SSM - Population Health 11 (2020) 100577



Contents lists available at ScienceDirect

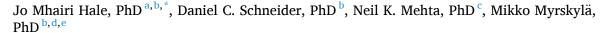
### SSM - Population Health

journal homepage: http://www.elsevier.com/locate/ssmph



#### Article

# Cognitive impairment in the U.S.: Lifetime risk, age at onset, and years impaired



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#### ARTICLE INFO

Keywords:
Cognitive impairment
Dementia
Health disparities
Race/ethnicity
Education

#### ABSTRACT

Prior studies have analyzed the burden of cognitive impairment, but often use potentially biased prevalencebased methods or measure only years lived with impairment, without estimating other relevant metrics. We use the Health and Retirement Study (1998-2014; n = 29,304) and the preferred incidence-based Markov-chain models to assess three key measures of the burden of cognitive impairment: lifetime risk, mean age at onset, and number of years lived impaired. We analyze both mild and severe cognitive impairment (dementia) and gender, racial/ethnic, and educational variation in impairment. Our results paint a multi-dimensional picture of cognitive health, presenting the first comprehensive analysis of the burden of cognitive impairment for the U.S. population age 50 and older. Approximately two out of three Americans experience some level of cognitive impairment at an average age of approximately 70 years. For dementia, lifetime risk for women (men) is 37% (24%) and mean age at onset 83 (79) years. Women can expect to live 4.2 years with mild impairment and 3.2 with dementia, men 3.5 and 1.8 years. A critical finding is that for the most advantaged groups (i.e., White and/ or higher educated), cognitive impairment is both delayed and compressed toward the very end of life. In contrast, despite the shorter lives of disadvantaged subgroups (Black and/or lower educated), they experience a younger age of onset, higher lifetime risk, and more years cognitively impaired. For example, men with at least an Associate degree have 21% lifetime dementia risk, compared to 35% among men with less than high school education. White women have 6 years of cognitively-impaired life expectancy, compared to 12 and 13 years among Black women and Latinas. These educational and racial/ethnic gradients highlight the very uneven burden of cognitive impairment. Further research is required to identify the mechanisms driving these disparities in cognitive impairment.

#### Introduction

Contemporary elders' unprecedentedly long lives fuel concern that they may spend a significant proportion of their lives suffering agerelated diseases. A particularly burdensome disease process, both personally and economically, is pathological cognitive decline. To provide a sense of the extent of cognitive impairment, a third of people in the U.S. aged 85 and older have Alzheimer's disease (Hebert, Weuve, Scherr, & Evans, 2013), the most common cause of pathological

cognitive decline (Qian, Schweizer, Munoz, & Fischer, 2016, p. P293). Alzheimer's disease accounts for 60–80% of dementias, is the sixth leading cause of death in the United States, and the only leading cause of death with no known prevention, efficacious treatment, or cure (Alzheimer's Association, 2019). Dementia more broadly, which includes Alzheimer's, Lewy body, cerebrovascular, and mixed dementias, is one of the most expensive diseases, as people with dementia can live for many years cognitively impaired and often require high levels of care (Hurd, Martorell, Delavande, Mullen, & Langa, 2013). Annual estimates

https://doi.org/10.1016/j.ssmph.2020.100577

Received 14 January 2020; Received in revised form 25 March 2020; Accepted 26 March 2020

Available online 31 March 2020

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for dementia costs in the U.S. in 2010 were between \$159 billion and \$215 billion (Hurd et al., 2013).

These individual, social, and economic costs have inspired research into the social factors that are associated with risk of cognitive impairment. This line of research has shown that the burden of dementia does not fall equally across the U.S. population. Two social risk factors that appear most highly correlated with later-life cognitive function are race/ ethnicity and educational attainment; gender disparities also exist (Crimmins et al., 2018; Farina, Hayward, Kim, & Crimmins, 2019; Langa et al., 2017; Mayeda, Glymour, Quesenberry, & Whitmer, 2016; Zhang, Hayward, & Yu, 2016). Dementia risk declines strongly with increasing education; Latinx and Blacks have approximately two to three times higher dementia risk than Whites; and, two-thirds of those with an Alzheimer's diagnosis are women (Mayeda et al., 2016; Plassman et al., 2007; Stern, 2012; Zhang et al., 2016). There are multiple plausible mechanisms through which these social factors may influence dementia risk, including differences in material deprivation, higher educational attainment, levels of occupational complexity, psychosocial stressors, treatment seeking, and overall life expectancy.

Although prior work has made important advances in documenting risk and burden of cognitive impairment, there are important limitations in existing research. First, most population-based research on cognitive impairment analyzes only relative risks of impairment, encompasses a limited set of survey years, or uses prevalence-based methods to calculate cognitive health expectancies. The prevalence-based methods are biased if incidence or mortality are changing (Barendregt, Bonneux, & Van der Maas, 1994; Imai & Soneji, 2007). The magnitude of the bias is difficult to estimate, but importantly, this bias is likely to vary across subpopulations (socioeconomic, racial/ethnic groups) if they are experiencing differential trends. Hence not only the overall level, but also estimates of disparities will be biased. Moreover, prevalence-based methods, by design, do not allow for recovery, which is likely questionable when analyzing mild cognitive impairment using survey data. We use incidence-based Markov chain multistate methods that are less prone to bias than the prevalence-based methods to estimate the burden of cognitive impairment in the U.S. by race/ethnicity, gender, and education using recent data covering the years 1998-2014.

Second, prior research that has focused on dementia life expectancy provides important insights into how long people live with very severe cognitive impairment (Farina et al., 2019); however, analyzing only dementia life expectancy misses the dynamics of incidence and recovery. It also does not help us to understand what fraction of the population will become cognitively impaired or when in life cognitive impairment is first experienced. Therefore, we work toward developing a more comprehensive understanding of the burden of cognitive impairment, complementing the analysis of cognitive health expectancies with two metrics of impairment that are novel in this line of research: lifetime risk of experiencing cognitive impairment and average age at which individuals first experience impairment. These metrics provide additional information beyond the number of years lived with impairment. They indicate the large fractions of the U.S. population directly affected by impairment and at what young ages cognitive impairment starts to impact individuals and their families.

Third, most existing research focuses only on severe cognitive impairment, intending to correspond to clinical dementia (exceptions Crimmins et al., 2018, 2016). In order to understand the burden of cognitive impairment in later life and not just the final years spent in dementia, we analyze any cognitive impairment, decomposed into mild cognitive impairment (MCI) and dementia. Cognitive decline progresses gradually. A much larger fraction of the population experiences MCI than dementia, and for much longer periods of life, with a high annual risk (10–15%) of transitioning to dementia (Roberts & Knopman, 2013). Neither behavioral nor medical interventions have been successful in curing Alzheimer's disease, and researchers hypothesize interventions earlier in the neurodegeneration process may increase efficacy of treatments or cures (Alzheimer's Association, 2019). Therefore,

describing the population burden and social inequalities in MCI has important policy implications.

Finally, a large fraction of research operationalizes cognitive impairment by using the entire modified Telephone Interview for Cognitive Status (TICS), which results in a 35-point scale that includes mental status questions (e.g., "Who is the U.S. President/Vice President?") and crystallized cognitive function measures, such as vocabulary (e.g., Reuser, Willekens, & Bonneux, 2011). These measures are more directly associated with education and other sociocultural factors and less reflective of underlying neuropathology (Ghisletta, Rabbitt, Lunn, & Lindenberger, 2012). Therefore, including them likely overstates the educational or racial/ethnic differentials. We use only variables reflective of fluid cognitive function (immediate and delayed word recall, backwards counting, and serial 7s), which should be more indicative of neurophysiological health (Ghisletta et al., 2012).

#### Data and methods

We use the Health and Retirement Study (HRS), a longitudinal study of U.S. residents aged 50 and older and their spouses, who are surveyed biennially on health and wealth measures. The HRS is sponsored by the National Institute on Aging (grant number NIA U01AG009740) and is conducted by the University of Michigan (RAND Center for the Study of Aging, 2017; University of Michigan, 2017). The HRS is nationally representative and oversamples minorities. We use RAND Version P of the HRS and years 1998–2014. We restrict our sample to respondents age 50 and over who had a cognitive function score or a proxy score in two or more waves. Less than one-half of one percent on any of the predictor variables is missing, and we use Fisher, Hassan, Faul, Rodgers and Weir (2017) imputed cognitive function scores. This results in a final sample size of 158,913 person-waves for 29,304 respondents.

#### Dependent variable

The dependent variable is a four-state variable that combines vital status (alive or not) and three categories of cognitive status among those alive: no cognitive impairment (NCI), cognitively impaired, but not demented (CIND), and dementia. The four states form the state space of the Markov model. Death is reported to the HRS and verified through the National Death Index (NDI).

In defining the three cognitive function states, we use the HRS's modified Telephone Interview for Cognitive Status (TICS), which was specifically modified to be sensitive to pathological cognitive decline and minimize ceiling effects (Fong et al., 2009; Karlamangla et al., 2009). We select a subset of the items contained in the TICS: immediate (0–10 points) and delayed recall (0–10 points), serial-7s (0–5 points), and backward counting from 20 (0–2 points). These items better reflect declines in neurophysiological health, in contrast to excluded measures (e.g., vocabulary), which are more influenced by education and other sociocultural factors (Ghisletta et al., 2012).

Our cut-points (scores: NCI 12–27, CIND 7–11, dementia 0–6) were validated against the clinical assessment from the Aging, Demographics, and Memory Study (ADAMS) (Crimmins, Kim, Langa, & Weir, 2011; Langa et al., 2005). These validated measures are expected to provide more accurate estimates for CIND and dementia than previously used cut-points. We follow Langa et al. (2017) in retaining respondents who have a proxy, which is important because cognitive impairment is the most common reason for use of a proxy. This incorporates the proxy's assessment of the respondent's cognitive status and instrumental activities of daily living, and after 2000 it also includes the interviewer's report of whether the respondent appeared cognitively impaired. As with in-person interviews, we used the ADAMS-validated cut-points to classify proxy interview scores (1998: NCI = 0–2, CIND = 3–4, and dementia = 5–9 points; 2000–2014: NCI 0–2, CIND 3–5, dementia 6–11).

#### Independent variables

We include gender, which HRS reports as a binary (man = 0; woman = 1). Race/ethnicity is self-reported as Non-Hispanic White, African American/Black Hispanic, Non-Black Hispanic, and "Other." We combine Black Hispanics with African American because they have more similar health outcomes to Blacks than to non-Black Hispanics (Chinn & Hummer, 2016). Hereafter we simplify to White, Black, and Latinx (Latino or Latina). We include in analyses, but do not display Other because it has small sample sizes at older ages. We categorize educational attainment as less than a high school diploma (henceforth, less than high school), high school diploma/general equivalency degree/some college (HS/GED), and Associate degree or higher (A/BA+). Although not ideal, we must combine HS/GED with some college, and Associate with college because of the low mean educational attainment of these birth cohorts, especially the racial/ethnic minorities, and the small samples with GED, some college, or Associates. Age is exact age in years at interview. We control for the number of cognition tests ("practice effects") taken using standard categories: first, second, third through sixth, and seven or more tests (Goldberg, Harvey, Wesnes, Snyder, & Schneider, 2015). A proxy response is coded as a separate practice effects category. This variable is lagged one wave, allowing for a non-missing value for those transitioning into the state of "dead."

#### Analytic strategy

We produce three metrics obtained from incidence-based Markov chain multistate models: lifetime risk of impairment, the mean age at first impairment, and state-specific life expectancies (cognitive health expectancies), all conditional on surviving to age 50. The first two metrics are conditional on being non-impaired at age 50. The Markov models are based on transition probabilities across states, which we estimate from a set of multinomial logistic regression models.

The multinomial logistic models are estimated separately for each of the three non-absorbing initial states (NCI, CIND, dementia) and for each gender. The models take the form:

$$\log\left(\frac{p_{ij}}{p_{iN}}\right) = a_{ij} + b_{1,ij} Age + b_{2,ij} Age^2 + \gamma_{ij} PE + \delta_{ij} \cdot DEMOGR$$

where  $p_{ij}$  is the probability of transitioning from state i to state j; state j includes death; j=N indicates the reference target state (NCI);  $a_{ij}$  is the intercept; Age is age over the follow-up measured at mid-interview; PE is the practice effect and is based on the number of prior tests taken, with  $\gamma_{ij}$  being the coefficient vector pertaining to the PE categories mentioned above;  $\delta_{ij}$  is a coefficient vector for the variables in DEMOGR, which contains race/ethnicity, education, and their full set of interactions.

We predict age (two-year intervals), gender, and subpopulationspecific transition probabilities using the logistic models. Probabilities are estimated by setting categorical indicators to either their sample proportion value to obtain the population average (e.g., "all education groups") or to 0/1, corresponding to a specific population subgroup (e.g., "White"). Practice effect is set to the second interview.

The predicted probabilities form the foundation of the Markov chain multistate model calculations. However, before we can calculate our outcome measures based on the transition probabilities, we must address the implications of measurement error. The observed state may not reflect true unobserved cognitive status. Participants may have a wave in which they earn a score on the cognitive function test that categorizes them as demented due to transient conditions that do not reflect a true state of dementia. For example, a participant may have an illness from which recovery is possible or may be experiencing unusually stressful life circumstances. Vacillation of cognitive function scores, even in a clinical setting, is common (Petersen et al., 2014; Roberts & Knopman, 2013). In addition, the test instrument itself may be intrinsically prone to random measurement error. As a consequence, we are

likely to misclassify individuals across cognition states. Importantly, the extent to which this may bias our results varies by outcome measure and can, to some extent, be anticipated. If misclassification occurs equally frequently across the states, state misclassifications may cancel each other out when calculating state occupancy times.

However, two of the key measures of this article, mean age at first incidence and fraction of people ever experiencing impairment, are both sensitive to measurement error. Increasing measurement error, even if random, decreases the age at which we first observe individuals in the impaired state, and increases the fraction of individuals ever experiencing impairment. To mitigate the potential downward bias of our calculation of age at first incidence and the potential upward bias in the fraction ever experiencing impairment, we apply more nuanced definitions for the occurrence of the first CIND episode and for the onset of dementia. We define the first CIND episode as being marked by two contiguous CIND observations, and similarly dementia onset as the first occurrence of two contiguous dementia observations. As these definitions can only be sensibly applied to completed (non-censored) life histories, we use a Markov chain multistate model that is based on estimated transition probabilities to simulate 10,000 completed life histories and calculate our outcome measures based on the simulated data, using our enhanced definitions of first CIND episode and dementia onset. Some aspects of the simulation procedure are further discussed below in the section on methodological considerations. Appendix I provides additional detail.

We calculate the three metrics of (i) the lifetime risk of any impairment or dementia conditional on not being impaired at age 50, (ii) the mean age at first incidence of any impairment or of dementia, conditional on not being impaired at age 50, and (iii) expected length of stay at age 50 in the states NCI, CIND, dementia, and total. All three metrics are based on simple averages and counts from the simulated trajectories. We obtain 95% confidence intervals by bootstrapping (500 replications). We conduct all analyses using Stata, version 16.

#### Results

Table 1 shows the sociodemographic composition of the sample over the 16-year period, overall and by cognitive function state. Of all personyears, 75% are non-impaired, 17% are cognitively impaired without dementia, and 8% are person-years with dementia. The average age is 70 years, and 57% of the observations are contributed by women. Men have a slightly higher percentage of person-waves in CIND (18% vs 17%), whereas women have a higher percentage in the dementia state (8.5% vs 6.7%). The racial/ethnic and educational disparities in CIND and dementia prevalence are more pronounced. Whereas 14% (CIND) and 6% (dementia) of Whites' person-years are in an impaired state, levels are nearly double for Latinx (27% CIND and 11% dementia) and Blacks (27% and 13%). Among those with less than a high school diploma, more than 50% of person-years are in an impaired state compared to only 9% among those with at least an Associate degree.

The bottom panel of Table 1 shows the transitions across states of impairment. This highlights that recoveries are common, as previously noted. CIND's liminal status is evident; there are almost as many transitions back to NCI as staying in CIND (34% versus 40%). Nevertheless, the highest percentage of transitions is to remain in the source state, regardless of the state, e.g., 84% of transitions from NCI are to NCI. 47% of source states categorized as dementia stay in a dementia state. Almost a third of the transitions from the dementia state are to death, i.e., a small fraction transition from being classified as demented to a less impaired state (more on this in the discussion).

Table 2 shows the estimated lifetime risk and age at first incidence of any cognitive impairment and dementia. Women have a 71% risk of experiencing any cognitive impairment before death, and 37% risk of experiencing dementia. Men have lower lifetime risks, 61% for any impairment and 24% for dementia. Among women, mean age at first incidence of any impairment and dementia is 73 and 83 years,

**Table 1**Descriptive characteristics of the HRS sample by person-waves (1998–2014). Total number of persons 29,304.

	Overall sample	No Cognitive Impairment (NCI)	Cognitive Impairment, no Dementia (CIND)	Dementia	
Total, %	100.0	74.9	17.3	7.7	
Age (years, mean)	69.8	67.2	72.8	79.5	
Gender, %					
Women	56.5	74.7	16.9	8.5	
Men	43.5	75.3	18.0	6.7	
Race/Ethnicity, %					
White	72.3	80.3	13.7	6.0	
Black	15.9	59.1	27.5	13.4	
Latinx	9.4	61.6	27.4	11.0	
Educational Attainment, %					
Less than high school	24.3	48.0	33.2	18.8	
HS/GED/ Some College	51.8	79.8	15.0	5.2	
Associate+	23.8	90.6	7.0	2.4	
Person-Waves	158,913	119,088	27,564	12,261	
Wave-to-wave transitions, %	From:				
To:	Any	NCI	CIND	Dementia	
NCI	69.0	83.7	33.6	4.9	
CIND			39.6	17.3	
Dementia	7.4	1.4	15.6	47.4	
Death			11.3	30.3	
Column Total	100	100	100	100	
n of transitions	138,133	103,798	23,766	10,569	

respectively, and among men 70 and 79 years.

The results by race/ethnicity and education show consistent and large disparities in the risk of cognitive impairment and mean age at first incidence of impairment. Table 2 shows the sub-population specific risks and mean age at first incidence, and Fig. 1 illustrates the disparities. For both women and men, lifetime risk of any cognitive impairment is lowest among Whites (women: 66%, men: 57%) and among those with an Associate degree or higher (women: 59%, men: 49%). These groups are the reference groups in Fig. 1, and the point estimates show how many percentage points higher the risk of any cognitive impairment is for other racial/ethnic and educational groups. Latinx and Blacks have 10-20 percentage points higher lifetime risk than Whites. Those with a high school/GED/some college education (henceforth, high school) have approximately 10 percentage point higher lifetime risk compared to the highest educated. The disparity is even greater for those with less than high school education who have 15-30 percentage points higher risk.

The same groups also have the oldest mean age at first incidence; therefore, Whites (women: age 75.0, men: age 71.3) and those with the highest education (women: age 79.0, men: age 76.3) act again as the reference groups. The racial/ethnic gradient is not quite as steep for men, where Latinos and Blacks experience the first impairment 3–6 years younger than Whites. Among women, however, the differences are 7–9 years. Those with a high school education experience the first impairment 5–6 years younger and those with less than high school education 13–14 years younger than their higher-educated counterparts.

Table 3 and Fig. 2 show expected years lived without impairment, with mild impairment, with dementia, and total life expectancy. Remaining life expectancy at age 50 is for women 32.6 years, of which they can expect to live 4.2 years with mild cognitive impairment and 3.2 years with dementia. Men have 27.6 years in total remaining life expectancy at age 50, of which 3.5 years are with mild cognitive

 Table 2

 Lifetime risk and age at first incidence of any impairment and dementia.

	Lifetime Risk (%) and [95% CI] of:					Age at first incidence and [95% CI] of:			
	Any	airment	Dem	entia	Any	airment	Dem	entia	
Men	61	[58,	24	[20,	70	[69,	79	[77,	
		65]		28]		71]		80]	
Education									
< High	76	[73,	35	[31,	63	[62,	74	[73,	
School		79]		40]		64]		75]	
High School/	62	[58,	22	[18,	70	[69,	79	[78,	
GED		65]		25]		71]		80]	
Associate,	49	[42,	20	[13,	76	[75,	82	[80,	
higher		54]		27]		78]		84]	
Race/Ethnicity									
White	57	[53,	22	[19,	71	[71,	79	[78,	
		60]		25]		72]		80]	
Latinx	77	[72,	36	[27,	69	[67,	78	[75,	
		84]		50]		70]		81]	
Black	72	[68,	28	[21,	64	[64,	76	[75,	
		76]		34]		66]		78]	
Women	71	[68,	37	[33,	73	[72,	83	[82,	
		74]		43]		74]		84]	
Education									
< High	80	[78,	42	[39,	65	[64,	78	[77,	
School		84]		47]		66]		79]	
High School/	71	[67,	36	[32,	74	[73,	84	[83,	
GED		74]		40]		75]		84]	
Associate,	59	[53,	32	[21,	79	[78,	86	[85,	
higher		64]		46]		81]		91]	
Race/Ethnicity									
White	66	[63,	33	[29,	75	[74,	83	[83,	
		69]		37]		76]		84]	
Latinx	82	[76,	48	[21,	69	[68,	84	[82,	
		861		721		71]		94]	
Black	83	[80,	46	[42,	66	[65,	79	[78,	
	50	851	.0	521	30	67]		80]	

impairment and 1.8 with dementia.

Fig. 3 shows the racial/ethnic and educational gradient for the number of years lived with any cognitive impairment. Whites (women: 5.9 years, men: 4.5 years) and those with an Associate degree or higher (women: 5.0 years, men: 3.3 years) are the reference group. Compared with these groups, Latinx and Black men have 4 more cognitively-impaired years than Whites; and Latinas and Black women 6–7 more cognitively-impaired years. Those with high school education have 2 more cognitively-impaired years, and those with less than high school education 6 more years.

#### Discussion

Using the high-quality Health and Retirement Study, we analyzed novel population summaries of cognitive impairment—lifetime risk and average age at which individuals first experience impairment, as well as number of years impaired. We take advantage of longitudinal, incidence-based approaches that are less prone to bias than prevalence-based approaches. Our findings demonstrate that the burden of cognitive impairment is very large and impacts individuals and populations well before advanced old ages and the extent of the disparities in the burden by gender, race/ethnicity, and educational attainment.

We first studied lifetime risk of any cognitive impairment or dementia, conditional on being non-impaired at age 50. Women carry a significant burden of both any impairment and dementia, having lifetime risk of dementia of 37% compared to 24% for men. This difference is partly attributable to women's longer life expectancies, which increase years of risk exposure. Lifetime risk of any impairment or dementia for Blacks, Latinx, and all those with lower education is significantly higher than for their White and higher-educated

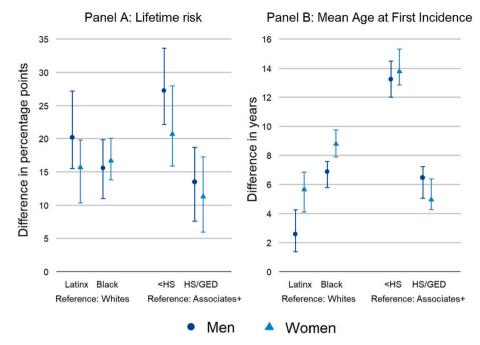


Fig. 1. Racial/ethnic and educational gradient in lifetime risk of any cognitive impairment (Panel A), mean age at first incidence of cognitive impairment (Panel B), and 95% confidence intervals.

**Table 3**Life expectancy with cognitive impairment no dementia (CIND), with dementia, without impairment, and total life expectancy.

	Life expectancy [95% CI] with:									
	CIND		Dementia	Dementia		No impairment		Total		
Men	3.5	[3.3, 3.9]	1.8	[1.4, 2.2]	22.3	[21.7, 23.2]	27.6	[26.9, 28.8]		
Education										
< High School	6.3	[5.8, 6.8]	3.7	[3.0, 4.3]	14.9	[14.0, 15.7]	24.9	[23.8, 26.0]		
High School/GED	3.6	[3.3, 3.9]	1.6	[1.2, 1.9]	22.7	[21.8, 23.4]	28.0	[26.9, 28.7]		
Associate, higher	2.1	[1.7, 2.4]	1.2	[0.6, 2.0]	27.6	[26.7, 28.9]	31.0	[29.7, 32.4]		
Race/Ethnicity										
White	3.0	[2.7, 3.3]	1.5	[1.2, 1.8]	23.4	[22.8, 24.3]	27.9	[27.1, 28.9]		
Latinx	5.5	[3.9, 6.5]	3.3	[0.6, 4.5]	20.5	[19.0, 22.5]	29.2	[26.2, 31.9]		
Black	5.9	[5.2, 6.6]	2.4	[1.7, 3.4]	17.1	[16.3, 18.3]	25.4	[24.3, 27.5]		
Women	4.2	[4.0, 4.7]	3.2	[2.5, 4]	25.2	[24.6, 26.3]	32.6	[31.7, 34.3]		
Education										
< High School	6.6	[6.1, 7.2]	4.7	[4.0, 5.4]	17.3	[16.5, 18.3]	28.5	[27.3, 30.2]		
High School/GED	4.0	[3.7, 4.4]	2.9	[2.6, 3.6]	26.2	[25.6, 27.0]	33.1	[32.4, 34.4]		
Associate, higher	2.7	[2.4, 3.7]	2.3	[0.8, 4.2]	30.5	[29.8, 32.5]	35.6	[34.2, 38.6]		
Race/Ethnicity										
White	3.3	[3.1, 3.7]	2.6	[2.2, 3.0]	27.1	[26.2, 27.7]	32.9	[32.0, 33.9]		
Latinx	7.6	[6.4, 13.2]	5.7	[0.7, 10.7]	23.1	[21.8, 26.5]	36.4	[32.1, 44.6]		
Black	6.6	[6.0, 7.2]	4.9	[4.2, 6]	19.4	[18.3, 20.1]	30.9	[29.4, 32.3]		

counterparts, despite Blacks and lower-educated individuals having shorter total life expectancy.

Lifetime risk estimates do not provide any information on when in the life-course cognitive impairment occurs or how long one is expected to live in an impaired state. The other two metrics we studied provided this important detail. The second metric, mean age at first impairment, is key to assessing how cognitive impairment impacts social and economic functioning. If individuals become impaired at an age when they are expected to be economically productive and independent, that has important consequences for labor force participation, as well as independent living. On average, women experience first impairment at age 73 years and dementia at age 83, and men at ages 70 and 79 years. Individuals with less than a high school degree had an expected onset of any impairment at age 65 or younger. Black men overall and men with less than high-school education fared the worst with a mean age at first impairment of 64 and 63 years, respectively.

The third metric, cognitive health expectancies, provides information about the burden of cognitive impairment and dementia over a lifecourse. We find that women have 7.4 years of cognitively-impaired life expectancy, of which 3.2 years are in dementia. For men, the respective numbers are lower, 5.3 and 1.8 years. Latinx and Blacks have 1.5 to two times more years in impairment than their White counterparts and spend a significantly longer share of their remaining life expectancy impaired. Higher education is associated with reduced number of years lived impaired, despite being associated also with higher life expectancy.

#### Interpretation

The goal of this study is to expand our understanding of the burden of cognitive impairment by estimating three different metrics for Black, Latinx, and White women and men of various educational levels. This

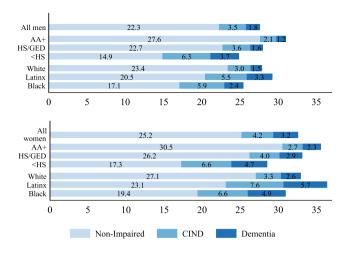
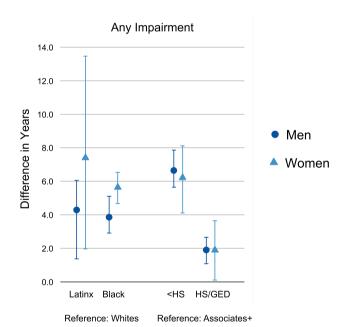


Fig. 2. Non-impaired, cognitive impairment no dementia (CIND), and dementia life expectancy at age 50 by gender, race/ethnicity, and education.



**Fig. 3.** Racial/ethnic and educational gradient in the expected number of years lived with any cognitive impairment and 95% confidence intervals.

contrasts with an approach that aims to control for mechanisms, in other words, estimating what racial/ethnic disparities would be if all else was equal, e.g., if there were no racial/ethnic disparities in educational attainment. We, thereby, paint a portrait of the burden of cognitive impairment as it exists in the U.S. for the contemporary age 50+ population.

Useful explanations for our findings of dramatic racial/ethnic disparities in cognitive impairment are likely to be multifaceted and require thoughtful analysis. For example, Blacks and Latinx are more likely to have disadvantaged early lives, attain lower-quality education even at equivalent educational level (Sisco et al., 2015), and accumulate stressors that may hasten aging, i.e., "weathering" (Das, 2013; Geronimus et al., 2010). More proximate factors may include health behaviors and disparities in healthcare access and treatment-seeking behavior (Williams, 2012). Studying mechanisms affecting cognitive health is an important area for future research, but understanding the burden of cognitive impairment in the population, as it is, is also

essential.

The connections between gender and dementia risk are also likely complicated. We document that women have a higher lifetime risk of cognitive impairment, and they spend more years with cognitive impairment than men, which is in line with other research, e.g., that two-thirds of those with Alzheimer's diagnoses are women (Plassman et al., 2007). On the other hand, they also experience the first incidence of cognitive impairment at a more advanced age than men and live more years not cognitively impaired than men. Thus, the higher lifetime risk and longer lifetime with impairment at least partially reflects longer life expectancy and not primarily higher age-standardized risk of impairment. Indeed, research suggests that age-specific differentials in prevalence may be small. For example, at ages 71 and above, women have only 5% higher age-specific prevalence than men (Plassman et al., 2007). In terms of mechanisms, women and men's risk profiles are likely to be quite different. For example, women in the current older-age population have lower educational attainment and worse physical and mental health, but may have denser, more supportive social networks, which may be protective (Fratiglioni, Wang, Ericsson, Maytan, & Winblad, 2000; Schafer & Vargas, 2016). More research is required to understand how these opposing forces drive gender disparities.

We find increasing education is strongly associated with deceasing risk of cognitive impairment for all subpopulations and for all three metrics considered. This is in line with a large body of research showing strong associations between educational attainment and later-life cognitive impairment (Crimmins et al., 2018; Farina et al., 2019; Reuser et al., 2011). Education may have protective effects via various mechanisms. The cognitive reserve hypothesis posits that education works through building a larger reserve capacity (structural and functional) (Jones et al., 2011; Meng & D'Arcy, 2012; Stern, 2012; Valenzuela & Sachdev, 2006). Thus, despite underlying neuropathology, those with higher education either delay dementia onset or never present as symptomatic prior to dying of other causes. Higher education may also increase the likelihood of engaging in occupations or post-retirement activities that are cognitively demanding, decreasing risk (Reed et al., 2011). And, directly or via social networks, education may shape behavioral profiles to be more protective against dementia (Pampel, Krueger, & Denney, 2010; Schafer & Vargas, 2016). Understanding how education affects cognitive function is an active and important line of research.

These racial/ethnic, gender, and educational disparities have important implications for the burden of cognitive impairment. The groups who face greater risk and longer expectancies in cognitive impairment – Blacks, Latinx, and those who are lower educated – are also those likely to have the fewest economic resources and the least access to quality healthcare. Regarding gender disparities, women appear to bear the greater burden both in terms of likelihood of providing care-partnering for men (as men have a younger mean age at onset) and in that women have higher lifetime risk and longer in impairment. Furthermore, women's longer life expectancies compared with men means they often face that increased risk whilst living alone and may require more years of social support.

#### Methodological considerations

We used incidence-based Markov chain multistate models. This has significant advantages over prevalence-based methods, which are biased if incidence or mortality are changing. It also makes it difficult to directly contrast our results on cognitively-impaired life expectancy with those using prevalence-based methods for calculating expectancies (Crimmins, Saito, Ki, & Kim, 2016, 2018; Garcia et al., 2017). Moreover, from prevalence-based estimates, one cannot estimate mean age at first impairment or lifetime risk or allow for recovery (important for estimates of CIND). Comparisons with the other incidence-based results (Farina et al., 2019; Fishman, 2017; Reuser et al., 2011) are possible but made challenging by both sample selection criteria (e.g., different age

ranges) and analytical focus (e.g., others do not estimate results by race/ethnicity or gender, and no other incidence-based studies consider CIND). Therefore, directly comparable estimates on lifetime risk of and expectancies in cognitive impairment do not exist in the literature, and we are not aware of any estimates of mean age at onset of cognitive impairment.

Reuser et al. (2011), however, estimated life expectancy with and without dementia by gender, race/ethnicity, and education. While results are not directly comparable, both studies find substantial educational and racial/ethnic disparities such that Whites and the higher educated spend fewer years cognitively impaired than Blacks, Latinx, and the lower educated. Several factors are likely to explain differences in estimates, including their findings of a wider racial/ethnic disparity. Plausibly most influential, Reuser et al. (2011) include measures of crystalized cognition, which is more associated with education and other cultural factors than fluid cognition (Ghisletta et al., 2012). Blacks and Hispanics (especially foreign-born Hispanics) are likely to have been exposed to different sociocultural contexts, even at equivalent levels of education. As such, lower crystallized cognition scores may reflect sociocultural differences, not neurophysiological decline.

In terms of risk, our findings are close to those of Fishman (2017), who estimate that the lifetime risk of dementia at age 70 for a U.S. 1920 birth cohort was 27% (male) and 35% (female), compared with our 24% for men and 37% for women. It is possible, however, that the proximity of our results is a function of several forces pulling to different directions and canceling each other. We start our calculations at age 50, and use more recent cohorts with higher life expectancy, which increases years at risk. Analyzing more recent cohorts may also mean that our cohorts have a different, perhaps lower age-standardized incidence, although the literature is not consistent on what these time trends are (Langa et al., 2017; Larson & Langa, 2017; Wu et al., 2017). More important, however, our analysis allows for recovery, which is reflective of clinical research showing vacillation in cognitive function scores is common (Petersen et al., 2014; Roberts & Knopman, 2013). Thus, we take a nuanced approached to accounting for random measurement error that would bias the lifetime risk upwards, if neglected. As explained above, instead of treating any cognition score below a certain threshold as indicative of impairment, independently of what the scores were before and after, we require two consecutive states of cognitive impairment before we classify a person as impaired. One would expect that this redefinition lowers the estimated lifetime risk of cognitive impairment; increases the mean age at first impairment; and leaves estimates of years impaired roughly unchanged. This is exactly what we observe when comparing the above estimates to the ones that use unaltered life history data (results available upon request). We conclude that our more restrictive incidence definitions reduce the noise that is present in the data and provide estimates that are less biased than previous estimates.

With regard to our study of racial/ethnic disparities, although "Hispanic" or "Latinx" homogenizes a non-homogenous population of native-born U.S. citizens and immigrants from multiple countries, the purpose of this analysis—to describe three metrics related to cognitive health—requires rather large sample sizes. This oversimplification is slightly less problematic because we do not attempt to identify mechanisms. We present each metric for those who identify as Hispanic or Latinx in the U.S. Garcia et al. (2017) found foreign-born Hispanics spend a greater share of their life expectancy at age 50 cognitively impaired than their native-born counterparts. The nativity question could be further explored using the incidence-based metrics developed in this study.

#### Conclusion

This paper paints a multi-dimensional picture of cognitive health, presenting the first comprehensive analysis of lifetime risk, mean age at first impairment, and years impaired for the U.S. population age 50 and older. We also include analysis of mild cognitive impairment, which

constitutes an important, but understudied, category. Our results show that approximately two out of three Americans experience cognitive impairment, at an average age of approximately 70 years. Women live over 7 years cognitively impaired, men over 5. The educational and racial/ethnic gradients are even larger than the gender differentials and highlight the uneven burden of cognitive impairment. A critical finding is that despite the shorter lives of disadvantaged subgroups (Black and/or lower educated), they experienced a younger age of onset and also spent more years cognitively impaired than their White, higher-educated counterparts who experienced a delayed onset. Thus, the early onset does not imply a quick death after onset. A corollary is that for the most advantaged groups (i.e., White and/or higher educated), cognitive impairment is both delayed and compressed toward the very end of life. Further research is required to identify the mechanisms driving these disparities in cognitive impairment.

#### Ethical approval

This study uses only secondary data analysis of the publicly available data in the Health and Retirement Study, a longitudinal project sponsored by the National Institute on Aging (NIA U01AG009740) and the Social Security Administration.

Ethical approval for the Health and Retirement Study was obtained from the University of Michigan Institutional Review Board.

#### CRediT authorship contribution statement

Jo Mhairi Hale: Conceptualization, Writing - original draft, Visualization. Daniel C. Schneider: Methodology, Validation, Formal analysis, Visualization. Neil K. Mehta: Conceptualization, Writing - review & editing. Mikko Myrskylä: Conceptualization, Writing - original draft, Visualization.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi. org/10.1016/j.ssmph.2020.100577.

### Appendix I. Calculation of Outcome Measures Based on Simulated Life Histories

The outcome measure calculations of this paper are somewhat non-standard, as they are based on simulated life histories. For an exposition of standard Markov chain multistate procedures, see Mehta and Myrskylä (2017) and Dudel (2018). Here we proceed as follows: Based on our multinomial logit model, we estimate transition probabilities for each cognition state combination, and two-year age classes 50, 52, ..., 110. Using these estimates and estimated initial state proportions, we generate 10,000 completed life histories. Underlying the entire procedure is the Markov assumption, which dictates that transition probabilities exclusively depend on the current state, and not on the history of past states.

The simulation is motivated by the problem of misclassification of states. As laid out in the main text, measurement error is likely to be present in the data and is likely to affect some of our outcome measures. To address this problem, we introduce more restrictive CIND and dementia onset definitions. We define dementia onset as the first occurrence of two contiguous dementia observations. We treat isolated dementia observations before that point as being CIND observations, but do not allow for recovery of any kind after dementia onset, i.e. we treat all observations after dementia onset as dementia observations, irrespective of their value that is recorded in the original simulated trajectory. We define the occurrence of the first CIND episode in a similar fashion, namely as being marked by two contiguous CIND observations. We ignore all CIND observations before that point, but, contrary to the dementia onset definition, do allow for recovery to no-impairment

#### afterwards.

These simple definitions entail a number of decisions for special cases: a) a single CIND or dementia observation immediately before death is counted as first CIND episode or dementia onset (if this has not occurred earlier). b) An analogous rule to a) holds for a single CIND observation right before dementia onset. c) An isolated succession of a CIND and dementia observation, in whichever order, is counted as the first CIND episode (if such an episode has not occurred earlier).

The above incidence definitions cannot be applied to observed life histories that are censored, since it is unclear how isolated CIND or dementia observations at the end of a censored history should be treated. This is a severe problem, since many subject trajectories in the data are censored at the last wave (year 2014). Therefore, we utilize completed, simulated life histories for the calculation of our outcome measures, using our more plausible definitions of dementia onset and first CIND episode.

All outcome measures are to a large extent just counts and averages from the simulated data: i) Lifetime risk simply counts the number of life histories that contain impairment episodes and divides by the number of simulated trajectories ii) Mean age at first incidence calculations determine, for each life history, the age at which impairment occurs, and then take the average. The HRS interview spacing dictates that model transitions take place every two years. To be consistent with the notion of mid-period transition timing (Dudel, 2018), one year is deducted from the raw average. iii) State occupancy times are calculated as averages of state counts across all simulated life histories. The mid-period transition assumption enters by weighing the first simulated state at age 50 with one year only instead of two.

We measure sample variation by applying a bootstrap procedure. A single replication of the bootstrap is based on the resampling of subjects and subsequently covers the whole analytic chain, consisting of multinomial regression, transition probability prediction, Markov-based life history simulation, and outcome measure calculation.

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## <u>Update</u>

## **SSM - Population Health**

Volume 12, Issue, December 2020, Page

DOI: https://doi.org/10.1016/j.ssmph.2020.100715

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#### **Erratum**



# Erratum regarding missing Declaration of Competing Interest statements in previously published articles

Erratum regarding missing Declaration of Competing Interest statements in previously published articles.

Declaration of Competing Interest statements were not included in the published version of the following articles that appeared in previous issues of SSM - Population Health.

The appropriate Declaration/Competing Interest statements, provided by the Authors, are included below.

- Were there long-term economic effects of exposure to polio vaccination? An analysis of migrants to Sweden 1946–2003 (SSM Population Health, 2020; 11C),https://doi.org/10.1016/j.ssmph.2020.100589.The authors were contacted after publication to request a Declaration of Interest statement.
- Communicating the benefits of population health interventions:
   The health effects can be on par with those of medication (SSM Population Health, 2018; 6C: 54–62), https://doi.org/10.1016/j.ssmph.2018.06.002. The authors were contacted after publication to request a Declaration of Interest statement.
- 3. A cohort longitudinal study of individual level social capital and depressive symptoms in the Wisconsin Longitudinal Study (SSM Population Health,2020; 10C),https://doi.org/10.1016/j.ssmph .2020.100544.The authors were contacted after publication to request a Declaration of Interest statement.
- 4. The impact of pharmaceutical innovation on the burden of disease in Canada, 2000–2016 (SSM Population Health, 2019; 8C) <a href="https://doi.org/10.1016/j.ssmph.2019.100457">https://doi.org/10.1016/j.ssmph.2019.100457</a> The authors were contacted after publication to request a Declaration of Interest statement.
- 5. Does sleep grow on trees? A longitudinal study to investigate potential prevention of insufficient sleep with different types of urban green space (SSM Population Health, 2019; 10C), https://doi.org/10.1016/j.ssmph.2019.100497.The authors were contacted after publication to request a Declaration of Interest statement.
- Advancing the study of health inequality: Fundamental causes as systems of exposure.(SSM - Population Health, 2020; 10C) http s://doi.org/10.1016/j.ssmph.2020.100555. The authors were

- contacted after publication to request a Declaration of Interest statement.
- Cohabitation and mental health: Is psychotropic medication use more common in cohabitation than marriage?. (SSM - Population Health, 2018; 4C:244–253. https://doi.org/10.1016/j.ssmph.20 18.01.001. The authors were contacted after publication to request a Declaration of Interest statement.
- 8. "Toxic" schools? How school exposures during adolescence influence trajectories of health through young adulthood (SSM Population Health, 2020; 11C),https://doi.org/10.1016/j.ssmph.2020.100623.The authors were contacted after publication to request a Declaration of Interest statement.
- Cognitive impairment in the U.S.: Lifetime risk, age at onset, and years impaired. (SSM - Population Health, 2020; 11C) https:// doi.org/10.1016/j.ssmph.2020.100577. The authors were contacted after publication to request a Declaration of Interest statement.
- Paid sex among men in sub-Saharan Africa: Analysis of the demographic and health survey (SSM Population Health, 2019; 11C).https://doi.org/10.1016/j.ssmph.2019.100459.The authors were contacted after publication to request a Declaration of Interest statement.
- 11. Health and economic scarcity: Measuring scarcity through consumption, income and home ownership indicators in Norway. (SSM Population Health, 2020; 11C). https://doi.org/10.1016/j.ssmph.2020.100582. The authors were contacted after publication to request a Declaration of Interest statement.
- Education and mental health: Do psychosocial resources matter? (SSM - Population Health, 2019; 7C) https://doi.org/10.1016/j.ssmph.2019.100392
   The authors were contacted after publication to request a Declaration of Interest statement.
- 13. An intersectional approach to understandings of mental health inequalities among men with disability (SSM Population Health, 2019; 9C) <a href="https://doi.org/10.1016/j.ssmph.2019.100464">https://doi.org/10.1016/j.ssmph.2019.100464</a>. The authors were contacted after publication to request a Declaration of Interest statement.
- 14. Disparities in functional disability among Arab Americans by nativity, immigrant arrival cohort, and country of birth (SSM -

 $DOIs of original article: \ https://doi.org/10.1016/j.ssmph.2019.100459, \ https://doi.org/10.1016/j.ssmph.2020.100589, \ https://doi.org/10.1016/j.ssmph.2020.100589, \ https://doi.org/10.1016/j.ssmph.2020.100589, \ https://doi.org/10.1016/j.ssmph.2020.100589, \ https://doi.org/10.1016/j.ssmph.2020.100589, \ https://doi.org/10.1016/j.ssmph.2018.100325, \ https://doi.org/10.1016/j.ssmph.2018.01.001, \ https://doi.org/10.1016/j.ssmph.2019.100498, \ https://doi.org/10.1016/j.ssmph.2019.100498, \ https://doi.org/10.1016/j.ssmph.2019.100497, \ https://doi.org/10.1016/j.ssmph.2019.100497, \ https://doi.org/10.1016/j.ssmph.2019.100497, \ https://doi.org/10.1016/j.ssmph.2019.100497, \ https://doi.org/10.1016/j.ssmph.2020.100555.$ 

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