

Published in final edited form as:

*Hypertension*. 2019 April ; 73(4): 812–819. doi:10.1161/HYPERTENSIONAHA.118.12164.

## Hypertension development by midlife and the roles of pre-morbid cognitive function, sex, and their interaction

Drew M. Altschul<sup>1,2,\*</sup>, Christina Wraw<sup>1,2</sup>, Geoff Der<sup>3</sup>, Catharine R. Gale<sup>2,4</sup>, and Ian J. Deary<sup>1,2</sup>

<sup>1</sup>The University of Edinburgh, Department of Psychology, 7 George Square, Edinburgh, EH8 9JZ, UK

<sup>2</sup>Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, EH8 9JZ, UK

<sup>3</sup>MRC/CSO Social & Public Health Sciences Unit, 200 Renfield Street, University of Glasgow, G2 3QB, UK

<sup>4</sup>MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton General Hospital, Southampton, SO16 6YD, UK

### Abstract

Higher early-life cognitive function is associated with better later-life health outcomes, including hypertension. Associations between higher prior cognitive function and less hypertension persist even when accounting for socioeconomic status, but socioeconomic status-hypertension gradients are more pronounced in women. We predicted that differences in hypertension development between sexes might be associated with cognitive function and its interaction with sex, such that higher early-life cognitive function would be associated with lower hypertension risk more in women than in men. We used accelerated failure time modeling with the National Longitudinal Study of Youth 1979. Cognitive function was assessed in youth, when participants were aged between 14 and 21. Of 2572 men and 2679 women who completed all assessments, 977 men and 940 women reported hypertension diagnoses by 2015. Socioeconomic status in youth and adulthood were investigated as covariates, as were components of adult socioeconomic status: education, occupational status, and family income. A standard-deviation of higher cognitive function in youth was associated with reduced hypertension risk (acceleration factor  $\hat{c} = 0.97$ , 95% CI: [0.96, 0.99],  $p = 0.001$ ). The overall effect was stronger in women (sex  $\times$  cognitive function:  $\hat{c} = 0.97$ , 95% CI: [0.94, 0.99],  $p = 0.010$ ); especially, higher functioning women were less at risk than their male counterparts. This interaction was itself attenuated by a sex by family income interaction. People with better cognitive function in youth, especially women, are less likely to develop hypertension later in life. Income differences accounted for these associations. Possible causal explanations are discussed.

---

\* corresponding author – drew.altschul@ed.ac.uk.

#### Conflict of interest disclosure

All authors declare that they have no conflict of interests.

## Keywords

hypertension; diagnosis; cognition; cognitive function; sex; socioeconomic position; income

---

## Introduction

Hypertension has been consistently linked to cardiovascular diseases such as coronary artery disease (CAD) and stroke.<sup>1</sup> It is also a risk factor for neurocognitive conditions such as early cognitive decline, vascular dementia, and possibly Alzheimer's disease.<sup>2</sup> Accelerated cognitive decline is associated with lower well-being, higher morbidity and mortality and, as cognitive function worsens, the clinical conditions of mild cognitive impairment and dementia can develop.<sup>3</sup> Some of hypertension's negative impacts on cognitive function have likely causal pathways: hypertension disrupts cerebral blood vessel structure and function, and is associated with stroke in relevant white matter regions.<sup>4</sup> Worldwide, hypertension, age-related cognitive decline, and dementia are on the rise.<sup>4, 5</sup>

Typically, hypertension is thought of as a risk factor for later cognitive decline. However, there is also evidence for the relationship operating in the opposite direction, i.e. that higher cognitive function in youth is associated with having lower risk of developing hypertension<sup>6</sup> and experiencing hypertension-related stroke and coronary artery events later in life.<sup>7</sup> These findings are part of a field known as cognitive epidemiology, which has found that higher cognitive function in early life is associated with lower risk of a number of physical and mental ailments later in life.<sup>8–12</sup>

Men are more likely to develop cardiovascular conditions than women,<sup>13</sup> a reason why men have been the subject of more intervention studies than women.<sup>14</sup> Nevertheless, cardiovascular disease is the leading cause of death in both women and men.<sup>15</sup> Some differences in hypertension are biologically based in differences between men and women, e.g. through hormones and gene dosage from the sex chromosomes, and these differences are consistent across different countries and ethnic groups.<sup>14</sup> Additionally, traditional gender roles are associated with men behaving in ways (e.g., higher smoking rates) that increase their risk for physical health conditions, including hypertension.<sup>16</sup>

Previous work on the cognitive epidemiology of CAD and stroke events found a significant interaction between sex and cognitive function in youth: individuals with higher cognitive function were at lower risk for CAD and stroke, and the associations were stronger in women.<sup>7</sup> However, the numbers of events in studies of CAD have been small.<sup>6, 7</sup> Here, we hypothesized that the development of hypertension, a condition that becomes increasingly common with age and is related to cardiovascular health and cognitive impairment, could differ by sex, such that higher early-life cognitive function is associated with lower risk of hypertension in women than it is in men.<sup>7</sup> We tested this hypothesis using the US National Longitudinal Survey of Youth 1979 (NLSY79), following prior work linking cognitive function in youth and physical health in midlife in this sample.<sup>6</sup> Socioeconomic factors, in particular education, have been implicated as mediators in the relationship between cognitive function in youth and cardiovascular risk;<sup>17–19</sup> these were examined in the present study, both as potential mediators and moderators.

## Methods

### Materials and Data Availability

Anonymized data and materials have been made publicly available from the United States Bureau of Labor Statistics' National Longitudinal Surveys website, and can be accessed at [www.nlsinfo.org/investigator](http://www.nlsinfo.org/investigator). The R code used in the present study is available upon request.

### Participants

The NLSY79 was initially sampled from non-institutionalized people aged 14-21 years, living in the United States.<sup>20</sup> The study consisted of 12,686 original participants, and was representative of the population at the time; 16% of participants were Hispanic, 25% were Black, and 59% were neither Black nor Hispanic.

The initial interview took place in 1979, and respondents were re-interviewed annually until 1994, and surveys were conducted biennially after. For the health modules, in which the hypertension diagnosis data were collected, not all individuals were surveyed every two years. Rather, each individual participating in the module(s) was surveyed for that module during the wave(s) when they were closest to 40 and 50 years of age, for each respective health module. The most recent data come from the 2014 health survey.

### Hypertension diagnosis

Respondents were asked if they had ever been told by a doctor that they had high blood pressure or hypertension. If respondents answered yes, they were asked for the month and year that this was first diagnosed. Right censored survival data were thus constructed as starting at the date of cognitive function measurement and ending at the time of hypertension diagnosis, or being censored at the most recent date of data collection in which they took part. Individuals who did not provide information on hypertension diagnosis were not included in the analyses, nor were individuals with hypertension prior to the study inception, as these cases more likely represent a congenital condition.<sup>21</sup> Kaplan-Meier survival curves were plotted to visualize the effect of different variables and interactions on hypertension diagnosis.

### Cognitive function

General cognitive function was assessed in the NLSY79 via the Armed Forces Qualifications Test (AFQT), scored using the 1989 re-norming.<sup>22</sup> The test was given in 1980, when participants were between 15 and 22 years of age; these tests' scores reflect pre-morbid cognitive function. The scores were derived from four subtests that assessed arithmetic reasoning, mathematical knowledge, word knowledge, and paragraph comprehension. The AFQT is a valid and reliable measure of cognitive function, having been associated with outcomes including academic achievement and job performance.<sup>23, 24</sup> To be consistent with previous work in this sample,<sup>6, 25</sup> we used the z-scored AFQT percentile score, taken from The Bell Curve website.<sup>26</sup>

## Covariates

Sex was originally determined by observation, and if it was not obvious, participants were asked directly by the interviewer during the initial survey in 1979. Every case was checked, and in 45 cases corrected, by the National Opinion Research Center in 1986. Men were coded as the reference level, i.e. 0, and women were coded as 1.

Several variables were incorporated as controls into progressive models. The age when the first interview was conducted in 1979 was included to control for lower test performance in younger individuals. Socioeconomic status (SES) in youth, i.e. parental SES, was included to control for confounding effects of an individual's rearing circumstances. Individuals from higher SES background may have access to more resources and benefit from higher cognitive functions in this way, although the existing literature suggests that these effects are slight.<sup>27</sup>

Adult SES, on the other hand, can have a much larger impact on associations between early-life cognitive function and later-life health.<sup>27</sup> We included adult SES as a variable of interest, although the mechanisms relating adult SES, cognitive function, and health are debated.<sup>12</sup> Adult SES is often theorized to have a mediating effect between cognitive function and health, but adult SES is also inherited: there are genetic correlations between cognitive function and SES,<sup>28</sup> and substantial environmental circumstances can carry-over from one generation to the next.<sup>29</sup> Including adult SES allows us to control for potential confounding, e.g. from inherited privilege, and consider the portion of adult SES that may mediate the relationship between early-life cognitive function and hypertension diagnosis. Adult SES is composed of adult measures of family income, education, and occupational status, each of which could have a different confounding or mediating effect. Thus each was also analyzed independently from the composite adult SES variable.

Youth SES and adult SES were averages of z-transformed income, education, and occupation status variables.<sup>26</sup> To calculate youth SES, participants' parents' information was used; to calculate adult SES, individuals' information from surveys from 2012 to 2014 were used. A higher SES value indicates more socioeconomic advantage.

The adult income variable was the total net family income in the past year, which was also log and z-transformed to be consistent with earlier work.<sup>6, 26</sup> Adult education was the highest grade completed by the most recent wave of the study. Occupation status was derived as a continuous variable using an updated version of the Duncan Socioeconomic Index.<sup>30, 31</sup>

## Statistical analyses

All analyses were conducted using accelerated failure time (AFT) regression models, a form of survival analysis that is fully parametric and not limited by the assumptions of proportional hazard modeling, which these data did not satisfy (Supplementary Table 1).<sup>32</sup> With selection of the best parametric distribution, AFT models also allow for better fit and more accurate inferences.<sup>33</sup> Complete case and multiply-imputed analyses using the same predictor variables yielded the same findings in previous work.<sup>6</sup> A similar pattern of missing

values could be expected in the following analyses, therefore only complete cases were analysed in the present study.

The outcome of AFT models was the event of a hypertension diagnosis and, if such a diagnosis was given, the date of the diagnosis. The log-logistic distribution was used as the error distribution in all models because it consistently produced better fit than the alternatives (Weibull, Gompertz, log-normal, and exponential distributions). The first model was our base model, and included cognitive function, sex, and age of testing in youth. The second model introduced an interaction between sex and cognitive function, i.e. asking the question of whether there was a stronger association in men or women between cognitive function in youth and hypertension by middle age. Model 3 added SES in youth as a covariate, and model 4 added adult SES to model 3. Because adult SES is composed of distinct subcomponents, i.e. income, education, and occupational status, it has been informative to analyse the effect of each variable independently, to investigate possible mechanisms. Models 5 through 7 broke down adult SES into its constituent parts, adding each in isolation to model 3 to examine the statistical effects of adult SES in greater detail. Model 8 investigates the specific importance of income and its interaction with sex.

For all models, acceleration factors ( $\hat{c}$ ) were presented, with 95% confidence interval, as the quantification of the regression coefficients that result from AFT modeling. A variable's acceleration factor represents the degree to which an event, i.e. hypertension diagnosis, occurs sooner than it would on average, which is the reference level for categorical variables (e.g. male, for sex) or the mean for continuous variables. If  $\hat{c} > 1$ , the acceleration is greater than average, meaning that the positive value of this variable increases the probability that the individual will be diagnosed with hypertension. If  $\hat{c} < 1$ , the opposite is true, and a positive value of the variable will decrease hypertension risk, relative to the average. Results were expressed per standard deviation of the exposure, i.e. the AFQT score.

## Results

A flow chart of individual participation and hypertension status is presented in Figure 1. Of the original sample of 12,686 individuals, data were incomplete for 7430, which mostly consisted of individuals who did not participate in health modules for either age 40 and 50. 5 more were hypertensive before the NLSY79 began. This yielded an analytic sample of 5251; 1917 of these individuals were diagnosed with hypertension.

Descriptive data for analysed variables are presented in Table 1. Expanded sample characteristics can be found in Wraw, Deary, Gale and Der 6 (Table 1, pg. 26). In ecologically relevant terms, adult annual incomes in the analytic sample ranged from \$1811 to \$595,986, with a mean of \$82,989; years of education ranged from only having completed the 3rd grade to more than 8 years of college, with a mean of 13.5 years of education stating from the 1st grade. Overall, the individuals in our analytic sample experienced slightly better socioeconomic circumstances in youth and adulthood than did the individuals who were missing data and not included in our analyses (Supplementary Table 2); the variable means in each subsample were between 0.05 and 0.59 of a standard deviation from the other. Contrary to some expectations,<sup>34, 35</sup> prevalence and average age of diagnosis of

hypertension were highly comparable across men and women, in both the full and analytic sample. The higher proportion of hypertension diagnoses in the analytic sample reflects the older age of this subsample.

Using cognitive function as a continuous variable, in our first model (Table 2) we found main effects of: cognitive function ( $\hat{c} = 0.96$ , 95% CI: [0.95, 0.97],  $p < 0.001$ ), indicating that higher functioning individuals were less likely to develop hypertension; sex ( $\hat{c} = 0.97$ , 95% CI: [0.95, 0.99],  $p = 0.019$ ), indicating that women were less likely to become hypertensive; and survey age in youth ( $\hat{c} = 0.99$ , 95% CI: [0.98, 1.00],  $p = 0.002$ ), which could be due to older individuals scoring higher on the AFQT. In subsequent analyses, we added a sex by cognitive function interaction to our AFT models (Table 2). We found an interaction between sex and cognitive function ( $\hat{c} = 0.97$ , 95% CI: [0.96, 0.99],  $p = 0.001$ ), indicating that the cognitive function and hypertension association was stronger in women than men.

Kaplan-Meier curves (Figure 2) illustrate the interaction between cognitive function and sex, and the relationship with hypertension diagnosis (Figure 2). We note that, although cognitive function is divided into tertiles in Figure 2 for the purpose of illustration, the analyses were conducted with cognitive function as a continuous variable. In women, there are three distinct curves for hypertension risk (Figure 2); by their 50s, those women with high cognitive function in youth had a lower risk of hypertension than average (mid) cognitive scorers, who are in turn at lower risk than those with low cognitive function from youth. In men, the high and average cognitive scorers from youth have similar risk of hypertension by middle age, and both have lower risk than lower cognitive scorers. In addition to these within-sex observations, Figure 2 shows between-sex differences, i.e. higher functioning women were less likely to be diagnosed with hypertension than higher functioning men.

Adding SES from youth had no effect on this interaction; it was not itself a predictor of hypertension diagnosis, nor did it interact with sex (Supplementary Table 3). Adding adult SES attenuated the main effect of cognitive function ( $\hat{c} = 0.99$ , 95% CI: [0.97, 1.01],  $p = 0.406$ ), but did not affect the interaction with sex. Adult SES also predicted hypertension development ( $\hat{c} = 0.97$ , 95% CI: [0.95, 0.99],  $p = 0.013$ ); higher SES individuals were less likely to be diagnosed with hypertension. We also fit the equivalent model separately in men and women (Supplementary Table 4). These models confirmed the effects of our sex  $\times$  cognitive function models, as significant effects of cognitive function and adult SES were present in women, but not men.

Of the adult SES subcomponents, only income was significant (Table 3); in this model, the sex by cognitive function interaction remained significant. Moreover, education and occupation status did not appear to individually predict hypertension diagnoses, independently or as a part of the adult SES composite. The Akaike Information Criterion (AIC), a measure of model fit,<sup>36</sup> for model 5 in Table 2 indicated that the adult family income model was a better fit than the model that used composite SES, as well as the models using occupation and education.

To test whether income differences between sexes could explain the sex by cognitive function interaction, we added a sex by family income interaction to model 5. The model (Table 4) indicated that women with higher family income are less likely to develop hypertension, and the inclusion of this interaction reduced the acceleration factor of the sex by cognitive function interaction from 0.97 (95% CI: [0.94 0.99]) to 0.98 (95% CI: [0.95, 1.01]).

Whereas the sex by income interaction was not significant in model 8 (Table 3), removing the sex by cognitive function interaction increased the sex by income interaction effect ( $\hat{\epsilon} = 0.97$ , 95% CI: [0.94, 1.00],  $p = 0.029$  – Supplementary Table 3), suggesting that the two interactions are accounting for the same outcomes. For additional sensitivity analysis, we evaluated a model with a sex by adult SES interaction, finding no evidence for an overall SES interaction. We also examined whether having a spouse or other partner accounted for any of the sex and income associations (Supplementary Table 3), and found no evidence for any such influence.

## Discussion

Our results show that sex and cognitive function from youth interact significantly to predict hypertension diagnosis by middle age. Women with higher cognitive function are less likely than higher cognitively functioning men to develop hypertension, as indicated by reported doctor diagnosis. The opposite is not necessarily true at the other end of the spectrum: lower functioning women appear about as likely to develop hypertension as lower functioning men.

SES from youth did not explain the effects of the interaction, and youth SES was only associated with hypertension diagnosis before the addition of adult SES variables. This is consistent with prior work,<sup>6, 25</sup> but is nonetheless notable, given that cognitive function and youth SES were assessed at the same time, and the correlation between the two is high ( $r = 0.56$ ).

Adult SES, on the other hand, did predict hypertension diagnosis, such that higher SES individuals were less likely to have hypertension. The association with adult SES attenuated the sex-independent effect of cognitive function on hypertension and made it non-significant, whilst preserving the sex by cognitive function interaction. The foundation for this can be seen in the curves presented in Figure 2: high and middle functioning males do not appear to differ. Adult SES and cognitive function are correlated strongly ( $r = 0.60$  for women;  $r = 0.66$  for men), and our findings suggest that the ‘anti-hypertensive benefit’ gained by those with higher cognitive function from youth that spans the sexes can be accounted for by adult family income.

Individuals with higher income were less likely to develop hypertension. Income alone did not affect the sex by cognitive function interaction, but including an interaction between sex and family income ablated the sex by cognitive function interaction. This suggests that the segment of higher cognitive functioning women, who are even less likely to become

hypertensive, overlaps with the segment of higher SES women, particularly women from higher income families, who also are less likely to become hypertensive.

Both men and women in this sample with higher cognitive function from youth tended to have a higher family income ( $r = .48$ ) in adulthood. It is difficult to causally determine whether the higher-cognitive-functioning segment of women benefitted directly from having higher family income. One explanation is that income mediates some or all of cognitive function's effect on hypertension, although an unmeasured confounder(s) could still be driving these associations. For instance, evidence from molecular genetic cognitive epidemiology suggests that cognitive function and hypertension share some genetic underpinnings.<sup>37</sup>

There is more evidence for the importance of lifestyle factors in explaining the associations between cognitive function and physical health. The Aberdeen Children of the 1950s cohort yielded results that were similar to ours; specifically, associations between childhood cognitive function and both stroke and coronary artery events were stronger in women.<sup>7</sup> However, in their analyses, the sex by cognitive function interaction effects on stroke and CAD outcomes could be accounted for by education, not income. The Aberdeen cohort began earlier than the NLSY79 and is from the UK not the US, so chronological and geographic-cultural cohort differences might explain this discrepancy.<sup>38–40</sup>

Developing hypertension is known to be robustly associated with adult SES, in particular education but, to lesser degrees, with income and occupation.<sup>18</sup> Women in particular seem to benefit more from having higher SES in all three categories, and women also appear to drive the meta-analytic association between hypertension and both income and occupation.<sup>41</sup> In the context of CVD, women are less likely to be diagnosed,<sup>42</sup> and lower SES adults and women are less likely to seek preventive treatments.<sup>43</sup> A key ecological reason for why lower SES adults may not seek preventive treatment is that in more socially and economically deprived areas, there is a lower concentration of and reduced access to primary care services, which is linked to increased CVD and mortality.<sup>44, 45</sup> Since women tend to use primary health care and preventative services more often than men,<sup>46</sup> the stronger association between cognitive function and hypertension observed among women may be influenced through the mediator of access to health care services. Higher cognitive function men with higher income might not put money toward health services, which we have speculated women might do;<sup>46</sup> instead, there might even be a tendency for men to spend some disposable income on health-harming habits, such as alcohol,<sup>47</sup> as men are more likely than women to drink alcohol.<sup>48</sup>

In general, our results are consistent with previous meta-analyses that have indicated that the effects of SES on hypertension diagnosis, as well as CVD, are stronger and more consistent in women.<sup>18, 49</sup> Our results suggest that both men and women with lower cognitive function are more generally at increased risk of developing hypertension. This group is more at risk for heart disease to begin with, not only because some individuals do not as readily seek treatment. On the other hand, the effect is different at the other end of the spectrum: higher functioning women are much less likely to develop hypertension than higher functioning men.



The present study is limited by a non-trivial proportion of missing data, particularly in the adult SES variables, which reduced our available analytical sample. The analytic sample we were left with was more affluent than the average across the whole sample. It was a limitation of our modeling software that we could not account for these differences with probabilistic weighting. However, prior imputation analyses suggested that our results would not be biased,<sup>6</sup> and our analyses were still able to make use of nearly a thousand cases of hypertension per sex. The diagnoses in the present study were self-reported and we were not able to cross-reference these reports with any physician records. Although we took steps to treat diagnoses and diagnosis dates conservatively, self-reported diagnoses of hypertension tend to have lower validity than those drawn from medical records,<sup>50</sup> although our use of diagnosis times would likely protect our analyses from some more common issues with low specificity in self-reports of hypertension.<sup>50</sup>

## Perspectives

Our study supports the association between cognitive function in youth and hypertension development, and finds a stronger association in women. Adult income appears to play an important, potentially mediating, role in the effects. These results further our understanding of the sex and gender risk factors that associate hypertension, cognitive function, and health inequalities. Future work should aim to elucidate the different contributions of cognitive function and SES on hypertension and other relevant physical health concerns that differ between the sexes. In finding clues to alleviating the population burden of hypertension, further attention could be given to what contributes to the especially low risk in women with higher cognitive ability.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Sources of funding

This work was conducted in the University of Edinburgh Centre for Cognitive Ageing and Cognitive Epidemiology, part of the cross council Lifelong Health and Wellbeing Initiative (MR/K026992/1). Funding from the Biotechnology and Biological Sciences Research Council (BBSRC), Economic and Social Research Council (ESRC) and Medical Research Council (MRC) is gratefully acknowledged.

## References

1. McInnes GT. Hypertension and coronary artery disease: Cause and effect. *Journal of Hypertension*. 1995; 13:S49–S56.
2. Barnes DE, Yaffe K. The projected effect of risk factor reduction on alzheimer's disease prevalence. *The Lancet Neurology*. 2011; 10:819–828. [PubMed: 21775213]
3. Salthouse T. Consequences of age-related cognitive declines. *Annual review of psychology*. 2012; 63:201–226.
4. Iadecola C, Yaffe K, Biller J, Bratzke LC, Faraci FM, Gorelick PB, Gulati M, Kamel H, Knopman DS, Launer LJ. Impact of hypertension on cognitive function: A scientific statement from the american heart association. *Hypertension*. 2016; 68:e67–e94. [PubMed: 27977393]
5. Matthews F, Stephan B, Robinson L, Jagger C, Barnes L, Arthur A, Brayne C, Collaboration ASC. A two decade dementia incidence comparison from the cognitive function and ageing studies i and ii. *Nature communications*. 2016; 7

6. Wraw C, Deary IJ, Gale CR, Der G. Intelligence in youth and health at age 50. *Intelligence*. 2015; 53:23–32. [PubMed: 26766880]
7. Lawlor DA, Batty GD, Clark H, McIntyre S, Leon DA. Association of childhood intelligence with risk of coronary heart disease and stroke: Findings from the aberdeen children of the 1950s cohort study. *Eur J Epidemiol*. 2008; 23:695–706. [PubMed: 18704700]
8. Calvin CM, Batty GD, Deary IJ. Cognitive epidemiology. *The Wiley-Blackwell Handbook of Individual Differences*. 2011:427–460.
9. Batty GD, Deary IJ, Gottfredson LS. Premorbid (early life) iq and later mortality risk: Systematic review. *Ann Epidemiol*. 2007; 17:278–288. [PubMed: 17174570]
10. Deary IJ. Cognitive epidemiology: Its rise, its current issues, and its challenges. *Personality and individual differences*. 2010; 49:337–343.
11. Deary IJ. Looking for ‘system integrity’ in cognitive epidemiology. *Gerontology*. 2012; 58:545–553. [PubMed: 22907506]
12. Lubinski D. Cognitive epidemiology: With emphasis on untangling cognitive ability and socioeconomic status. *Intelligence*. 2009; 37:625–633.
13. Jousilahti P, Vartiainen E, Tuomilehto J, Puska P. Sex, age, cardiovascular risk factors, and coronary heart disease. *Circulation*. 1999; 99:1165–1172. [PubMed: 10069784]
14. Sandberg K, Ji H. Sex differences in primary hypertension. *Biology of sex differences*. 2012; 3:7. [PubMed: 22417477]
15. Bots SH, Peters SA, Woodward M. Sex differences in coronary heart disease and stroke mortality: A global assessment of the effect of ageing between 1980 and 2010. *BMJ global health*. 2017; 2:e000298.
16. Courtenay WH. Constructions of masculinity and their influence on men's well-being: A theory of gender and health. *Social science & medicine*. 2000; 50:1385–1401. [PubMed: 10741575]
17. Hagger-Johnson G, Möttus R, Craig LC, Starr JM, Deary IJ. Pathways from childhood intelligence and socioeconomic status to late-life cardiovascular disease risk. *Health Psychol*. 2012; 31:403. [PubMed: 22309883]
18. Leng B, Jin Y, Li G, Chen L, Jin N. Socioeconomic status and hypertension: A meta-analysis. *Journal of hypertension*. 2015; 33:221–229. [PubMed: 25479029]
19. Backholer K, Peters SAE, Bots SH, Peeters A, Huxley RR, Woodward M. Sex differences in the relationship between socioeconomic status and cardiovascular disease: A systematic review and meta-analysis. *J Epidemiol Community Health*. 2017; 71:550–557. [PubMed: 27974445]
20. Rothstein DS, Carr D, Cooksey E. Cohort profile: The national longitudinal survey of youth 1979 (nlsy79). *Int J Epidemiol*. 2018
21. Dionne JM, Abitbol CL, Flynn JT. Hypertension in infancy: Diagnosis, management and outcome. *Pediatric nephrology*. 2012; 27:17–32. [PubMed: 21258818]
22. Kilburn, MR, Hanser, LM, Klerman, JA. Estimating afqt scores for national educational longitudinal study (nels) respondents. ERIC; 1998.
23. Palmer P, Hartke DD, Ree MJ, Welsh JR, Valentine LD Jr. Armed services vocational aptitude battery (asvab): Alternate forms reliability (forms 8, 9, 10, and 11). 1988
24. Welsh JR Jr, Kucinkas SK, Curran LT. Armed services vocational battery (asvab): Integrative review of validity studies. 1990
25. Der G, Batty GD, Deary IJ. The association between iq in adolescence and a range of health outcomes at 40 in the 1979 us national longitudinal study of youth. *Intelligence*. 2009; 37:573–580. [PubMed: 19907663]
26. Herrnstein, RJ, Murray, C. *Bell curve: Intelligence and class structure in american life*. Simon and Schuster; 2010.
27. Calvin CM, Deary IJ, Fenton C, Roberts BA, Der G, Leckenby N, Batty GD. Intelligence in youth and all-cause-mortality: Systematic review with meta-analysis. *Int J Epidemiol*. 2010; 40:626–644. [PubMed: 21037248]
28. Marioni RE, Davies G, Hayward C, Liewald D, Kerr SM, Campbell A, Luciano M, Smith BH, Padmanabhan S, Hocking LJ. Molecular genetic contributions to socioeconomic status and intelligence. *Intelligence*. 2014; 44:26–32. [PubMed: 24944428]

29. Kalil, A, DeLeire, T. Family investments in children's potential: Resources and parenting behaviors that promote success. Psychology Press; 2004.
30. Hauser RM, Warren JR. 4. Socioeconomic indexes for occupations: A review, update, and critique. *Soc Method.* 1997; 27:177–298.
31. Frederick, C, Hauser, RM. A crosswalk for using pre-2000 occupational status and prestige codes with post-2000 occupation codes. Center for Demography and Ecology: University of Wisconsin-Madison; 2010. PMID. 25506974
32. Kalbfleisch, JD, Prentice, RL. The statistical analysis of failure time data. John Wiley & Sons; 2011.
33. Swindell WR. Accelerated failure time models provide a useful statistical framework for aging research. *Experimental gerontology.* 2009; 44:190–200. [PubMed: 19007875]
34. Ong KL, Tso AW, Lam KS, Cheung BM. Gender difference in blood pressure control and cardiovascular risk factors in americans with diagnosed hypertension. *Hypertension.* 2008; 51:1142–1148. [PubMed: 18259031]
35. Hajjar I, Kotchen TA. Trends in prevalence, awareness, treatment, and control of hypertension in the united states, 1988-2000. *Jama.* 2003; 290:199–206. [PubMed: 12851274]
36. Akaike H. A new look at the statistical model identification. *IEEE transactions on automatic control.* 1974; 19:716–723.
37. Davies G, Lam M, Harris SE, Trampush JW, Luciano M, Hill WD, Hagenaars SP, Ritchie SJ, Marioni RE, Fawns-Ritchie C. Study of 300,486 individuals identifies 148 independent genetic loci influencing general cognitive function. *Nature communications.* 2018; 9
38. Tucker-Drob EM, Bates TC. Large cross-national differences in gene× socioeconomic status interaction on intelligence. *Psychol Sci.* 2016; 27:138–149. [PubMed: 26671911]
39. Preston SH, Wang H. Sex mortality differences in the united states: The role of cohort smoking patterns. *Demography.* 2006; 43:631–646. [PubMed: 17236538]
40. Allender S, Scarborough P, O'Flaherty M, Capewell S. Patterns of coronary heart disease mortality over the 20 th century in england and wales: Possible plateaus in the rate of decline. *BMC Public Health.* 2008; 8:148. [PubMed: 18452595]
41. Bernstein IS. Dominance relationships and ranks - explanations, correlations and empirical challenges. *Behavioral and Brain Sciences.* 1981; 4:449–453.
42. Wenger NK. Women and coronary heart disease: A century after herrick: Understudied, underdiagnosed, and undertreated. *Circulation.* 2012; 126:604–611. [PubMed: 22850362]
43. Pilote L, Dasgupta K, Guru V, Humphries KH, McGrath J, Norris C, Rabi D, Tremblay J, Alamian A, Barnett T. A comprehensive view of sex-specific issues related to cardiovascular disease. *Canadian Medical Association Journal.* 2007; 176:S1–S44.
44. Starfield B, Shi L, Macinko J. Contribution of primary care to health systems and health. *The milbank quarterly.* 2005; 83:457–502. [PubMed: 16202000]
45. Shi L, Macinko J, Starfield B, Wulu J, Regan J, Politzer R. The relationship between primary care, income inequality, and mortality in us states, 1980–1995. *The Journal of the American Board of Family Practice.* 2003; 16:412–422. [PubMed: 14645332]
46. Wang Y, Hunt K, Nazareth I, Freemantle N, Petersen I. Do men consult less than women? An analysis of routinely collected uk general practice data. *BMJ open.* 2013; 3:e003320.
47. Briasoulis A, Agarwal V, Messerli FH. Alcohol consumption and the risk of hypertension in men and women: A systematic review and meta-analysis. *The Journal of Clinical Hypertension.* 2012; 14:792–798. [PubMed: 23126352]
48. Wilsnack RW, Vogeltanz ND, Wilsnack SC, Harris TR. Gender differences in alcohol consumption and adverse drinking consequences: Cross-cultural patterns. *Addiction.* 2000; 95:251–265. [PubMed: 10723854]
49. Backholer K, Peters SAE, Bots SH, Peeters A, Huxley RR, Woodward M. Sex differences in the relationship between socioeconomic status and cardiovascular disease: A systematic review and meta-analysis. *J Epidemiol Community Health.* 2016
50. Gonçalves VS, Andrade KR, Carvalho K, Silva MT, Pereira MG, Galvao TF. Accuracy of self-reported hypertension: A systematic review and meta-analysis. *Journal of hypertension.* 2018; 36:970–978. [PubMed: 29232280]

## Novelty and Significance

### What is new?

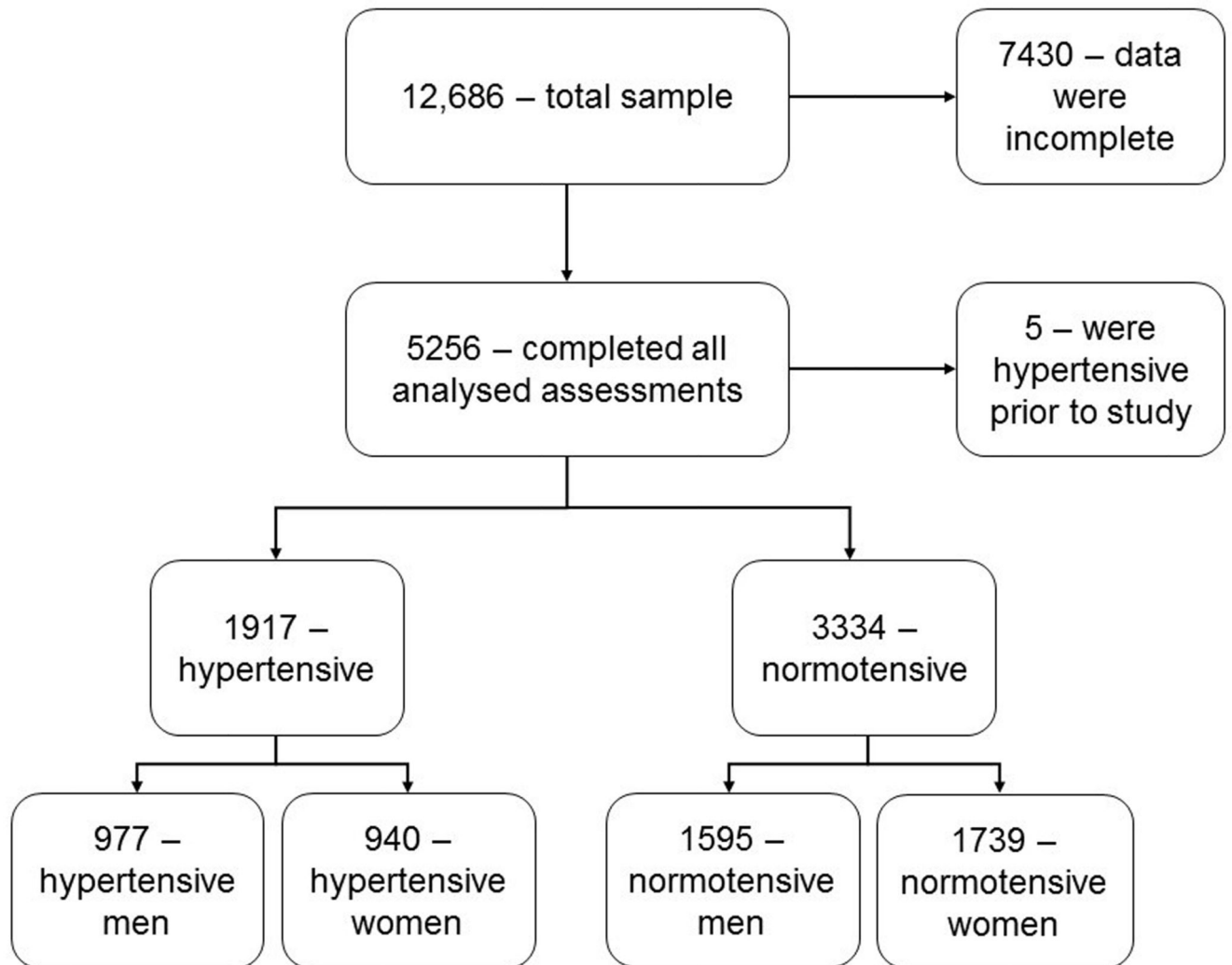
- Women with higher early life cognitive function are at lower risk for developing hypertension than their male counterparts.
- The relationship is unaffected by the inclusion of youth and adult SES variables.
- Family income is a potential mediator of the relationship.

### What is relevant?

- Women with higher cognitive ability could provide insights into how to protect populations from the risk of hypertension.
- Understanding root causes and mediating relationships will open up useful avenues for future treatment and intervention.

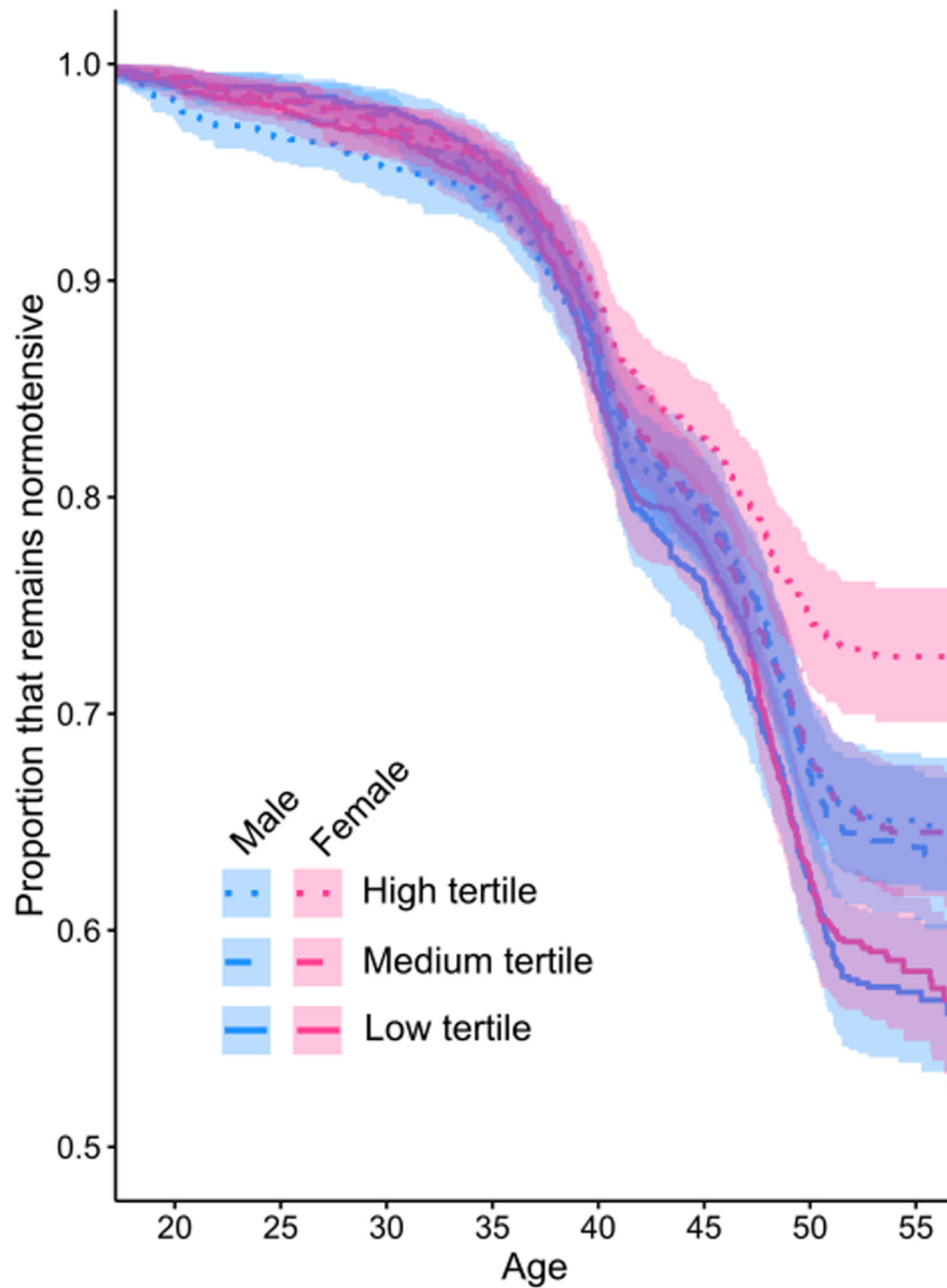
### Summary

Higher early-life cognitive function is associated with better later-life health outcomes, including hypertension. These associations persist even when accounting for SES, although SES-hypertension gradients are stronger in women. We found that higher functioning women were less at risk for hypertension than their male counterparts. Income differences could account for these associations, and may mediate the relationship between early-life cognitive function and hypertension.



**Figure 1. Flow chart of NLSY participants analyzed in this study.**

From the full NLSY sample, individuals were only analyzed if they had complete sex, cognitive function, youth SES and adult SES data, and hypertension diagnosis information from either the age 40 or 50 health module.



**Figure 2. Kaplan-Meier curves of time to hypertension diagnosis.**

For visualisation purposes, cognitive function across all individuals was divided into tertiles. Individuals in these tertiles were subdivided by sex, producing six curves. The band around each curve is the 95% confidence region.

**Table 1**  
**Descriptive statistics of explanatory, control, and outcome variables, split by sex.**

Full sample	Male (N = 6401)			Female (N = 6282)		
	Cases (%)	Mean	SD	Cases (%)	Mean	SD
AFQT (Cognitive Function)	5949 (93)	-0.25	1.06	5926 (93)	-0.27	0.96
Youth SES	5949 (93)	-0.35	1.06	5926 (93)	-0.37	1.07
Adult SES	2753 (43)	0.08	0.79	2806 (44)	0.08	0.76
Family Income	3099 (48)	0.08	0.96	3270 (51)	-0.05	0.93
Education	3729 (58)	-0.06	1.00	3945 (61)	0.06	1.00
Occupation Status	3272 (51)	-0.03	0.99	3327 (52)	0.03	1.01
Hypertension diagnoses	1584 (24)			1517 (24)		
Age at diagnosis		41.50	8.23		41.47	8.13
Analytic Sample	Male (N = 2572)			Female (N = 2679)		
	Cases (%)	Mean	SD	Cases (%)	Mean	SD
AFQT (Cognitive Function)		-0.16	1.06		-0.24	0.93
Youth SES		-0.24	1.09		-0.32	1.06
Adult SES		0.10	0.78		0.09	0.76
Family Income		0.19	0.88		0.04	0.85
Education		0.06	0.98		0.17	0.96
Occupation Status		0.04	0.99		0.06	1.01
Hypertension diagnoses	977 (38)			940 (35)		
Age at diagnosis		40.98	8.78		41.68	7.97

AFQT: Armed Forces Qualification Test, a measure of general cognitive function. SES = Socioeconomic Status.



**Table 2**  
**Accelerated failure time models of hypertension, predicted by sex, cognitive function, and SES variables.**

	Model 1			Model 2			Model 3			Model 4		
	$\hat{\epsilon}$	95% C.I.	p	$\hat{\epsilon}$	95% C.I.	p	$\hat{\epsilon}$	95% C.I.	p	$\hat{\epsilon}$	95% C.I.	p
Sex	0.97	[0.95, 0.99]	0.019	0.96	[0.94, 0.99]	0.003	0.96	[0.94, 0.99]	0.003	0.96	[0.94, 0.99]	0.003
Cognitive Function	0.96	[0.95, 0.97]	< 0.001	0.97	[0.96, 0.99]	0.001	0.98	[0.96, 1.00]	0.034	0.99	[0.97, 1.01]	0.406
Youth survey age	0.99	[0.98, 1.00]	0.002	0.99	[0.98, 1.00]	0.002	0.99	[0.98, 1.00]	0.001	0.99	[0.98, 1.00]	< 0.001
Sex * Cog Function				0.97	[0.94, 0.99]	0.010	0.97	[0.94, 0.99]	0.012	0.97	[0.94, 0.99]	0.013
Youth SES							0.99	[0.97, 1.00]	0.040	0.99	[0.97, 1.00]	0.104
Adult SES										0.97	[0.95, 0.99]	0.013
AIC	20022.81			20018.24			20016.01			20011.82		
Log-likelihood	-10008.41			-10005.12			-10003.01			-9999.91		

$\hat{\epsilon}$ : acceleration factor, the degree to which an outcome is accelerated after the first observation. A  $\hat{\epsilon} < 1$  indicates that an event will happen later than at baseline. SES: socioeconomic status. AIC: Akaike Information Criterion.

**Table 3**  
**Accelerated failure time models of hypertension, adding individual adult SES predictors.**

	Model 5			Model 6			Model 7		
	$\hat{\epsilon}$	95% C.I.	p	$\hat{\epsilon}$	95% C.I.	p	$\hat{\epsilon}$	95% C.I.	p
Sex	<b>0.96</b>	<b>[0.93, 0.98]</b>	<b>0.001</b>	<b>0.94</b>	<b>[0.94, 0.99]</b>	<b>0.003</b>	<b>0.96</b>	<b>[0.94, 0.99]</b>	<b>0.003</b>
Cognitive Function	0.99	[0.97, 1.01]	0.467	<b>0.98</b>	<b>[0.96, 1.00]</b>	<b>0.043</b>	0.98	[0.96, 1.00]	0.091
Youth survey age	<b>0.99</b>	<b>[0.98, 1.00]</b>	<b>&lt;0.001</b>	<b>0.99</b>	<b>[0.98, 1.00]</b>	<b>&lt;0.001</b>	<b>0.99</b>	<b>[0.98, 1.00]</b>	<b>0.001</b>
Sex * Cog Function	<b>0.97</b>	<b>[0.94, 0.99]</b>	<b>0.016</b>	<b>0.97</b>	<b>[0.94, 0.99]</b>	<b>0.012</b>	<b>0.97</b>	<b>[0.94, 0.99]</b>	<b>0.012</b>
Youth SES	0.99	[0.97, 1.00]	0.112	<b>0.98</b>	<b>[0.97, 1.00]</b>	<b>0.040</b>	0.99	[0.97, 1.00]	0.051
Family income	<b>0.96</b>	<b>[0.95, 0.98]</b>	<b>&lt;0.001</b>						
Education				1.00	[0.98, 1.02]	0.865			
Occupation Status							0.99	[0.98, 1.01]	0.315
AIC	19996.41			20017.98			20017.00		
Log-likelihood	-9992.21			-10002.99			-10002.50		

$\hat{\epsilon}$ : acceleration factor, the degree to which an outcome is accelerated after the first observation. SES: socioeconomic status. AIC: Akaike Information Criterion.

**Table 4**  
**Accelerated failure time model of hypertension, adding sex by income interactions.**

Model 8				
	$\hat{\epsilon}$	95%	C.I.	p
Sex	<b>0.96</b>	<b>[0.94,</b>	<b>0.99]</b>	<b>0.003</b>
Cognitive Function	0.99	[0.97,	1.01]	0.292
Youth survey age	<b>0.99</b>	<b>[0.98,</b>	<b>1.00]</b>	<b>0.001</b>
Sex * Cog Function	0.98	[0.95,	1.01]	0.110
Youth SES	0.99	[0.97,	1.00]	0.108
Family Income	<b>0.97</b>	<b>[0.95,</b>	<b>0.99]</b>	<b>0.012</b>
Sex * Family income	0.98	[0.95,	1.01]	0.224
AIC	19996.94			
Log-likelihood	-9991.47			

$\hat{\epsilon}$ : acceleration factor, the degree to which an outcome is accelerated after the first observation. AIC: Akaike Information Criterion.