Pathways to disability and mortality in mid-ages: Estimates from the Health and Retirement Study Data

Lakshmi K. Raut

Social Security Administration
Lakshmi.Raut@ssa.gov

April 5, 2019

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Slides presented at the Annual Conference of Society for Government Economists, April 5, 2019, Washington, DC, USA.

Overview

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Objective

- The homeostatic regulatory mechanism controls physiological systems including the respiratory, cardiovascular, neuroendocrine, immune, and metabolic systems.
  Aging weakens homeostatic health, making one too fragile to cope with internal and external stressors, leading to diseases, disabilities and death.
- I draw from the molecular biology literature examining the genetic and epigenetic mechanisms for aging and incidence of age related disease, disability and death.
- I use the HRS data on demographics, education, biomarkers (such as BMI, CES-D, cognition) and health related behaviors such as smoking, drinking, exercising and preventative care use over the life-course.
- How these factors affect the risks of disease, disability and death before reaching age 65?
  How they affect the risk of following various paths through the states of normal health, one-or-more diseases, disability and death.
- I use a multi-state time-to-event statistical model, a generalization of the competing risk models and use R and SAS statistical software to estimate the model.

Literature

Previous Models

Disablement Models: Nagi (1965); Nagi (1976); Nagi (1991) Verbrugge and Jette (1994); Verbrugge, Latham, et al. (2017)

Biomedical Mechanism of Health Developments

- Genetic: Barondes (1999); Khoury et al. (2009); Bookman et al. (2011)
- Telomere: Hayflick (1965); Blair et al. (1989); Vaupel (2010); Austad and Fischer (2016); Zarulli et al. (2018); Epel et al. (2004); Shalev, Entringer, et al. (2013); DiLoreto and Murphy (2015); Shalev and Belsky (2016); Simons et al. (2016)
- Epigenetic: Esteller (2008); Barres and Zierath (2011); Alisch et al. (2012); Horvath (2013); Hannum et al. (2013)
- Programming and important milestones: Barker (1998); Barker (1990); Barker (2007); Gluckman et al. (2008); Thornburg et al. (2010); Kanherkar et al. (2014); Simons et al. (2016)

Economics and Social Sciences

Wallace and Herzog (1995); Steffick (2000); Renna (2008); Conti et al. (2009); Karakus and Patton (2011); Seib et al. (2014); Fisher and Ryan (2017)

The Basic Model

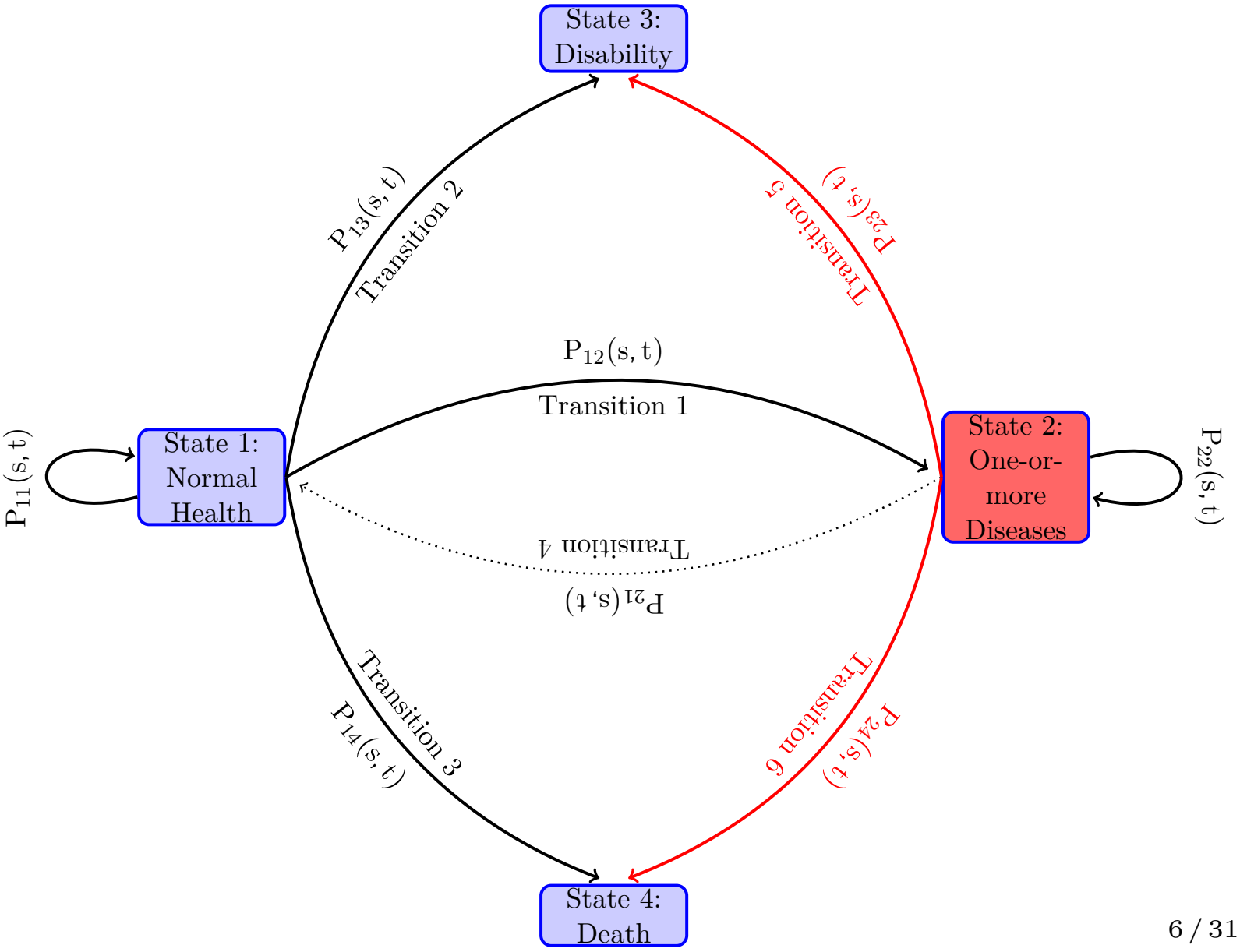
Assume that health outcomes over the life-cycle follow a multi-state continuous time Markov process $X(t), t \in T$ with the finite state space $S = \{1, ..., 4\}$.
$T = [51, 65]$ and unit of time is a year.
$1 =$ Healthy or normal health,
$2 =$ Ill with one or more chronic diseases,
$3 =$ Disability qualifying for the DI or SSI programs, and
$4 =$ Death.
The transition probabilities of the stochastic process $X(t)$

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

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

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

Path Diagram of health evolution over the life-span



Mathematics of Transition Probabilities

$P(s,t)$ satisfies the Chapman-Kolmogorov equation

$$P(s,t) = P(s,u) \cdot P(u,t), \forall s,u,t \in T \text{ with } s < u < t \quad (3)$$

Population distribution $\pi(t)$ over time follows

$$\pi(t) = \pi'(s)P(s,t), 0 \leq s < t. \quad (4)$$

Define transition intensity by

$$\alpha_{hj}(t) = \lim_{\Delta t \to 0} P_{hj}(t, t+\Delta t)/\Delta t \quad (5)$$

Define the matrix $\alpha(t) = (\alpha_{hj}(t))_{h,j=1,\ldots,p}$. Equation (3) reduces to Kolmogorov forward equation

$$\frac{\partial P(s,t)}{\partial t} = P(s,t) \cdot \alpha(t) \quad (6)$$

Note that $P(s,s) = I$ for all $s \in T$, serves as the initial condition of the above system of differential equation.

Solution of the system of differential equations: time-varying case

For the disability-disease-death model, transition intensities in (6)

$$\alpha(t) = \begin{pmatrix} -(\lambda_{12}(t) + \lambda_{13}(t) + \lambda_{14}(t)) & \lambda_{12}(t) & \lambda_{13}(t) & \lambda_{14}(t) \\ 0 & -(\lambda_{23}(t) + \lambda_{24}(t)) & \lambda_{23}(t) & \lambda_{24}(t) \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \tag{7}$$

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

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

$$\begin{aligned} P_{13}(s,t) &= \int_s^t \lambda_{13}(u)\,P_{11}(s,u)\,du + \int_s^t \left[P_{11}(s,u)\lambda_{12}(u)\int_u^t P_{22}(u,\tau)\,\lambda_{23}(\tau)\,d\tau\right]du \quad (10)\\ &= Q_{13}(s,t) + Q_{123}(s,t) \quad (11)\end{aligned}$$

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

$$P_{22}(s,t) = \exp\left(-\int_s^t (\lambda_{23}(u) + \lambda_{24}(u))\,du\right) \tag{13}$$

$$P_{2h}(s,t) = \int_s^t \lambda_{2h}(u)\,P_{22}(s,u)\,du, h = 3,4 \tag{14}$$

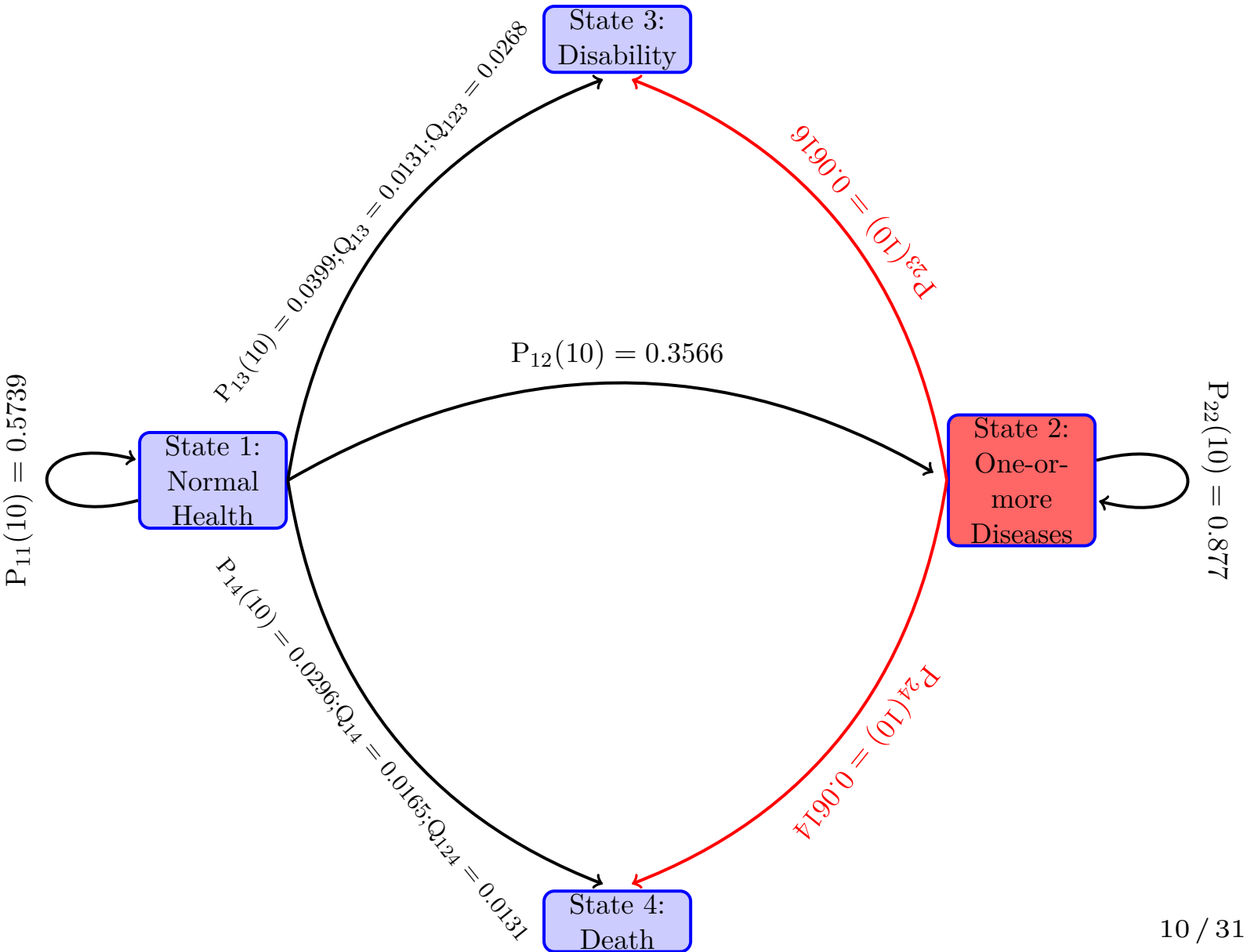
Solutions for the time-constant case

$$
\begin{aligned}
P_{11}(t) &= \exp(-\lambda_1 t), \\
P_{22}(s,t) &= \exp(-\lambda_2 (t-s)), \\
P_{12}(t) &= \frac{\lambda_{12}}{\lambda_2 - \lambda_1}\left[\exp(-\lambda_1 t) - \exp(-\lambda_2 t)\right] \\
P_{13}(t) &= \frac{\lambda_{13}}{\lambda_1}\left[1 - \exp(-\lambda_1 t)\right] + \frac{\lambda_{12}\lambda_{23}}{\lambda_2}\left[\frac{\exp(-\lambda_2 t) - \exp(-\lambda_1 t)}{\lambda_2 - \lambda_1} + \frac{1 - \exp(-\lambda_1 t)}{\lambda_1}\right] \\
&= Q_{13}(t) + Q_{123}(t) \\
P_{14}(t) &= \frac{\lambda_{14}}{\lambda_1}\left[1 - \exp(-\lambda_1 t)\right] + \frac{\lambda_{12}\lambda_{24}}{\lambda_2}\left[\frac{\exp(-\lambda_2 t) - \exp(-\lambda_1 t)}{\lambda_2 - \lambda_1} + \frac{1 - \exp(-\lambda_1 t)}{\lambda_1}\right] \\
P_{2h}(t) &= \frac{\lambda_{2h}}{\lambda_2}\left(1 - \exp(-\lambda_2 t)\right), h = 3, 4.
\end{aligned}
\tag{15}
$$

What is done

Given estimates of the intensities $\lambda_{hj}(t; X_h(t), \beta_{hj})$—time constant or time varying, with covariates or for a specific demographic group—probabilities of various health trajectories, and distribution of population $\pi(t)$ occupying various health states over time can be studied. Shown next.

Probabilities of pathways for $\hat{\lambda}_{12} = 0.04990, \hat{\lambda}_{13} = 0.00349, \hat{\lambda}_{14} = 0.00215, \hat{\lambda}_{23} = 0.00657, \hat{\lambda}_{24} = 0.00656.$



Econometric Specification and Estimation

Parameterization of transition intensities, for h → j

$$\lambda_{hj}\left(t; X_h, \beta_{hj}\right) = \lambda_{hj,0}(t)\exp^{\beta'_{hj}X_h}$$

Likelihood function of the data

- $Y_{h,i}(t) = 1$ if i is in health state h, $h = 1, 2$ at time t.
- $T^*_{h,i}$ = completed duration in state h or censoring time
- $N_{hj,i}(t)$ = # of transitions of type h → j by i during $[0, t]$.
- Likelihood of the sample

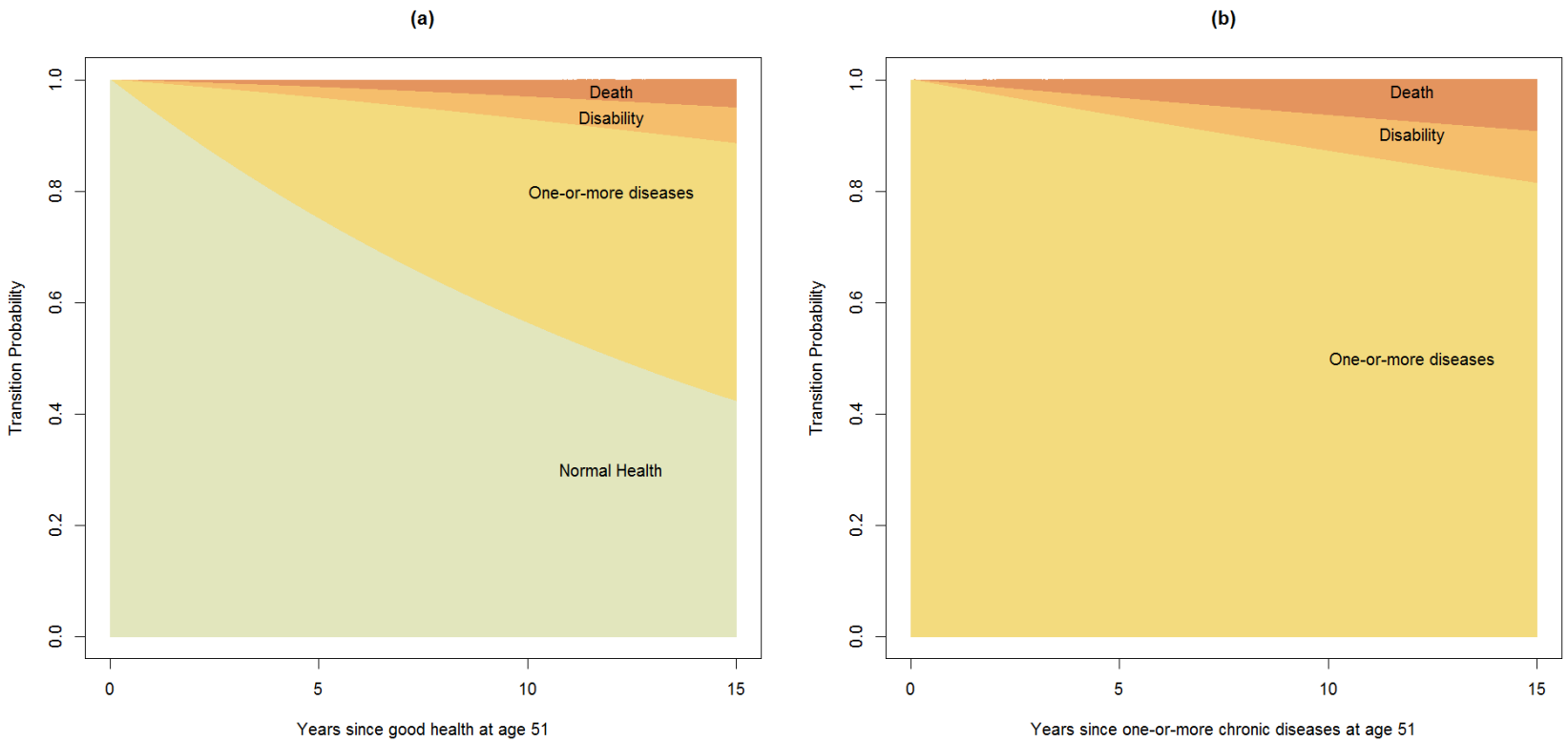
$$L(\theta) = \prod_i \prod_{h \to j, h \neq j, \substack{h=1,2 \\ j=2,3,4}} \left(\prod_t \lambda_{hj,i}\left(t|X_{hj,i}\right)^{\triangle N_{hj,i}(t)}\right) \exp\left(-\int_0^{T^*_{h,i}} \lambda_{hj,i}\left(u|X_{hj,i}\right) du\right)$$

- m.l.e for time-constant intensities

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

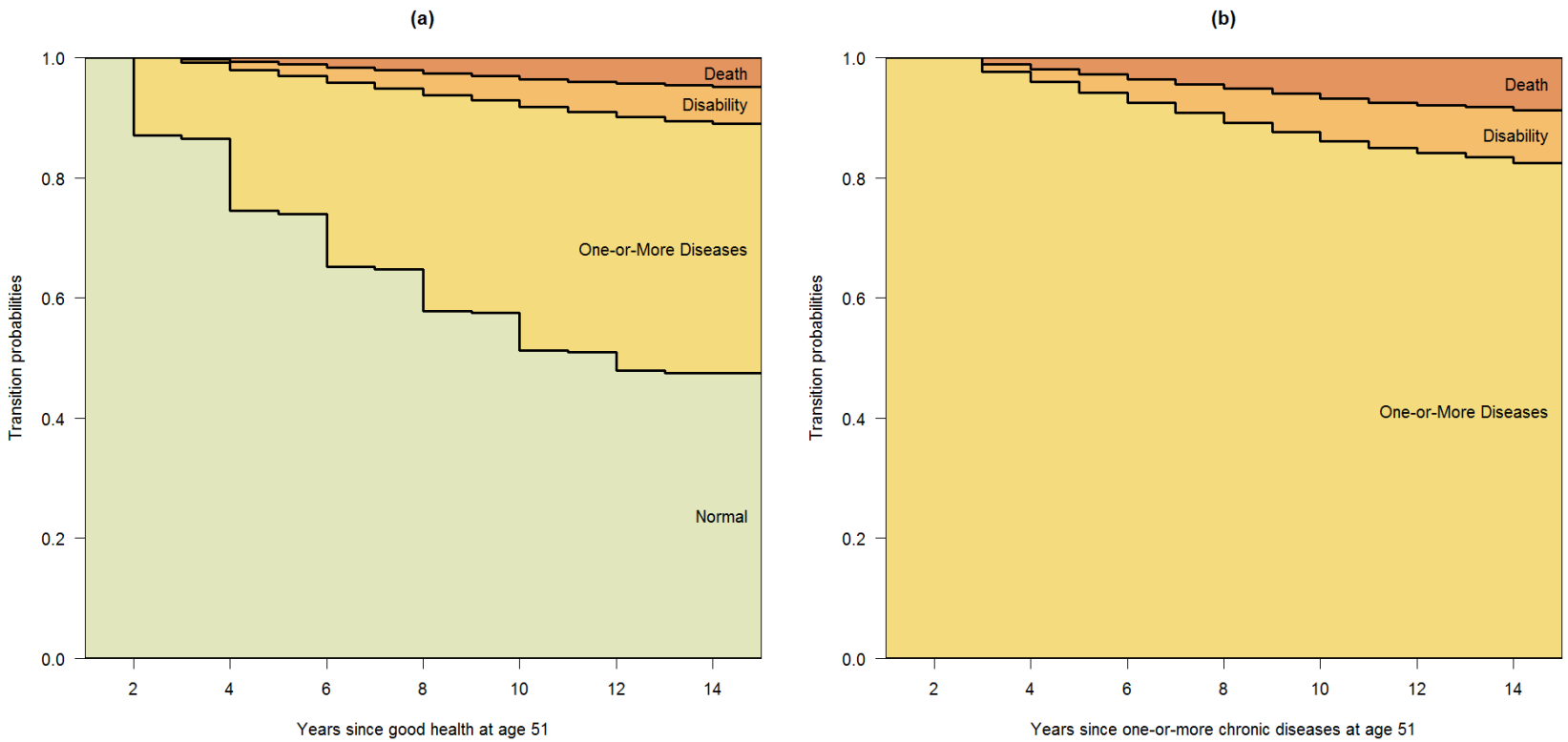
Transition probabilities: time constant intensities

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



Transition probabilities: time varying intensities

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



Transition Probabilities

duration	$1 \to 1$	$2 \to 2$	$1 \to 2$	$1 \to 3$	$2 \to 3$	$1 \to 4$	$2 \to 4$
1	0.9460	0.9870	0.0482	0.0036	0.0065	0.0023	0.0065
2	0.8949	0.9741	0.0932	0.0072	0.0130	0.0047	0.0129
3	0.8465	0.9614	0.1351	0.0110	0.0193	0.0073	0.0193
4	0.8008	0.9488	0.1742	0.0149	0.0256	0.0101	0.0256
5	0.7575	0.9365	0.2105	0.0189	0.0318	0.0130	0.0317
6	0.7166	0.9243	0.2443	0.0230	0.0379	0.0161	0.0378
7	0.6779	0.9122	0.2757	0.0271	0.0439	0.0193	0.0439
8	0.6413	0.9003	0.3048	0.0313	0.0499	0.0226	0.0498
9	0.6066	0.8886	0.3317	0.0356	0.0558	0.0261	0.0557
10	0.5739	0.8770	0.3566	0.0399	0.0616	0.0296	0.0614
11	0.5429	0.8655	0.3797	0.0443	0.0673	0.0332	0.0672
12	0.5135	0.8543	0.4009	0.0487	0.0729	0.0369	0.0728
13	0.4858	0.8431	0.4204	0.0531	0.0785	0.0407	0.0784
14	0.4596	0.8321	0.4384	0.0576	0.0840	0.0445	0.0839
15	0.4347	0.8213	0.4548	0.0621	0.0895	0.0484	0.0893

Source: The author.

Maximum likelihood estimates of the time constant intensities and transition probabilities by group

sample	n	λ_{12}	λ_{13}	λ_{14}	λ_{23}	λ_{24}	$P_{13}(10)$	$P_{23}(10)$	$P_{14}(10)$	$P_{24}(10))$
overall	11095	0.050	0.003	0.002	0.007	0.007	0.040	0.062	0.030	0.061
White	8900	0.050	0.003	0.002	0.006	0.006	0.037	0.057	0.026	0.056
Non-White	2195	0.050	0.005	0.004	0.009	0.009	0.051	0.079	0.046	0.080
Female	5841	0.052	0.003	0.002	0.007	0.005	0.037	0.062	0.023	0.048
Male	5254	0.048	0.004	0.003	0.007	0.008	0.042	0.061	0.037	0.077
College	1967	0.043	0.001	0.001	0.003	0.004	0.015	0.027	0.017	0.041
No college	9128	0.052	0.004	0.002	0.007	0.007	0.046	0.068	0.033	0.065
bmi $>$ 25	6980	0.057	0.004	0.002	0.007	0.006	0.042	0.064	0.029	0.057
bmi $<=$ 25	4113	0.042	0.003	0.002	0.006	0.008	0.037	0.055	0.031	0.072
Smoker	6891	0.051	0.004	0.003	0.008	0.009	0.044	0.070	0.041	0.079
Nonsmoker	4092	0.049	0.003	0.001	0.005	0.003	0.030	0.047	0.011	0.032
Drinker	4421	0.052	0.003	0.001	0.004	0.003	0.030	0.042	0.017	0.032
Non-drinker	6674	0.048	0.004	0.003	0.008	0.009	0.047	0.073	0.038	0.079
Exercise	8604	0.050	0.003	0.001	0.005	0.003	0.033	0.052	0.018	0.030
No exercise	2490	0.049	0.007	0.006	0.010	0.017	0.071	0.088	0.074	0.150

Source: Author's calculation.
Notes: All hazard intensities are significant at 1 percent level.

Definition of variables:

White and Female: Definitions are standard.

- Age: This is a time varying covariate not perfectly correlated with the duration of occupancy in a health state.
- cesd: Based on the score on the Center for Epidemiologic Studies Depression (CESD) measure, capturing the level of stress and depression.
- cogtot: A measure of cognitive functioning based on the aggregate scores on word recall, counting backwards, naming tasks (e.g., date-naming), and vocabulary questions.
- bmi: Using the standard body-mass-index (BMI) value, I define this binary variable to take 1 if BMI > 25 and 0 otherwise.
- behav_prev: Using the dynamic IRT (item response theory) on a set of preventive care responses in the HRS, I used the first dominant factor's loadings for each individual, and define this variable to take value 1 if the loading of the variable in a survey year is above the mean of the factor loading score and 0 otherwise.
- behav_smoke: A binary variable taking value 1 if the respondent ever smoked and 0 otherwise.
- behav_drink: Like the creation of the variable behav_prev, this variable is created using the dynamic IRT on the categorical variables reporting the number of days per week the respondent drank.
- behav_vigex: This variable takes value 1 if the respondent did vigorous exercises 3 or more times per week.

Estimates of Cox regression models separately for each transition

	1->2	1->3	1->4	2->3	2->4
White	−0.0143	−0.3263	−0.7321**	−0.3650***	−0.4121***
	(0.0628)	(0.2308)	(0.2650)	(0.1012)	(0.1006)
Female	0.0479	−0.2105	−0.5196*	−0.0644	−0.5104***
	(0.0463)	(0.1904)	(0.2499)	(0.0911)	(0.0922)
Age	−0.0823***	−0.0568	0.0058	−0.1132***	−0.0499***
	(0.0081)	(0.0324)	(0.0421)	(0.0143)	(0.0135)
AIC	25259.8561	1740.3244	1063.5163	8073.3477	8057.7550
R^2	0.0249	0.0016	0.0031	0.0102	0.0081
Max. R^2	0.9992	0.3756	0.2537	0.6949	0.6935
Num. events	1602	112	69	476	475
Num. obs.	3583	3695	3652	6856	6855
Missings	0	0	0	0	0
PH test	0.0000	0.0125	0.0772	0.0000	0.0000

$^{***}p < 0.001$, $^{**}p < 0.01$, $^{*}p < 0.05$

1:h = healthy; 2:i = ill with one-or-more diseases; 3:d = disability; 4:D = death.

Misleading effects

With only demographic covariates (most that can be done with Administrative data) shows significantly lower risks of transitions h → D; i → d; i → D for whites and h → D and i → D for women.

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

	1->2	1->3	1->4	2->3	2->4
White	0.0086	0.0038	−0.3675	−0.1056	−0.1622
	(0.0671)	(0.2939)	(0.5095)	(0.1102)	(0.1624)
Female	0.0772	−0.3895	−0.4448	−0.2038*	−0.2308
	(0.0511)	(0.2390)	(0.4995)	(0.1037)	(0.1508)
College	−0.1768**	−0.9687*	−0.7994	−0.6165**	−0.5416*
	(0.0641)	(0.4333)	(0.7701)	(0.1950)	(0.2635)
Age	−0.0907***	−0.0849*	−0.1386*	−0.1076***	−0.1102***
	(0.0085)	(0.0378)	(0.0693)	(0.0150)	(0.0215)
cesd	0.5065***	1.8802***	0.0940	1.2030***	0.4952*
	(0.1092)	(0.3641)	(1.0818)	(0.1631)	(0.2526)
cogtot	−0.0112	−0.0662*	0.0192	−0.0328***	−0.0028
	(0.0058)	(0.0260)	(0.0440)	(0.0096)	(0.0160)
bmi	0.0398***	−0.0088	0.0141	0.0158	−0.0233
	(0.0055)	(0.0315)	(0.0536)	(0.0095)	(0.0170)
behav_prev	0.3828***	0.7397**	−19.7473***	0.1402	−1.5869***
	(0.0487)	(0.2270)	(0.2451)	(0.0974)	(0.1845)
behav_smoke	0.0436	0.2626	2.5071*	0.4057***	0.8133***
	(0.0504)	(0.2264)	(1.0096)	(0.1093)	(0.1817)
behav_drink	0.0307	−0.3579	0.5318	−0.4993***	−0.2507
	(0.0497)	(0.2414)	(0.4481)	(0.1118)	(0.1518)
behav_vigex	−0.2467***	−1.0293***	−0.9911	−0.5974***	−1.0397***
	(0.0702)	(0.2535)	(0.5155)	(0.1058)	(0.1447)
AIC	23182.4941	1370.5925	309.5095	7250.9572	3212.5472
R^2	0.0689	0.0302	0.0159	0.0471	0.0415
Max. R^2	0.9993	0.3529	0.0990	0.7050	0.4406
Num. events	1500	95	23	446	207
Num. obs.	3239	3334	3262	6165	5926
Missings	344	361	390	691	929
PH test	0.0000	0.0034	0.1191	0.0000	0.0000

$^{***}p < 0.001$, $^{**}p < 0.01$, $^{*}p < 0.05$

Conclusions

- The model with only demographic covariates leads to misleading inferences that whites and women have some inherent advantages (probably better genetic disposition) so that they have lower risks for death and disability.
- The above are misleading effects, capturing effects of epigenetic and behavioral factors, controlling which make those disappear.
- Most important factors are — CES-D measuring level of depression and stress, and college education, with positive effect on all transitions with the exception of no effect on h $\rightarrow$ D.
- Other important ones: Smoking with significant adverse effect and exercising regularly with favorable effects on most transitions.
- The framework is useful to calculate the probabilities of becoming disabled or dying by a given age from a health state.

The End

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