interval $[s,t]$ is subdivided into a partition of m sub-intervals with cut-off points $s = t_0 < t_1 < ... < t_m = t$. Denote the partition by $P(m)$. Denote the largest size of the sub-intervals by $|P(m)| \equiv \max\{|t_i - t_{i-1}|, i = 1, ..., m\}$. Applying repeatedly the Chapman-Kolmogorov equation

Eq. (7) on the sub-intervals of the partition, we have

$$P(s,t) = P(t_0,t_1) \cdot P(t_1,t_2) \cdot \ldots \cdot P(t_{m-1},t_m) = \prod_{i=1}^{m} P(t_{i-1},t_i) \tag{20}$$

Note that as $|t_{i-1} - t_i| \rightarrow 0$, the transition probability matrix $P(t_{i-1},t_i) \rightarrow P(t_{i-1},(t_{i-1}+dt) = I + \Gamma(t)dt$.[4] With finer subdivisions of the interval $[s,t]$ such that the maximum length of the sub intervals tends to 0, the right hand side of Eq. (20) converges to a matrix called the *the product integral*[5] of the integrated hazard functions $\Lambda(s,t)$. This product integral is denoted as $\widetilde{\prod}_s^t (I + d\Lambda(u))$. Or in other words, the transition probabilities of a stochastic process parameterized via an intensity process is given by the product integral of the integrated transition intensity functions.

$$P(s,t) = \widetilde{\prod}_s^t (I + d\Lambda(u)). \tag{21}$$

The above product-integral solution is a generalization of the Kaplan-Meier (Kaplan and Meier (1958)) product-limit formula for the survival function in survival analysis. The product integral formula unifies both discrete time and continuous time Markov processes. It is an extremely useful apparatus for statistical analysis of Markov processes.

The most widely used statistical procedure to estimate the transition probabilities $P(s,t),\ s,t \in T, s < t$ is to plug in an estimate $\Lambda(u)$ in Eq. (21). The effect of covariates is incorporated by conditioning the transition intensity functions $\Gamma(t;X(t))$ on the covariates process $X(t)$. There are many ways to get these estimates. I will follow two approaches in this paper: First, I will explore the more widely used non-parametric Aalen-Johnson-Fleming method via Nelson Aalen estimates for each-component of the $\hat{\Lambda}(u;X(u))$ with Cox proportional hazard model to incorporate the time-varying covariate effects in the next sub-section. Second, the Neural network approach explored in a later section.

4.1 Aalen-Johansen Estimator of Transition Probabilities

Most widely used statistical procedure incorporates the time-varying covariates for the transition probabilities by specifying a semi-parametric functional forms for the intensity hazard

[4] From the definition of transition intensity and writing it in matrix form, we have $\Gamma(t) = \lim_{\Delta t \downarrow 0} \frac{P(t,t+\Delta t)-P(t,t)}{\Delta t} = \lim_{\Delta t \downarrow 0} \frac{P(t,t+\Delta t)-I}{\Delta t}$. From this it follows that for small Δt, we have $P(t,t+\Delta t) = I + \Gamma(t)\Delta t$.

[5] For a more formal treatment of product integral see Gill and Johansen (1990) and for a lucid exposition with some applications, see Gill (2005).

functions

$$\lambda_{hj}\left(t;X\left(t\right)\right)=\lambda_{hj}^{0}\left(t\right)e^{\beta_{hj}^{\prime}X(t)}. \tag{22}$$

In the above specification, $\lambda_{hj}^{0}\left(t\right)$ is known as the *baseline hazard function*. The specification of transition intensity in Eq. (22) is known as the *proportional hazard model*. It aggregates the effects of the regressors linearly as a measure of some kind of latent factor, and that latent factor shifts the baseline hazard proportionately, i.e., the effect on hazard is uniform over time. Two papers (Fleming (1978) and Aalen and Johansen (1978)) independently extended the Kaplan-Meier nonparametric product limit estimator from survival analysis to the multi-state time to event models. While Fleming (1978) gave the estimator for complete data, Aalen and Johansen (1978) gave the estimator for censored data. To describe the Aalen-Johansen estimator, let me introduce some concepts and notation. For each individual $i, i=1,2,...,n$ and corresponding to each transient health state, $h, h=1,2$, define two types of stochastic processes: (1) the counting processes $N_{hj,i}(t)$ denoting the **observed** number of transitions from health state h to health state j that the individual i has made by time t—which in our case is either 0 or 1, since by assumption when an individual exits a health state, the individual does not return to it in future ; and (2) $Y_{h,i}(t)$, taking value 1 if individual i is at risk at time t for transition to another possible health state, and taking value 0 otherwise.

Let us focus on one transition $h\rightarrow j$. Denote by $\bar{N}_{hj}(t)=\sum_{i}^{n}N_{hj,i}(t)$, a counting process measuring the number of transitions of the $h\rightarrow j$ in the sample at time t, $\bar{Y}_{h}(t)=\sum_{i}^{n}Y_{h,i}(t)$, a counting process measuring the number of individuals in the sample at risk for a transition at time t, and $\bar{M}_{hj}(t)=\sum_{i}^{n}M_{hj,i}(t)$. In any empirical study the data will be at the discrete times, say in ordered times $0=t_{0}<t_{1}<...<t_{m}$. At each time t_{i}, we calculate

$$\hat{\lambda}_{hj}\left(t_{i}\right)=\frac{\triangle\bar{N}_{hj}\left(t_{i}\right)}{\bar{Y}_{h}\left(t_{i}\right)},j\neq h, \tag{23}$$

Without covariates, the *Nelson-Aalen non-parametric estimate* of the integrated intensity functions is given by, for each $h=1,2$

$$\begin{aligned}\hat{\Lambda}_{hj}\left(t\right) &= \sum_{i:t_{i}\leq t}\hat{\lambda}_{hj}\left(t_{i}\right),j\neq h,\\ \hat{\Lambda}_{hh}\left(t\right) &= -\sum\hat{\Lambda}_{hj}\left(t\right)\\ \hat{\Lambda}_{hj}\left(t\right) &= 0\text{ for all other }h,j\text{ combinations}\end{aligned} \tag{24}$$

The *Aalen-Johansen estimator* $\hat{P}(s,t),s,t,\in T,s<t$ for the transition probabilities is obtained by substituting for each component hj the Nelson-Aalen estimates $\hat{\Lambda}_{hj}(t)$ and

then applying the product integral formula Eq. (21) as follows

$$\hat{P}(s,t) = \prod_{s<u<t} \left(I + d\hat{\Lambda}(u)\right) = \prod_{i:t_i \leq t} \left(I + \left[\hat{\Lambda}(t_i) - \hat{\Lambda}(t_{i-1})\right]\right). \tag{25}$$

In the counting process framework, Andersen, Borgan, et al. (1993) derive the following generalized Cox partial likelihood to get parameter estimates of the Cox regression models

$$CL(\beta) = \prod_i \prod_{h=1,2j=2,3,4h\neq j} \prod_t \left(\frac{Y_{h,i}(t) \exp\left(\beta'_{hj} X_{h,i}(t)\right)}{\sum_r Y_{h,r}(t) \exp\left(\beta'_{hj} X_{h,r}(t)\right)} \right)^{\triangle N_{hj,i}(t)} \tag{26}$$

With covariates, one obtains the Cox partial likelihood estimate for $\hat{\beta}_{hj}$ for each transition $h \to j$ separately and then computes an weighted risk set defined by

$$\bar{Y}^*_{hj}(t) = \sum_{i=1}^{n} Y_{hj,i}(t) \exp\left(\hat{\beta}'_{hj} X_{h,i}(t)\right). \tag{27}$$

The estimates of cumulative intensities with covariates are obtained from Eq. (23) by replacing, $\bar{Y}_h(t)$ with $\bar{Y}^*_{hj}(t)$.

Nelson-Aalen estimator has nice statistical property. For instance, using Martingale calculus it can be shown that the estimator is asymptotically unbiased. Using the results from Martingale theory, one can derive the formula for variance-covariance estimates of parameter estimates and the normalized estimate is normally distributed (central limit theorem holds for normalized parameter estimates), for details see, (Aalen, Borgan, et al., 2008; Andersen, Borgan, et al., 1993; Fleming and Harrington, 2005).

The likelihood of the sample is given by[6] ,

$$L(\theta) = \prod_i \prod_{h=1,2j=2,3,4h\neq j} \left(\prod_t \lambda_{hj,i}\left(t|X_{h,i}(t)\right)^{\triangle N_{hj,i}(t)} \right) \exp\left(- \int_0^{T^*_{h,i}} \lambda_{hj,i}\left(u|X_{h,i}(u)\right) \right) du \tag{28}$$

Parametric models specify distributions for $\lambda_{hj,i}(t)$'s in Eq. (28) such as Weibull and Gamma. Even without covariates, close-form solution of the maximum likelihood parameter estimates for the Weibull model is difficult. But for without covariates time-constant intensity processes, close form solutions can be derived (see next subsection).

4.2 Time constant transition intensities without covariates

For time constant hazard with no covariates, $\lambda_{hj}(t) = \lambda_{hj}$, i.e. for exponential model, close-form solution can be derived, which after simplification is given by

[6] For details, see (Andersen, Borgan, et al., 1993; Andersen and Perme, 2008; Commenges, 2002).

$$\hat{\lambda}_{hj} = \frac{\overline{N}_{hj}}{\bar{T}_h^*}; V\left(\hat{\lambda}_{hj}\right) = \frac{\lambda_{hj}^2}{\overline{N}_{hj}}; \widehat{s.e}\left(\hat{\lambda}_{hj}\right) = \frac{\sqrt{\overline{N}_{hj}}}{\bar{T}_h^*}$$

where $\overline{N}_{hj} = \sum_{i=1}^{n_h} \int_0^t N_{hj,i}(t)\, dt$ is the total number of transitions of type $h \to j$, n_h is the total number of individuals in the health state h, and the common denominators in all the expression $\bar{T}_h^* = \sum_{i=1}^{n_h} T_{h,i}^*$ is the total of all completed transition times and censor times of individuals who are in health state h, $(h = 1, 2)$ in the extended sample.

I first report the estimates of time constant transition intensities for the overall sample and illustrate the interdependence of the transition probabilities and how they evolve over time. Then I compare these estimates of transition intensities and transition probabilities for a selected few groups in **??**.

Probabilities of following various paths for the estimated time constant parameters: $\hat{\lambda}_{12} = 0.0407, \hat{\lambda}_{13} = 0.0039, \hat{\lambda}_{14} = 0.0018, \hat{\lambda}_{23} = 0.0049, \hat{\lambda}_{24} = 0.0055$

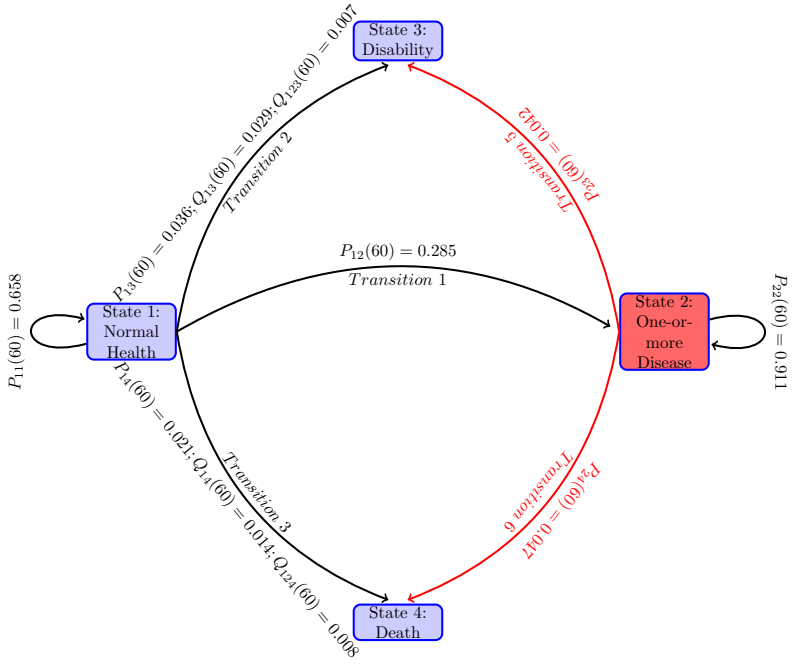

Figure 2: Path diagram of health trajectors.

To get an idea about these transition probabilities over time, I plot transition probabilities out of state 1 in Figure 3 panel (a) and out of state 2 in Figure 3 panel (b).

It will be interesting to compute the distributions of waiting times T_{13} and T_{123} and compare them empirically. For various groupsd the maximimum likelihood parameter estimates

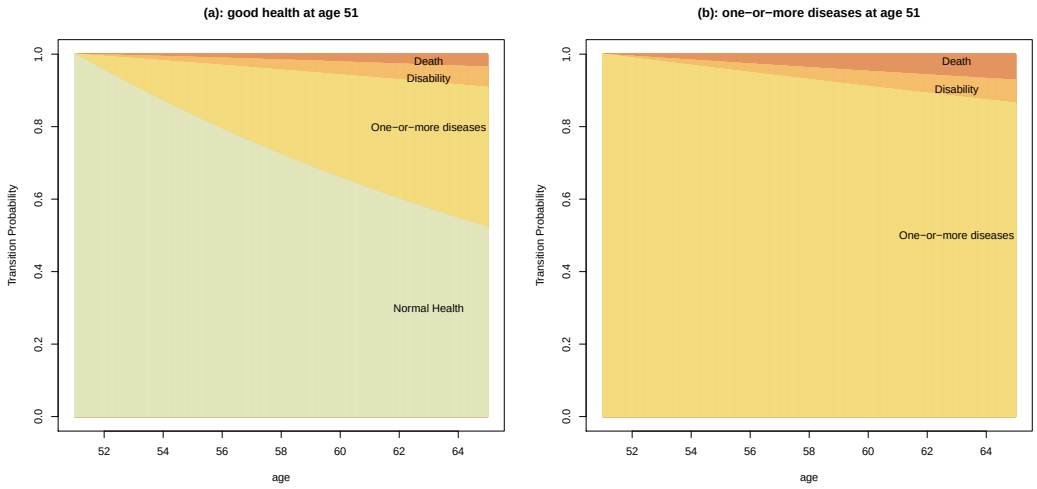

Figure 3: Transition probabilities (a) from normal health state, (b) from one-or-more diseased health state

and selected transition probabilities at 10 years are given in **??**.

Table 3: Maximum likelihood estimates of the time constant intensities and transition probabilities at 10 years for various groups

group	#nobs	λ_{12}	λ_{13}	λ_{14}	λ_{23}	λ_{24}	$P_{13}(10)$	$P_{23}(10)$	$P_{14}(10)$	$P_{24}(10)$
overall	15440	0.041	0.004	0.002	0.005	0.005	0.040	0.046	0.024	0.052
White	9086	0.040	0.003	0.001	0.004	0.005	0.034	0.042	0.020	0.048
NonWhite	2340	0.042	0.007	0.004	0.006	0.007	0.064	0.061	0.040	0.068
Female	5986	0.041	0.004	0.001	0.005	0.004	0.037	0.048	0.018	0.040
Male	5440	0.040	0.004	0.002	0.005	0.007	0.042	0.045	0.030	0.066
College	2010	0.039	0.001	0.001	0.002	0.003	0.014	0.020	0.013	0.034
Nocollege	9416	0.041	0.005	0.002	0.005	0.006	0.046	0.051	0.027	0.056
bmi>25	7280	0.046	0.004	0.002	0.005	0.005	0.044	0.048	0.023	0.049
bmi<=25	4144	0.035	0.003	0.002	0.004	0.006	0.034	0.042	0.025	0.059
Smoker	9674	0.040	0.005	0.003	0.006	0.007	0.046	0.052	0.033	0.066
Nonsmoker	5766	0.041	0.003	0.001	0.004	0.003	0.030	0.036	0.009	0.027
Drinker	8503	0.045	0.003	0.000	0.004	0.002	0.033	0.039	0.007	0.018
Nondrinker	6937	0.035	0.005	0.004	0.006	0.010	0.050	0.055	0.046	0.092
Exercise	11447	0.041	0.003	0.001	0.004	0.003	0.030	0.040	0.014	0.027
No exercise	3993	0.040	0.010	0.005	0.007	0.014	0.086	0.063	0.060	0.122

4.3 Time varying transition intensities without covariates

I compute the Aalen-Johansen estimates of the transition probabilities and their standard errors using the R package, *mstate*, developed and described by the authors in Wreede et al. (2010).

Figure 4 panel(a) shows the probabilities of a representative individual (i.e., one with the mean value of all the regressors) of age 51 to remain in normal health, contact one-or-more diseases, become disabled or die as the years pass by. Similarly, Figure 4 panel(b) shows the corresponding probabilities for an individual of age 51 who is in the health state of one-or more diseases.

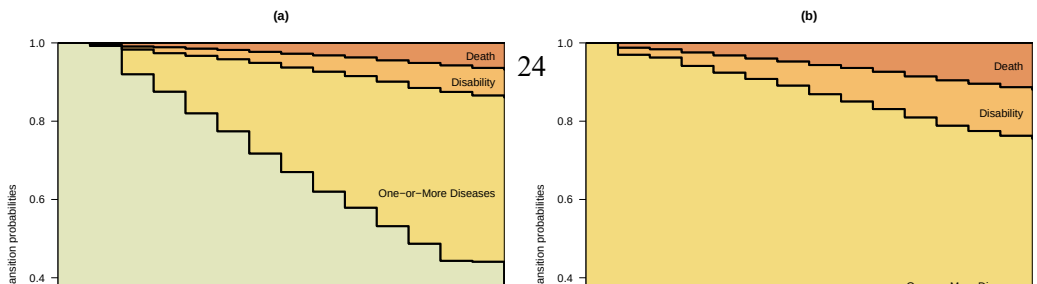

Table 2: Transition Probabilities for transitions i -> j by duration of stay in each state 1 and 2 for the model with time constant intensities

Duration	1 -> 1	2 -> 2	1 -> 2	1 -> 3	2 -> 3	1 -> 4	2 -> 4
51	1.000	1.000	0.000	0.000	0.000	0.000	0.000
52	0.955	0.990	0.040	0.004	0.005	0.002	0.005
53	0.911	0.980	0.077	0.008	0.010	0.004	0.011
54	0.870	0.969	0.112	0.012	0.014	0.006	0.016
55	0.830	0.959	0.145	0.016	0.019	0.008	0.021
56	0.793	0.950	0.177	0.020	0.024	0.011	0.027
57	0.757	0.940	0.206	0.024	0.028	0.013	0.032
58	0.722	0.930	0.234	0.028	0.033	0.016	0.037
59	0.690	0.920	0.260	0.032	0.037	0.018	0.042
60	0.658	0.911	0.285	0.036	0.042	0.021	0.047
61	0.628	0.902	0.308	0.040	0.046	0.024	0.052
62	0.600	0.892	0.330	0.044	0.051	0.027	0.057
63	0.573	0.883	0.350	0.048	0.055	0.030	0.062
64	0.547	0.874	0.369	0.052	0.059	0.033	0.067
65	0.522	0.865	0.387	0.056	0.063	0.036	0.072

Compare the non-parametric time non-homogeneous transition probability estimates in Table 4 with the parametric time-homogeneous estimates in **??** for the overall sample without covariates. They are very close to each other.

4.4 Time varying transition intensities and covariates

For the Cox regression parameter estimates, I have used both the R package *mstate* (see, Wreede et al. (2010) for details) and also used the SAS procedure *phreg* (both produced the same estimates) and used the *mstate* package to estimate all the transition probabilities (SAS does not have readily available procedure for this purpose). The parameter estimates are shown in Table 5 and Table 6.

With only demographic covariates (most that can be done with the Administrative data) the parameter estimates in Table 5 show that significantly lower risks of transitions $1 \rightarrow 4$; $2 \rightarrow 3$; $2 \rightarrow 4$ for whites and $1 \rightarrow 4$ and $2 \rightarrow 4$ for women. This may entail that the genetic make-up of being white or female sex yield favorable genetic predisposition to have better health outcomes and longer life. This is a misleading inference as we will see next that when we control for epigenetic factors that the biomedical literature pointed out to have significant effects on aging process and health outcomes, the above effects disappear.

Table 6 shows the Cox regression coefficient estimates of the effects of various factors

Table 4: Transition probabilities for transition i -> j by age in health state 1 and 2 from the semi-parametric multistate model

Duration	1 -> 1	2 -> 2	1 -> 2	1 -> 3	2 -> 3	1 -> 4	2 -> 4
51	1.0000	1.0000	0.0000	0.0000	0.0000	0.0000	0.0000
52	0.9933	0.9699	0.0000	0.0022	0.0181	0.0045	0.0120
53	0.9201	0.9629	0.0633	0.0078	0.0211	0.0089	0.0160
54	0.8756	0.9412	0.0983	0.0152	0.0347	0.0109	0.0241
55	0.8203	0.9242	0.1468	0.0184	0.0441	0.0144	0.0317
56	0.7744	0.9080	0.1841	0.0237	0.0524	0.0179	0.0396
57	0.7176	0.8912	0.2315	0.0281	0.0616	0.0227	0.0472
58	0.6701	0.8691	0.2673	0.0353	0.0744	0.0274	0.0565
59	0.6202	0.8506	0.3065	0.0417	0.0854	0.0316	0.0640
60	0.5791	0.8310	0.3362	0.0479	0.0954	0.0368	0.0735
61	0.5319	0.8098	0.3694	0.0544	0.1049	0.0443	0.0853
62	0.4871	0.7887	0.3978	0.0639	0.1159	0.0511	0.0953
63	0.4434	0.7749	0.4315	0.0680	0.1211	0.0572	0.1040
64	0.4411	0.7630	0.4249	0.0702	0.1240	0.0638	0.1129
65	0.3733	0.7556	0.4877	0.0712	0.1254	0.0678	0.1190

on the risk of having transitions $h \rightarrow j$ from health status $h = 1, 2$ to health status $j, j = 2, 3, 4$.

These estimates show that the parameter estimates for the demographic covariates in Table 5 are biased as they are capturing the effects of excluded epigenetic and behavioral factors in that model. After controlling for these epigenetic and behavioral factors, the significance of those effects disappear. Furthermore, women show significantly lower probability of transition from diseased health states onto the disability health state.

Most important factors in Table 6 are cesd, measuring depression and stress and college graduation or higher level of education, with positive effect on all transitions with the exception of no effect on transition from normal health to death. Other important factors are smoking, with significant adverse effect on transitions, and exercising three or more times regularly has significant favorable effect on most transitions. The alcohol use has no significant detrimental effect. Instead it reduces the risk of disability and death for people with diseases.

To understand the quantitative significance of these estimates, say the parameter estimate of -1.0042 in Table 6 for the parameter of $behav\_vigex$ in the model for transition $1 \rightarrow 3$ is that given all other factors equal, an individual of a given age with normal health will have a $0.37 \equiv exp(-1.0042)$ times lower risk of becoming disabled before age 65 if

Table 5: Estimates of Cox regression models separately for each transition

	1->2	1->3	1->4	2->3	2->4
White	0.008	-0.247	-0.921 ***	-0.355 ***	-0.392 ***
	(0.065)	(0.234)	(0.224)	(0.099)	(0.093)
Female	0.058	-0.301	-0.506 *	-0.003	-0.557 ***
	(0.048)	(0.191)	(0.219)	(0.090)	(0.085)
N	1759.000	113.000	90.000	504.000	568.000
R2	0.000	0.001	0.005	0.002	0.008
logLik	-13506.916	-862.010	677.209	4206.226	4781.869
AIC	27017.831	1728.019	1358.419	8416.453	9567.737

*** p $<$ 0.001; ** p $<$ 0.01; * p $<$ 0.05.

the person does moderately vigorous exercise compared to the probability of one who does not. The corresponding probability of becoming disabled before age 65 from the diseased health state is $0.56 \equiv exp(-0.5811))$ times lower compared to the probability of one who does not. The effect of other parameters can be easily read from the table.

Is there evidence for the racial reversal in mortality rates for the middle age non-college educated non-Latino white population that is found in Case and Deaton (2015). They found higher mortality rates for mid-age non-college educated white population. I also examine if disability entitlement rates for the group were also rising in the early 1990s. I calculated various transition probabilities analogous to transition probability estimates in Table 4 for these two groups. These are plotted in **??** (compare with the plots in Figure 4) and also reported in **??** (compare with Table 2. It appears that the non-college educated whites still show lower mortality and disability rates than the non-white non-college educated population.

As I have shown above that it is not the genetic make-up of race that is important for the pathways to diseases, disability and to death. The other behavioral and biomedical factors reported in Table 6 are important. To see if the non-college educated non-white group had on the average higher values of the behavioral and biomedical indicators that lead to higher probabilities of diseases, disability and death, I computed these averages for the two groups shown in **??**. We saw from the estimates in Table 6 that a level of cesd, higher level of cogtot, lower level of bmi, no smoking and moderate amount of vigorous exercising lower incidence of diseases, disability and death. From **??**, however, we see that the white has all the good attributes—lower cesd, higher cogtot, lower bmi, higher percent of population doing moderately vigorous exercising—all leading to lower probabilities of diseases, disability and death. Although they have slightly higher percent smoke and drink, which are detrimental, but these did not offset the other conducive effects mentioned above.

These estimates do not quite negate the Case and Deaton (2015) hypothesis for several reasons. First the population considered here is older and no new cohorts are added in each period as compared to their case. Estimation of the model and transition probabilities for the younger cohorts in the HRS data can shed better light on this issue.

Table 7: Transition probabilities for transition $i \rightarrow j$ by duration of stay in state 1 and 2 for non-college non-white (denoted with subscript 0) and non-college white (denoted with subscript 1)

X.your.data.frame.
your data frame

Table 8: Average values of various covariates for the non-college educated non-white and non-college educated white population

X.your.data.frame.
your data frame

Table 6: Estimates of Cox regression models separately for each transition with health measures

	1->2	1->3	1->4	2->3	2->4
White	0.024	0.172	-0.623	-0.064	-0.137
	(0.069)	(0.268)	(0.391)	(0.108)	(0.144)
Female	0.092	-0.415	-0.371	-0.086	-0.126
	(0.052)	(0.218)	(0.420)	(0.099)	(0.129)
College	-0.099	-0.826 *	-0.792	-0.588 **	-0.263
	(0.065)	(0.382)	(0.761)	(0.187)	(0.223)
cesd	0.460 ***	1.777 ***	-0.747	1.192 ***	0.760 ***
	(0.116)	(0.346)	(1.222)	(0.152)	(0.231)
cogtot	-0.004	-0.056 *	-0.003	-0.029 **	0.018
	(0.006)	(0.021)	(0.041)	(0.010)	(0.013)
bmi	0.039 ***	0.004	0.021	0.022 **	0.018
	(0.006)	(0.024)	(0.040)	(0.008)	(0.011)
behav_prev	-0.164 ***	-0.008	2.896 ***	0.099	2.600 ***
	(0.030)	(0.120)	(0.541)	(0.056)	(0.146)
behav_smoke	0.097 *	0.192	2.625 **	0.319 **	0.673 ***
	(0.052)	(0.219)	(1.030)	(0.104)	(0.161)
behav_drink	0.053	-0.197	-0.530	-0.332 ***	-0.073
	(0.055)	(0.212)	(0.405)	(0.099)	(0.136)
behav_vigex	-0.234 ***	-1.002 ***	-0.055	-0.427 ***	-0.279 *
	(0.074)	(0.231)	(0.443)	(0.102)	(0.128)
N	1667.000	101.000	30.000	478.000	267.000
R2	0.035	0.023	0.037	0.035	0.123
logLik	-12570.841	-722.863	-165.596	-3833.741	-1861.680
AIC	25161.682	1465.726	351.191	7687.483	3743.360

*** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$.

5 Conclusion

In this paper, I study the determinants of falling chronically ill with one-or-more diseases, the likelihood of getting on the Social Security's DI (Disability Insurance) program or the SSI (Supplemental Security Income) program and the likelihood of dying before becoming disabled by age 65. I use the Health and Retirement Studies (HRS) dataset. I surveyed the biomedical literature to gain insights into the genetic and epigenetic mechanisms at the molecular (i.e., cellular) level for the process of aging and developing age related chronic diseases, disability and death. I view aging as depletion in one's homeostatic regulatory health level that controls physiological body systems—such as respiratory, cardiovascular, neuroendocrine, immune, and metabolic. The higher rate of depletion of one's homeostatic health level makes the individual become more and more frail in his/her ability to face internal and external stressors. The depleted level of homeostatic health leads to one-or-more chronic diseases (such as diabetes, cancer, vascular, musculoskeletal, cognitive and mental disorders), and to disability or death. The general consensus in the biomedical literature is that much of an individual's later life health outcomes is programmed at an early stage of life—as early as the prenatal stage, most importantly right after the conception stage. The programming is strongly modulated by the epigentic inputs created by the environment in mother's womb. The genetic predisposition also matters. But epigentic factors modulate quite strongly the programming for later life developments in cognitive and non-cognitive health. The most important epigenetic factor is stress of any kind— psychological, financial, social and chemical—and other significant factors are diet, smoking, substance use, and exercising. These modulating factors are important throughout life, with stronger effects imparted in early stages of life.

I used a multi-state time-to-event model to estimate the effects of the above epigenetic factors (that include health related behaviors), demographic factors, education level (taken as college graduated or not). I use biomarkers like BMI, CES-D and cognition scores as noisy measurements of internal homeostatic health level, depression and stress level. I then study their effects on the probabilities of following various transition paths through the health states of normal health, illness with one-or-more chronic diseases, disability and death before reaching age 65. Disability and death are both treated as an absorbing state(i.e., final state) for this analysis. Death is always an absorbing state. I have treated disability also as an absorbing state because the focus of this study is the determinants of DI/SSI enrollments. Individuals are entitled to these programs only up to age 65 with severe disabilities.

I first estimate the model with only demographic variables as covariates, and found that whites have significantly lower risk of transiting from good health to death and from diseased health state to disability or death. The women found to have significantly lower risk of death than men, both from normal health and diseased health, and have no difference with men in becoming disabled. These are commonly observed phenomena found in other studies. These are the effects one can study using only the Administrative data.

After controlling for other variables from our list of variables, I find that the above effects for women and for whites disappeared. I find that college graduates have significantly lower probability of all transitions. The variable CES-D measuring the level of depression and stress has significant positive effects on transiting from normal health to acquiring one-or-more diseases, from normal health to becoming disabled and from diseased health state to becoming disabled or dying. The other most significant behavioral variables are smoking and sufficiently vigorous level of exercising regularly. The smoking has significantly adverse effects and exercising has favorable effects on most transitions.

For individuals in their early fifties in normal health, I have computed the risks of their acquiring diseases, or becoming disabled or dying before certain age. Similarly, for individuals who are ill with one-or-more diseases in their early fifties, I have calculated their risks of becoming disabled or dying before certain age. These probabilities can also be calculated for individuals with given values of the covariates of the Cox regression model of the paper.

Unlike the findings of Case and Deaton (2015), the non-Hispanic whites in their mid-ages, 50-60 in 1992, do not show higher morbidity, higher incidence of disability nor higher mortality. This could be due to the fact that the cohort in this study is older and the studied period is little earlier, 1992-2006, as compared to the age-group, 40-45, and the period, 1999-2013, for which their findings hold. Future work using the younger cohorts in the HRS data can shed better light on this issue, and on the effects of other variables studied in this paper.

6 Appendix

The system of differential equations in Eq. (7) becomes,

$$\frac{\partial P_{11}(s,t)}{\partial t} = -(\lambda_{12}(t) + \lambda_{13}(t) + \lambda_{14}(t))P_{11}(s,t) \tag{29}$$

$$\frac{\partial P_{12}(s,t)}{\partial t} = \lambda_{12}(t) P_{11}(s,t) - (\lambda_{23}(t) + \lambda_{24}(t))P_{12}(s,t) \tag{30}$$

$$\frac{\partial P_{13}(s,t)}{\partial t} = \lambda_{13}(t) P_{11}(s,t) + \lambda_{23}(t) P_{12}(s,t) \tag{31}$$

$$\frac{\partial P_{14}(s,t)}{\partial t} = \lambda_{14}(t) P_{11}(s,t) + \lambda_{24}(t) P_{12}(s,t) \tag{32}$$

$$\frac{\partial P_{22}(s,t)}{\partial t} = -(\lambda_{23}(t) + \lambda_{24}(t)) P_{22}(s,t) \tag{33}$$

$$\frac{\partial P_{23}(s,t)}{\partial t} = \lambda_{23}(t) P_{22}(s,t) \tag{34}$$

$$\frac{\partial P_{24}(s,t)}{\partial t} = \lambda_{24}(t) P_{22}(s,t) \tag{35}$$

with the initial condition, $P(s,s) = I$.

Note that Eq. (29) and Eq. (33) are differential equations of the form $dy(t)/dt = \lambda(t)y(t)$, which has the solution $y(t) = exp\left[\int_s^t \lambda(u)du\right]$. Thus Eq. (8) and Eq. (12) follows.

The differential equation Eq. (30), is of the form

$$dy(t)/dt + \lambda(t)y(t) = g(t) \tag{36}$$

which is more difficult to solve. Various techniques are available to solve this type of differential equations. I use the integrating factor technique. Define the integrating factor $exp\left[\int_s^t \lambda(u)du\right]$, multiply both sides of Eq. (36) by this integrating factor and then simplifying the left hand side using the multiplicative rule for differentiation, one gets $\frac{d}{dt}y(t)exp\left[\int_s^t \lambda(u)du\right] = g(t)exp\left[\int_s^t \lambda(u)du\right]$. This has the solution,

$$y(t)exp\left[\int_s^t \lambda(u)du\right] = \int_s^t \left[g(u)exp\left[\int_s^u \lambda(\tau)d\tau\right]\right]du.$$

Dividing both sides by the integrating factor, and utilizing the fact that, $exp\left[\int_s^t \lambda(u)du\right] = exp\left[\int_s^u \lambda(u)du + \int_u^t \lambda(u)du\right]$, one gets $y(t) = \int_s^t \left[g(u)exp\left[-\int_u^t \lambda(\tau)d\tau\right]\right]du$. Now substituting the original values for $g(t)$ and $\lambda(t)$, and noting that the exponential term is indeed the already solved $P_{22}(u,t)$ (see Eq. (12)), we have the solution Eq. (9).

Finally note that given the above solutions, Eq. (31), Eq. (32), Eq. (34) and Eq. (35) are of the form $dy(t)/dt = g(t)$ where the function $g(t)$ does not depend on $y(t)$. The solution for this is easily derived to be $y(t) = \int_s^t g(u)du$. This gives solutions Eq. (10), Eq. (11) and Eq. (13).

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