Investigating life-course pathways to sex differences in later-life cognitive health among older adults in rural South Africa

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Across sub-Saharan Africa (SSA), research on cognitive impairments and dementias has illuminated an emerging trend: the older generations of women are currently experiencing a far higher burden of mild cognitive impairment (MCI) and dementia than men (Guerchet et al., 2014, 2013; Payne, Kohler, Bandawe, Lawler, & Kohler, 2017; Pilleron et al., 2015). These findings are at odds with research from higher-income contexts, where a consistent body of work has found a persistent female advantage in episodic memory and other facets of cognitive health in older ages, and similar rates of cognitive aging, impairment, and dementia diagnosis when compared to men. This trend portends a potentially large burden of dementia emerging in a region that is largely lacking the infrastructural supports to care for it. Potentially worse, these findings may be an early indicator that there will be a large population of old-age dependents in a context that is still being ravaged by a high burden of HIV across younger age groups. As such, the causes of the disproportionately high burden of poor cognitive health among older women in this region warrant investigation.

An increasing body of research has investigated risk factors for dementia, with researchers highlighting a number of key risk factors including, for example, age, education, and cardiovascular disease. To date, however, relatively little is known about risk factors for dementia outside of high-income contexts, especially in low-income regions such as sub-Saharan Africa (SSA), where clinical diagnoses of the disease are rare due to inadequate health systems. There are also reasons to believe that the existing evidence about risk factors for dementia from high-income contexts, and the policy and health recommendations countries derived from this evidence, may not be directly applicable to older adults in SSA. Older individuals in SSA have had widely divergent life histories from those in high-income settings, including increased exposure to chronic undernutrition and infectious diseases, economic shocks, severe poverty, and high levels of uncertainty, all of which have been linked to reduced cognitive abilities and accelerated cognitive aging (Haan, Al-Hazzouri, & Aiello, 2011; Lynch, Kaplan, & Shema, 1997; Madsen, 2016).

In South Africa in particular, little research has examined gender differences in cognitive health of the older population. Early data from “Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa” (HAALSI) has demonstrated that women over 40 living in a rural region of the country have lower cognitive function scores and lower literacy, on average, than men of the same age range (Humphreys et al., 2017). South Africa is unique within the SSA region due to the traumatic history of Apartheid from 1948 to 1994, whereby the black population was subject to forced racial segregation that included poor access to and quality of schooling, limited and hazardous employment, and day-to-day discrimination. In particular, women had lower schooling completion rates than men and were not engaged in formal employment to the same degree as men during Apartheid. However, these factors have not been investigated as potential causes for gender-based disparities in later-life cognitive health among older South African adults.

In a large, population-based study of older men and women living in rural South Africa, we aimed to investigate the drivers of sex-based differentials in later-life cognitive functioning. We find that that controlling for formal schooling greatly diminishes the sex gap in cognitive well-being among individuals who have received some schooling. However, a sizable sex gap persists among older adults in the HAALSI sample who received no formal schooling. We explore a number of potential factors that could explain why not receiving schooling would be worse for women than men in terms of cognitive outcomes. Our results suggest that differential sex patterns of widowhood in later life, childhood economic conditions, and women’s more rapid decline in physical functioning with age, are all strongly related to the female-male gap in cognition in later life.

Data and Measures

Data

The HAALSI study is a population-based survey that aims to examine and characterize a population of older men and women in rural South Africa with respect to health, well-being, and physical and cognitive function, as well as the social, environmental, and biological factors affecting these domains.

Setting

The study was conducted in the Agincourt sub-district in the Mpumalanga Province, South Africa, where the MRC/Wits Rural Public Health and Health Transitions Research Unit has been running the Agincourt Health and Demographic Surveillance System site since 1992 (Kahn et al., 2012). In 2015 the study area covered around 450sq km including 32 villages with a population of approximately 110,000 people. The primary health care system consists of six clinics and two health centers. Three hospitals covering the district are 45 to 60 km from the study site. The social situation of this community has improved in the past 20 years but there are still huge gaps in availability of electricity, water and tarred road coverage. Unemployment rates are high, putting stress on families and leading to high rates of work migration and reliance on remittances as an important source of income.

Sampling

Participants were sampled from the existing framework of the Agincourt Health and Socio-Demographic Surveillance System (AHDSS) site in Mpumalanga province (Kahn et al., 2012). Individuals 40 years and older as of July 1, 2014 and permanently living in the study site during the 12 months previous to 2013 census round were eligible for this study. Using the full 2013 Census data, we identified a sampling frame of 8,974 women and 3,901 men aged 40 and older who met the residence criteria. Our target sample size was approximately 5,000 completed interviews. Assuming an 80% response rate, we selected a total of 6,281 women and men for the main household study.

Data Collection

All sampled individuals were visited at home from November 2014 to November 2015. Trained, local fieldworkers collected survey data electronically using Computer Assisted Personal Interviews (CAPI). Surveys were conducted in the local Shangaan language, with instruments translated from English and back-translated to ensure reliability. Out of the 6,281 selected for the study, 391 had moved outside of the study site or were deceased. Out of the remaining 5,890 eligible individuals, 5,059 (86%) participated in the baseline survey. Additional waves of longitudinal follow up of the cohort are planned every 3 years. The data and questionnaires for HAALSI are publicly available at http://haalsi.org/.

Ethics and Grant Information

Ethical approval for HAALSI was obtained from the University of the Witwatersrand Human Research Ethics Committee (#M141159), the Harvard T.H. Chan School of Public Health Office of Human Research Administration (#13–1608), and the Mpumalanga Provincial Research and Ethics Committee.

Measures

Measures of cognition

Cognitive function was assessed during the in-person interview using a brief screening instrument for dementia adapted from validated measures used in the US Health and Retirement Study. The screening instrument assessed time orientation (ability to state the correct day, month, year, and South African President; 4 points total), immediate and delayed recall of 10 common nouns read out loud (1 point for each word; 20 points total), forward count (the ability to count correctly from 1 to 20; 1 point), and number skip pattern (the ability to complete the final digit of the number skip pattern beginning with 2, 4, 6, if the respondent was able to correctly count from 1 to 20; 1 point). The total score was 26 points. The outcome variable was a z-standardized latent cognitive function derived from a confirmatory factor analysis of the above cognitive items. This latent cognitive score has several methodological advantages over a simple summary score: it allows non-linear relationships between each individual cognitive test and overall cognitive function, it utilizes only common covariation between the cognitive tests to reduce measurement error that may be present in any one test, it estimates the cognitive outcome variable using all available test data even if some items are missing, and it does not assume equal difficulty or contribution of each cognitive test to overall cognitive function. The confirmatory factor model used to derive the z-standardized latent cognitive score was of good fit to the data, with RMSEA = 0.032 (95% CI: 0.025, 0.039), CFI = 0.998, and TLI = 0.997. Acceptable thresholds for these fit statistics are RMSEA<0.05, CFI>0.95, and TLI>0.95 (Hu & Bentler, 1999). Cognitive impairment was defined as scoring ≤1.5 standard deviations below the mean composite score, or requiring a proxy interview with “fair” or “poor” proxy-reported memory (Kobayashi et al., n.d.).

Sociodemographic indicators

Educational attainment was grouped into four categories: no formal schooling, some primary education (1–7 completed years), some secondary education (8–11 completed years), and completed secondary education or more (12+ years). The HAALSI household asset index was calculated following DHS methodology (Rutstein & Johnson, 2004) that combines information on household durable goods and infrastructures through principal component analysis, we utilize quantiles of household asset index as a measure of SES. Other demographic indicators included: age and 5-year age groups (40–85+), sex (men and women), marital status (never married, married/cohabiting, divorced/separated, widowed), total household size, and whether the individual had ever worked outside of the home.

Childhood conditions

The four childhood conditions of interest were: country of birth (South Africa; Mozambique or other), father's education (any formal schooling; no formal schooling), father's occupation during childhood according to the International Standard Classification of Occupations (ISCO) 2008 (skilled; unskilled; don't know; other), and self-rated health in childhood (excellent; very good; good; fair; poor). We retain the 'don't know' category in the father's occupation variable, as this response was associated with significantly worse cognitive function, and it may indicate not having a father present either at all, or for frequent enough periods for the respondent to know what his or her father did for work.

Cardiovascular health

For both hypertension, we applied the set of criteria listed in the South African and US guidelines (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001; Klug et al., 2013; National High Blood Pressure Education Program, 2004; Seedat, Rayner, & Veriava, 2014). One will be considered hypertensive if systolic blood pressure is greater than or equal to 140 mmHg or diastolic blood pressure is 90 mmHg or higher, or if use of anti-hypertensive medication is reported at the time of interview. Diabetes was diagnosed using the guideline published by the American Diabetes Association (American Diabetes Association, 2015): fasting glucose (defined as >8 hours) >7 mmol/L (126 mg/dL) or non-fasting glucose level >11.0 mmol/L (200 mg/dL), reported ever being diagnosed with diabetes, or if use of medication is reported at the time of interview. Height and weight were measured by interviewers, and body mass index (BMI) calculated from these measures. Respondents also reported whether they had previously received a physician diagnosis of a stroke.

Mental health

Symptoms of depression were screened using the Center for Epidemiological Studies – Depression Scale (CES-D) 8-item questionnaire. We used a cutoff of three or more symptoms as a diagnosis of depression (Steffick, 2000). PTSD was diagnosed using a seven-symptom screening scale developed by (Breslau, Peterson, Kessler, & Schultz, 1999), and individuals who score four or more on this scale were classified as having PTSD.

Results

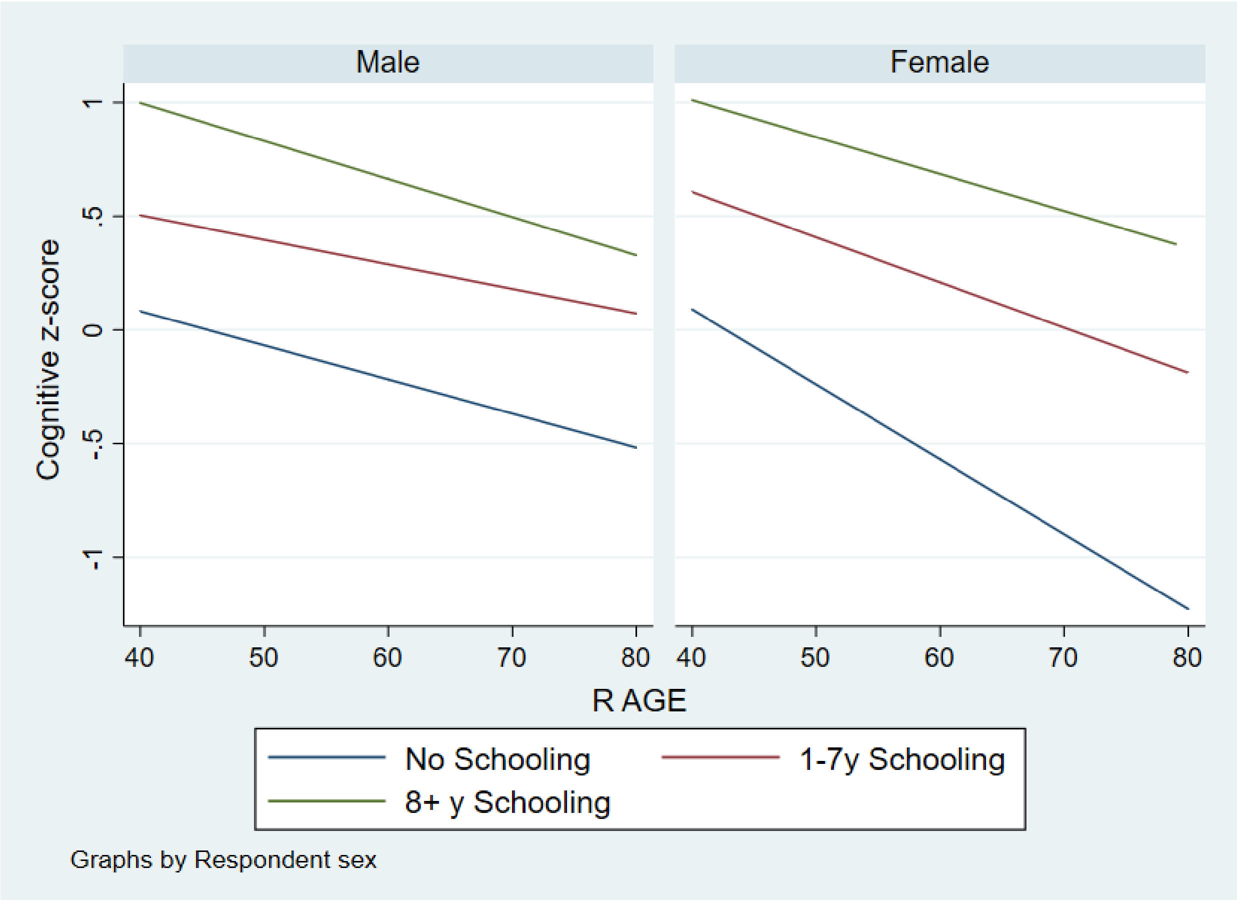
Summary statistics

Table 1 presents the baseline characteristics of the sample (by males, females, and the total sample), as well as results from a baseline linear regression on the cognitive z-score measure to establish a general pattern of linear relationships. We see that the mean age of the sample is just below 62 years, and that there are some differences in demographics by sex—women are somewhat less likely to have received schooling, less likely to be currently married, much less likely to have worked outside the home, have higher BMIs, and are slightly more likely to report higher rates of both depressive and PTSD symptoms. In our baseline linear regression, we see that women on average have lower cognitive z-scores, and that cognitive score decreases with increasing age. Schooling is highly related to cognitive z-score—on average, individuals with 8 or more years of schooling score nearly .9 standard deviations higher than those with no formal schooling. Higher household wealth, higher grip strength and gait speed, better self-rated health and being currently married are all associated with higher cognitive scores, while Mozambican origin is associated with lower scores.

Exploring the gender gap in functioning by schooling

Though these baseline associations are interesting, it is very likely that they mask several important interactions in the data. In particular, previous work in the HAALSI sample (Kobayashi et al., n.d.) finds that the sex gap in cognitive well-being disappears for those who have received some formal schooling once a three-way multiplicative interaction between age, sex, and education is included. As seen in Figure 1, the level of cognitive z-score, and the negative slope of cognitive change with increasing age, was similar between men and women for those who received some formal schooling. Indeed, with just these simple controls, the differences between these groups become non-significant at $p<0.05$. However, women with no formal education scored considerably worse, and had a much steeper age-gradient in cognitive change over increasing age.

Figure 1: Age gradients in Cognitive z-score, by sex and schooling attainment



Exploration of factors associated with the age and gender patterning of cognitive health

In the above sections, we have demonstrated that the gender gap in cognitive well-being among older adults in the HAALSI sample exists almost completely among those who received no schooling. Receiving any level of education appears to diminish or eliminate this gap in cognitive well-being. But this finding raises further questions--why might not receiving schooling be worse for women than men in terms of cognitive outcomes? What gendered mechanisms might mediate the education-cognition relationship in SSA? Does controlling for any of these reduce the age-gradient and male-female gap in cognition (as compared to the baseline model)?

In this section, we explore a number of potential relationships, seeking to gain insight into the factors that may explain some of the gender and age gaps in cognition among those with no formal schooling. Our analyses in this section are exploratory, seeking to gain a preliminary insight into how differential exposures to life-course and health factors may influence these gender gaps in cognition among those with no formal schooling. As such, our sample in the below analyses is limited to only those who received no formal schooling—45% of our total sample, comprising 916 men and 1296 women.

We explore five different broad sources of variation—sociodemographic and family sources, early-life conditions, cardiovascular conditions, mental health factors, and physical health factors. Our analyses take the form of non-nested models, testing how different sources of variation associate with cognitive health, and how their inclusion changes the female-male gap and age gradient in cognitive health. Our baseline model includes age, age^2, a female dummy, and an age*female interaction. Due to the number of interactions in our model, raw coefficients are somewhat difficult to interpret. As such, our discussion of results will center the average marginal effects of age and gender on cognitive health, and how the age gradient and female-male gap changes in response to the inclusion of different factors from our five hypothesized sources of variation.

Sociodemographic characteristics

Prior research has found that cognitive well-being in later life is tightly linked with sociodemographic characteristics, including partnership status, household composition, wealth, and occupational history (Cacioppo & Hawkley, 2009; Glymour & Manly, 2008; Haslam, Cruwys, & Haslam, 2014; Payne et al., 2017). In South Africa, we hypothesize that these characteristics may have an outsized effect, particularly among those with no formal schooling, as these factors may associate with a more active and enriching social life, potentially reducing the adverse effects of having no formal schooling. Table 2 presents results investigating the role of sociodemographic characteristics in explaining the gender gap in cognition in the HAALSI sample, as well as the age-gradient in cognitive health. The first panel of Table 2 presents means of each sociodemographic factor by age groups, as well as the average female-male difference in the factor. The second panel shows the average marginal effect of a 1-unit change in the factor on cognitive z-score, and the third panel provides the percent change in the age-gradient and female-male difference after controlling for the factor. We see that the factor with the largest influence is current marital status—women in the HAALSI sample are substantially less likely to be currently married than men, and married individuals on average have cognitive z-scores that are 0.1 standard deviations higher than unmarried individuals. Controlling for differences by marital status reduces the female-male difference in cognitive scores by over 30%, though the age-gradient remains unchanged. In the Agincourt region, remarriage rates among widowed women are low, and male spouses tend to be older. Controlling for household wealth actually increases the gender gap and age gradient slightly, while controlling for working outside the home marginally reduces the female-male difference.

Childhood conditions

Early-life conditions are well-known to have later life effects in almost all domains of health, including cognitive functioning (Kobayashi et al., 2017). We explore the associations between four measures of early-life conditions and later-life cognitive health, in order to see whether any of these factors helps explain our observed gender differences and age gradient in cognition. The first panel of Table 3 presents means of each childhood factor by age groups, as well as the average female-male difference in the factor. The second panel shows the average marginal effect of a 1-unit change in the factor on cognitive z-score, and the third panel provides the percent change in the age-gradient and female-male difference after controlling for the factor. We see that overall, early-life factors have relatively little association with the age gradient and female-male differences among those without formal schooling. Including dummies for Mozambican origin and father's education results in little change in these gradients, though controlling for father's type of employment (whether a high-skill or low-skilled occupation) does reduce the female-male difference by over 18%. Self-rated health in childhood is significantly associated with cognitive z-score, but does little to explain the age gradient or gender gap in cognition in the HAALSI sample.

Cardiovascular health

Cardiovascular conditions have well-established relationships with cognitive functioning in later life. Long-term exposure to hypertension is associated with more rapid cognitive decline (Breteler, Claus, Grobbee, & Hofman, 1994; Lithell et al., 2003; Skoog et al., 2005), and a substantial portion of cases of incident dementia are known to have cerebrovascular origins. More directly, hypertension substantial raises the incidence of strokes, which can have substantial repercussions for cognitive functioning. In addition, poor control of diabetes mellitus can lead to neurological and vascular decline. Though increased BMI is known to be a risk factor for a variety of cardiovascular and cardiometabolic conditions, prior evidence directly linking elevated BMI to cognitive health has found mixed results, with some studies suggesting that high BMI may be somewhat protective against cognitive decline (Atkinson et al., 2005) . Table 4 displays the associations between four markers of cardiovascular and cardiometabolic health—a binary measure of hypertension, continuous body mass index, a binary measure of diabetes mellitus, and a binary measure of prior doctor diagnosis of stroke. We see that BMI, diabetes, and history of stroke are all associated with the cognitive z-score measure, and that a substantial female-male difference exists in rates of hypertension, BMI, and rates of diabetes. However, only controlling for BMI makes a difference in the female-male difference in cognition, and controlling for BMI actually increases the cognition gap between unschooled men and women.

Physical health

Prior research in SSA has found a strong relationship between late-life cognitive functioning and markers of physical health (Payne et al., 2017). Table 5 investigates whether differences in physical health, as measured through ADL limitations, grip strength, gait speed, and self-rated health, can explain the sex-gap in cognitive outcomes in the HAALSI population. We find that all of the markers of physical health are strongly associated with cognition—ADL disabled individuals, on average, score almost .3 standard deviations lower than non-disabled individuals, and higher grip strength, faster gait speed, and better self-rated health are all highly associated with improved cognitive functioning. We also find evidence that this decline in physical health with age is strongly associated with both the age-gradient and sex-gap in cognitive health. Controlling for grip strength reduces the age-gradient in cognition by nearly a third, and reduces the sex-gap by over 12%. Similarly, controlling for gait speed reduces the female-male difference by 23%, and reduces the age gradient by nearly 15%. Self-rated health has somewhat smaller effects, reducing the age-gradient by 11.5% and the female-male difference by 8%.

Mental health

Mental health is known to highly associate with cognitive functioning in high-income contexts (Rock, Roiser, Riedel, & Blackwell, 2014; Wang & Blazer, 2015), and evidence also suggests that anxiety and depression associate strongly with cognitive functioning in SSA (Kohler, Payne, Bandawe, & Kohler, 2017; Payne et al., 2017). In Table 6 we find a large female-male difference in measures of both depression (measured via the CESD score) and post-traumatic stress disorder (measured via the short PTSD scale), and find that both of these factors are strongly associated with the cognitive z-score. However, introducing these factors into the baseline regression has minimal effects on the age-gradient in cognitive z-scores, and only a small effect on the female-male difference. Controlling for CESD score reduces the sex-difference by slightly over 4%, and controlling for PTSD score reduces it by 8%.

Discussion

In a large, population-based study of older men and women living in rural South Africa, we aimed to investigate the drivers of sex-based differentials in later-life cognitive functioning. We find that that controlling for formal schooling greatly diminishes the sex gap in cognitive well-being among individuals who have received some schooling. However, a sizable sex gap persists among older adults in the HAALSI sample who received no formal schooling. We explored a number of potential factors that could explain why not receiving schooling would be worse for women than men in terms of cognitive outcomes. Our results suggest that differential sex patterns of widowhood in later life, childhood economic conditions, and women's more rapid decline in physical functioning with age, are all strongly related to the female-male gap in cognition in later life.

Our exploratory analysis centered on attempting to discern a potential set of factors that could explain why women lag behind men in late-life cognition in SSA. As such, our analyses are not causal in nature, but rather seek as an initial investigation to find relationships that warrant further study. With the second round of HAALSI data being collected in late 2018, these analyses will be a useful baseline for identifying relationships to explore using longitudinal data.

Table 1: Baseline characteristics and linear associations with cognitive z-score, HAALSI 2015 sample

	Means			
	Male	**Female**	**All**	**Linear assoc w/Cognitive z-score**
Obs	2345	2714	5059	
Age (continuous)	61.7	61.7	61.7	--
	(12.8)	(13.3)	(13.1)	
Female	--	--	0.54	-0.24**
Age group				
40-49	0.18	0.18	0.18	ref
50-59	0.27	0.29	0.28	-0.12**
60-69	0.27	0.24	0.26	-0.27**
70-79	0.19	0.16	0.17	-0.45**
80+	0.091	0.12	0.11	-0.61**
Level of schooling				
No formal schooling	0.41	0.5	0.46	ref
1-7y schooling	0.36	0.33	0.34	0.55**
8+ y schooling	0.23	0.17	0.2	0.89**
Born in Mozambique	0.29	0.31	0.3	-0.10**
Currently married	0.68	0.36	0.51	0.095**
Household size	5.18	5.46	5.33	-0.0039
	(3.4)	(3.3)	(3.3)	
Wealth asset index quintile				
First (lowest)	0.21	0.2	0.21	ref
Second	0.19	0.2	0.2	0.057
Third	0.19	0.2	0.2	0.13**
Fourth	0.19	0.2	0.2	0.11**
Fifth (highest)	0.21	0.2	0.2	0.22**
Never worked outside home	0.11	0.52	0.34	-0.085**
Father had any schooling	0.13	0.15	0.14	-0.04
Self-rated child health				
Very bad	0.065	0.063	0.064	ref
Bad	0.067	0.051	0.059	0.089
Fair	0.19	0.18	0.18	0.089
Good/very good	0.68	0.71	0.69	0.26**
ADL disabled	0.09	0.091	0.09	-0.086
Grip strength (standardized by sex)	0	0	0	0.092**
	(1.0)	(1.0)	(1.0)	
Gait speed (M/s)	0.71	0.67	0.68	0.22**
	(0.3)	(0.3)	(0.3)	
Self-rated current health				
Very bad	0.018	0.022	0.02	ref
Bad	0.15	0.19	0.17	0.28*
Fair	0.13	0.13	0.13	0.27
Good	0.48	0.47	0.48	0.22
Very good	0.22	0.19	0.2	0.50**
CESD score	1.61	1.8	1.72	-0.018
	(1.4)	(1.5)	(1.4)	

PTSD score	0.43	0.6	0.52	-0.0031
	(1.2)	(1.4)	(1.3)	
Hypertensive	0.59	0.68	0.63	0.0026
BMI	24.9	29.2	27.2	0.016**
	(5.4)	(6.9)	(6.6)	
Diabetic	0.11	0.13	0.12	-0.056
Prior stroke	0.027	0.031	0.029	-0.067

Table 2: Sociodemographics

	Baseline model +			
	Currently married	HH Size	HH wealth	Never worked outside home
Mean, by age group, and female-male difference (age adjusted)				
Age group				
40-49	0.57	5.62	2.65	0.44
50-59	0.52	5.64	2.97	0.32
60-69	0.58	5.34	3.50	0.27
70-79	0.48	5.08	3.38	0.24
80+	0.37	4.47	3.14	0.18
Female-male difference	-0.27**	0.50**	0.19**	0.38**
AME of 1 unit change on cog Z score[a]	0.10**	0.0016	0.052**	-0.035
	(0.039)	(0.0052)	(0.014)	(0.046)
Change in age-gradient and female-male difference after controlling for factor (%)[b]				
Age gradient	-2.4%	-0.2%	10.3%	6.3%
Female-male difference	-31.7%	1.0%	11.5%	-11.6%

Notes: AME: average marginal effect. Currently married: =1 if currently married, =0 if currently unmarried (divorced, widowed, never married). HH size= # of persons in household. HH wealth: quintile of HH asset index (1=lowest, 5=highest). Ever worked outside home: =1 if ever worked outside home, =0 if never worked outside home.

[a]Average marginal effect of a one-unit change in each sociodemographic factor obtained from linear regressions of cognitive z-score on the respective factor, age, age*age, female, and age*female.

[b]Change in the age gradient and female-male difference in cognitive z-score if the sociodemographic factor is included in a regression of the cognitive z-score on age, age*age, female, and age*female.

†p < .10; *p < .05; **p < .01

Table 3: Childhood conditions

	Baseline model +			
	Former Mozambican	Father's education	Father's employment	Self-rated child health
Mean, by age group, and female-male difference (age adjusted)				
Age group				
40-49	0.34	0.19	0.52	3.44
50-59	0.17	0.16	0.47	3.46
60-69	0.10	0.19	0.51	3.47
70-79	0.16	0.14	0.47	3.49
80+	0.17	0.13	0.51	3.62
Female-male difference	-0.028	0.024	-0.087**	-0.027
AME of 1 unit change on cog Z score[a]	-0.0051	-0.0045	0.17**	0.14**
	(0.049)	(0.044)	(0.037)	(0.018)
Change in age-gradient and female-male difference after controlling for factor (%)[b]				
Age gradient	0.3%	0.0%	-1.0%	2.8%
Female-male difference	0.2%	-0.1%	-18.6%	-5.6%

Notes: AME: average marginal effect. Former Mozambican: =1 if born in Mozambique, =0 if born in South Africa. Father's education: =1 if father had formal schooling, =0 if father had no formal schooling. Father's employment: =1 if father worked in a skilled occupation, =0 if father worked in unskilled occupation. Self-rated child health: 1=very poor, 2=poor, 3=fair, 4=good, 5=very good.

[a]Average marginal effect of a one-unit change in each early-life factor obtained from linear regressions of cognitive z-score on the respective factor, age, age*age, female, and age*female.

[b]Change in the age gradient and female-male difference in cognitive z-score if the early-life factor is included in a regression of the cognitive z-score on age, age*age, female, and age*female.

†p < .10; *p < .05; **p < .01

Table 4: Cardiovascular and cardiometabolic diseases

	Baseline model +			
	Hypertension	BMI	Diabetic	Prior stroke
Mean, by age group, and female-male difference (age adjusted)				
Age group				
40-49	0.44	27.07	0.08	0.01
50-59	0.57	27.61	0.10	0.02
60-69	0.68	27.95	0.16	0.04
70-79	0.78	27.37	0.19	0.04
80+	0.86	26.12	0.16	0.07
Female-male difference	0.12**	5.49**	0.037*	0.0086
AME of 1 unit change on cog Z score[a]	-0.0092	0.016**	-0.10*	-0.19+
	(0.040)	(0.0031)	(0.053)	(0.11)
Change in age-gradient and female-male difference after controlling for factor (%)[b]				
Age gradient	-0.8%	4.7%	-2.8%	-1.3%
Female-male difference	-1.6%	55.3%	-6.0%	-2.5%

Notes: AME: average marginal effect. Hypertension: =1 if measured BP over 140 systolic or over 90 diastolic, or self-report on medication. =0 if measured BP under thresholds and not on medication. BMI=body mass index (continuous). Diabetic: =1 if random glucose >XXX mm/l or self-report diabetic, =0 if random glucose <XXX mm/L and not on diabetes treatment. Prior stroke: =1 if prior doctor diagnosed stroke, =0 if no prior diagnosed stroke.

[a]Average marginal effect of a one-unit change in each cardiovascular/cardiometabolic health factor obtained from linear regressions of cognitive z-score on the respective factor, age, age*age, female, and age*female.

[b]Change in the age gradient and female-male difference in cognitive z-score if the cardiovascular/cardiometabolic health factor is included in a regression of the cognitive z-score on age, age*age, female, and age*female.

†p < .10; *p < .05; **p < .01

Table 5: Physical health

	Baseline model +			
	ADL limited	Grip strength (standardized)	Gait speed (standardized)	Self-rated health
Mean, by age group, and female-male difference (age adjusted)				
Age group				
40-49	0.05	0.40	0.18	3.94
50-59	0.05	0.25	0.15	3.75
60-69	0.07	-0.06	-0.01	3.65
70-79	0.08	-0.32	-0.10	3.63
80+	0.26	-0.79	-0.58	3.11
Female-male difference	-0.0072	-0.033	-0.096+	-0.071
AME of 1 unit change on cog Z score[a]	-0.27**	0.15**	0.082**	0.10**
	(0.069)	(0.024)	(0.019)	(0.019)
Change in age-gradient and female-male difference after controlling for factor (%)[b]				
Age gradient	-4.8%	-31.9%	-14.6%	-11.5%
Female-male difference	2.2%	-12.5%	-23.0%	-8.2%

Notes: AME: average marginal effect. ADL limited: =1 if report limitation on 1+ ADLs (eating, walking, bathing, toileting, transferring), =0 if no reported ADL limitations. Grip strength: dominant hand grip strength, z-standardized by sex. Gait speed: average gait speed (meters/second) over 5 meter walking course, z-standardized by sex. Self-rated health: current self-rated health, 1=very poor, 2=poor, 3=fair, 4=good, 5=very good.

[a]Average marginal effect of a one-unit change in each physical health factor obtained from linear regressions of cognitive z-score on the respective factor, age, age*age, female, and age*female.

[b]Change in the age gradient and female-male difference in cognitive z-score if the physical health factor is included in a regression of the cognitive z-score on age, age*age, female, and age*female.

†p < .10; *p < .05; **p < .01

Table 6: Mental health

	Baseline model +	
	CESD score	PTSD score
Mean, by age group, and female-male difference (age adjusted)		
Age group		
40-49	1.56	0.57
50-59	1.78	0.64
60-69	1.79	0.71
70-79	1.90	0.75
80+	2.55	0.98
Female-male difference	0.15*	0.25**
AME of 1 unit change on cog Z score[a]	-0.026*	-0.028*
	(0.013)	(0.014)
Change in age-gradient and female-male difference after controlling for factor (%)[b]		
Age gradient	-1.3%	-0.7%
Female-male difference	-4.4%	-8.0%

Notes: AME: average marginal effect. CESD score: score on CESD-9 depression index (0=lowest, 8=highest). PTSD score: score on short PTSD scale (0=lowest, 7=highest).

[a]Average marginal effect of a one-unit change in each mental health factor obtained from linear regressions of cognitive z-score on the respective factor, age, age*age, female, and age*female.

[b]Change in the age gradient and female-male difference in cognitive z-score if the mental health factor is included in a regression of the cognitive z-score on age, age*age, female, and age*female.

†p < .10; *p < .05; **p < .01

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