

# Panel 2: Cognitive Health



**STANFORD**  
SCHOOL OF MEDICINE

*Stanford University Medical Center*

# **THE ROLE OF COGNITIVE DECLINE ON EARLY RETIREMENT: A MENDELIAN APPROACH**

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August 4, 2016

# Research Aims

Estimate the causal role of cognitive decline on early retirement decisions.

Use an instrumental variable approach called Mendelian Randomization.

# Dementia as a population health issue

- More than 35.6 million people living with dementia worldwide, increasing to 65.7 million by 2030 and 115.4 million by 2050.
- Total estimated worldwide costs of dementia are US\$604 billion in 2010.
- Important consequences on health care, caregiving, finance and savings, etc.

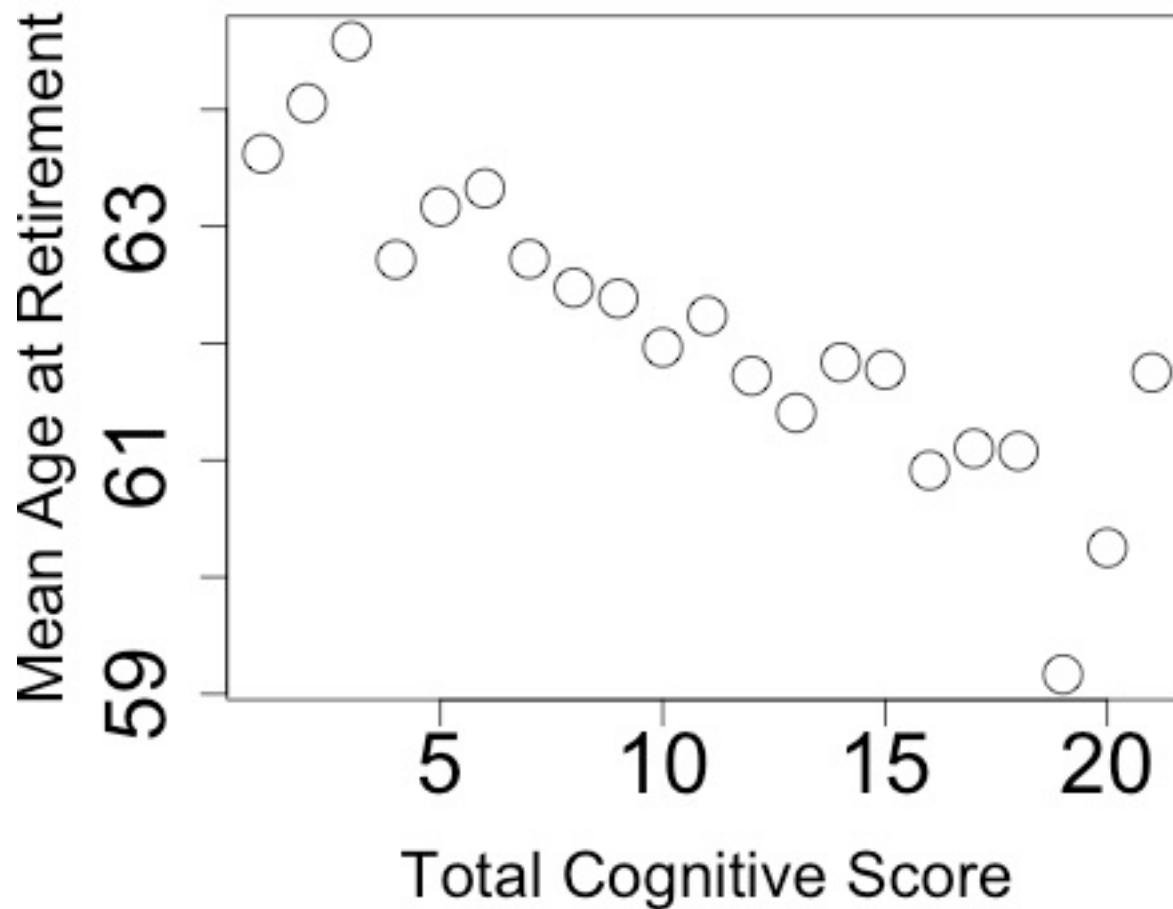
# What about earlier forms of cognitive decline?

- Still, what remains relatively understudied is the role of more mild forms of cognitive decline.
- Occurs earlier in the lifecourse and impact a different set of considerations: labor market participation, financial literacy, etc.
- Different biological pathologies may be at play with different trajectories

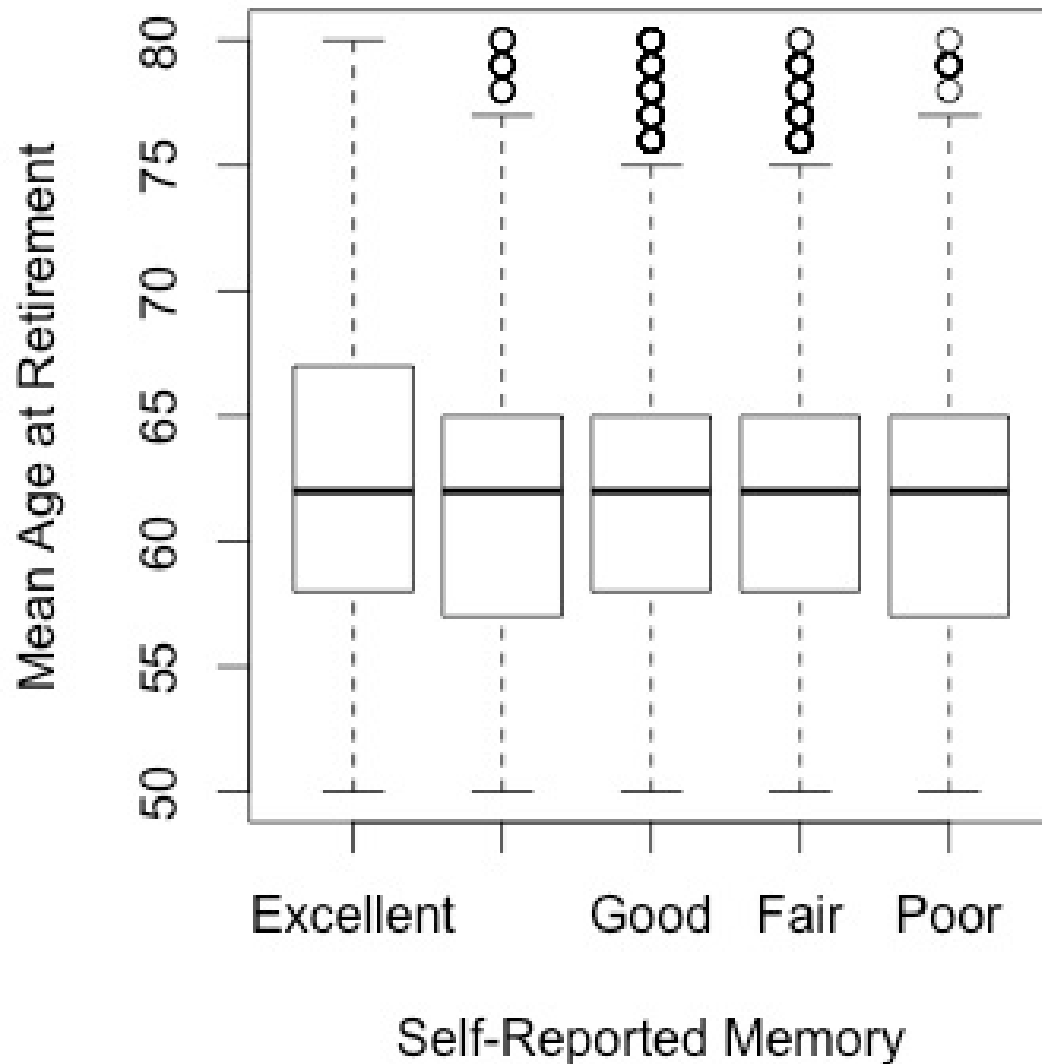
# Retirement and Cognitive Decline

- Evidence that physical health impacts early retirement
- Causal evidence that retirement → cognitive decline (Rohwedder and Willis, 2010)
- What about the other direction? This remains an open question
- Endogeneity concerns

Earlier retirement age is associated with lower cognitive scoring



# Earlier retirement age is not associated with lower self-rated memory





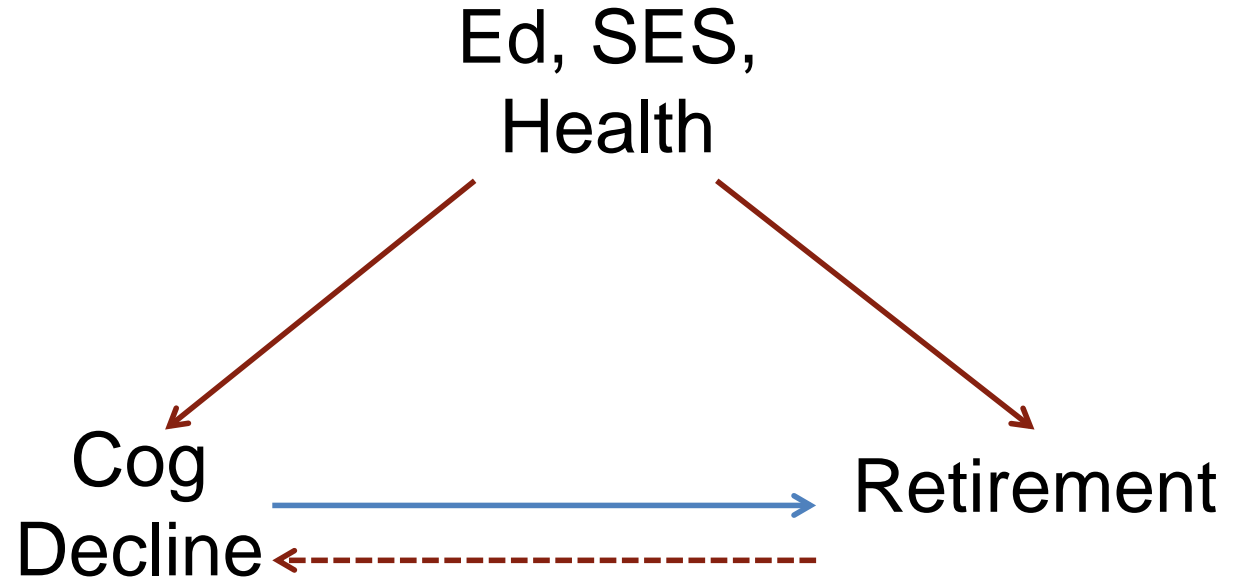
# Mendelian Randomization Approach

- An instrumental variable approach using a genetic instrument
- If assumptions are met, it can calculate an unbiased causal estimate
- 179 + studies in epidemiology (Beof et al. 2015)
- Limited number in economics (Norton and Han, 2008; Ding et al. 2009; Fletcher and Lehrer, 2011)

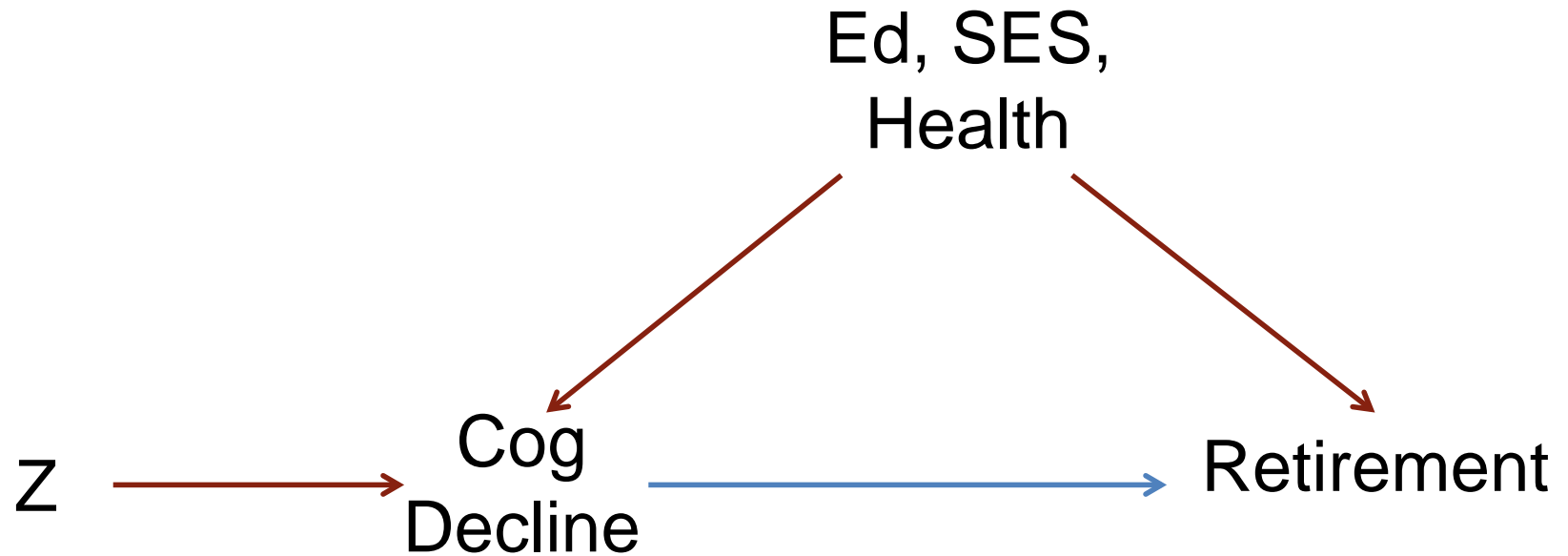
# Instrumental Variables Approaches Using Genetic Instruments



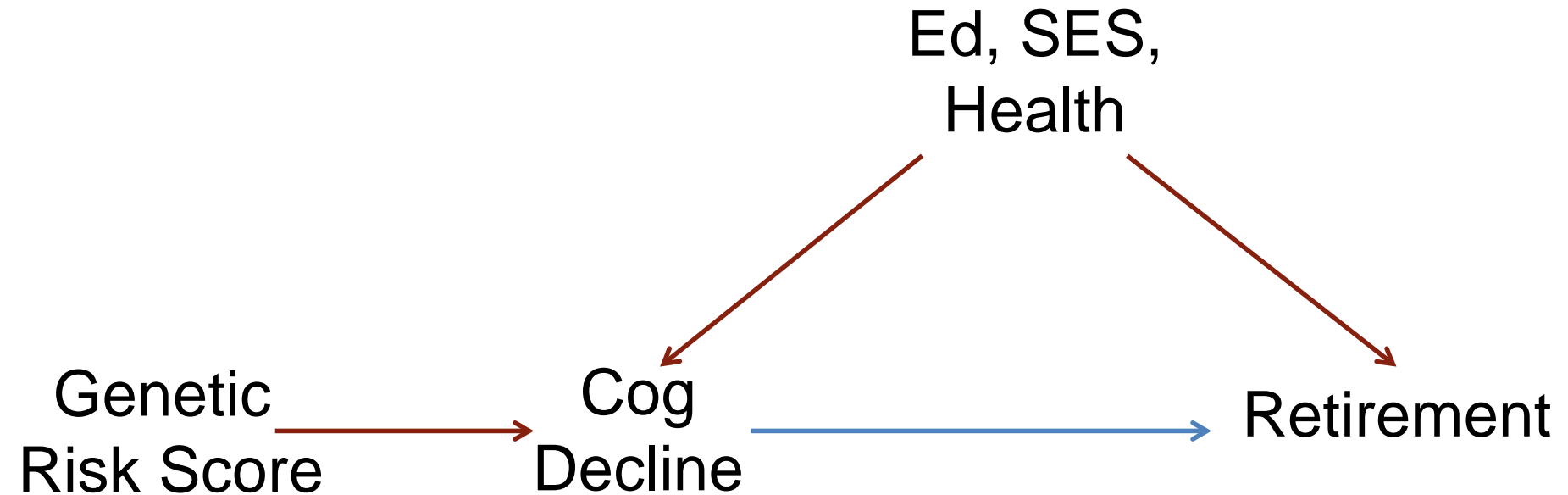
# Instrumental Variables Approaches Using Genetic Instruments



# Instrumental Variables Approaches Using Genetic Instruments



# Instrumental Variables Approaches Using Genetic Instruments



# Data and sample

## Health and Retirement Study (HRS)

Biennial Survey 1992-2014

Nationally-representative of U.S. 50+

N= 37,131 respondents;

298,536 observations over time

## HRS Genetic Data

2.5 million Single-Nucleotide Polymorphisms

12,595 respondents

# Measures

- Cognitive Decline= Cognitive Age Slope between Wave 3 and Wave 10
- Retirement = Age at Full or Partial Retirement
- Instrument= Genetic Risk Score

# Sample Restrictions

N= 20,652 with cognitive measures

N=12,595 total genotyped

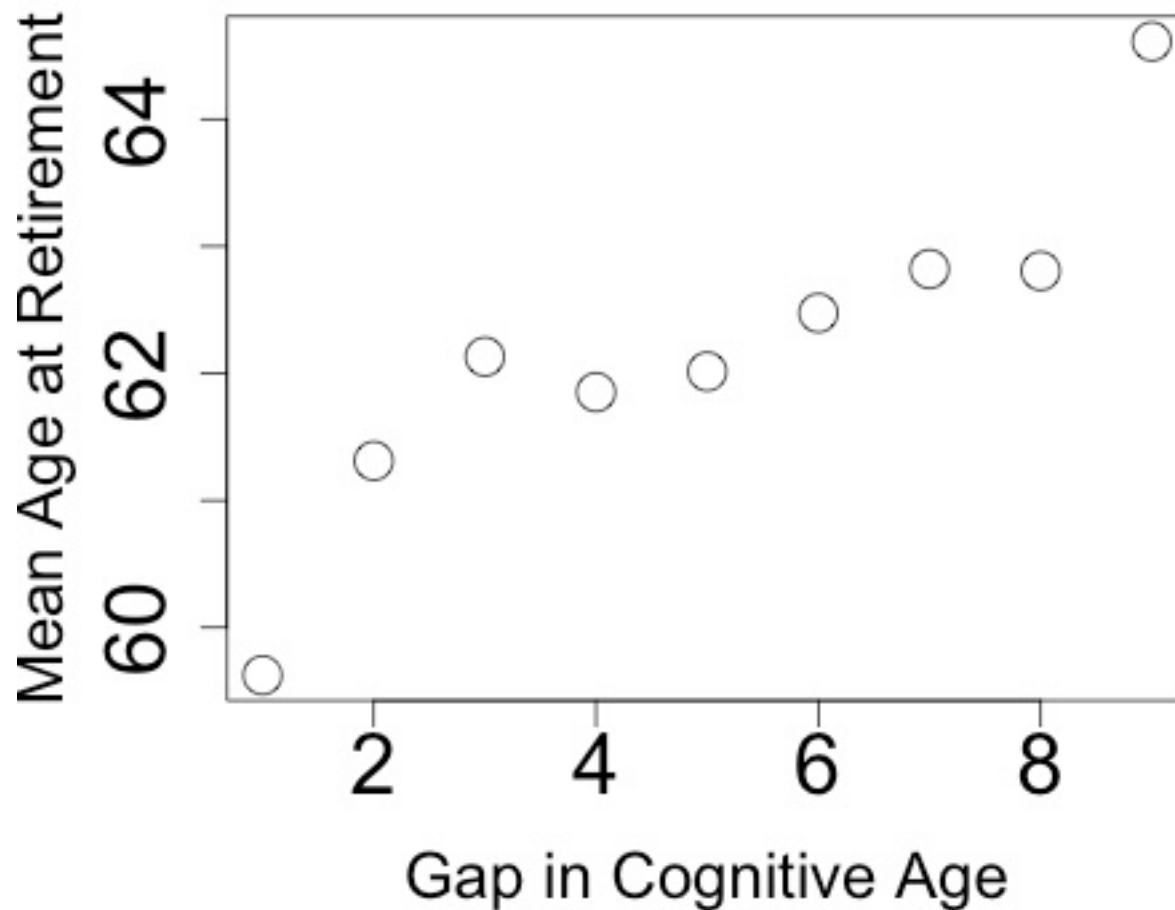
N= 9,218 non-Hispanic whites only

N= 6,836 post-retirement (non-Hispanic whites)

N= 6,438 retired and genotyped



Earlier retirement age is associated with lower cognitive age



# Genes as Instruments: Mendelian Randomization

- Mendel's First Law: Genes segregate randomly and independently of environmental factors
- Mendel's Second Law: Genes segregate independently of other traits
- Little individual knowledge of genetic makeup

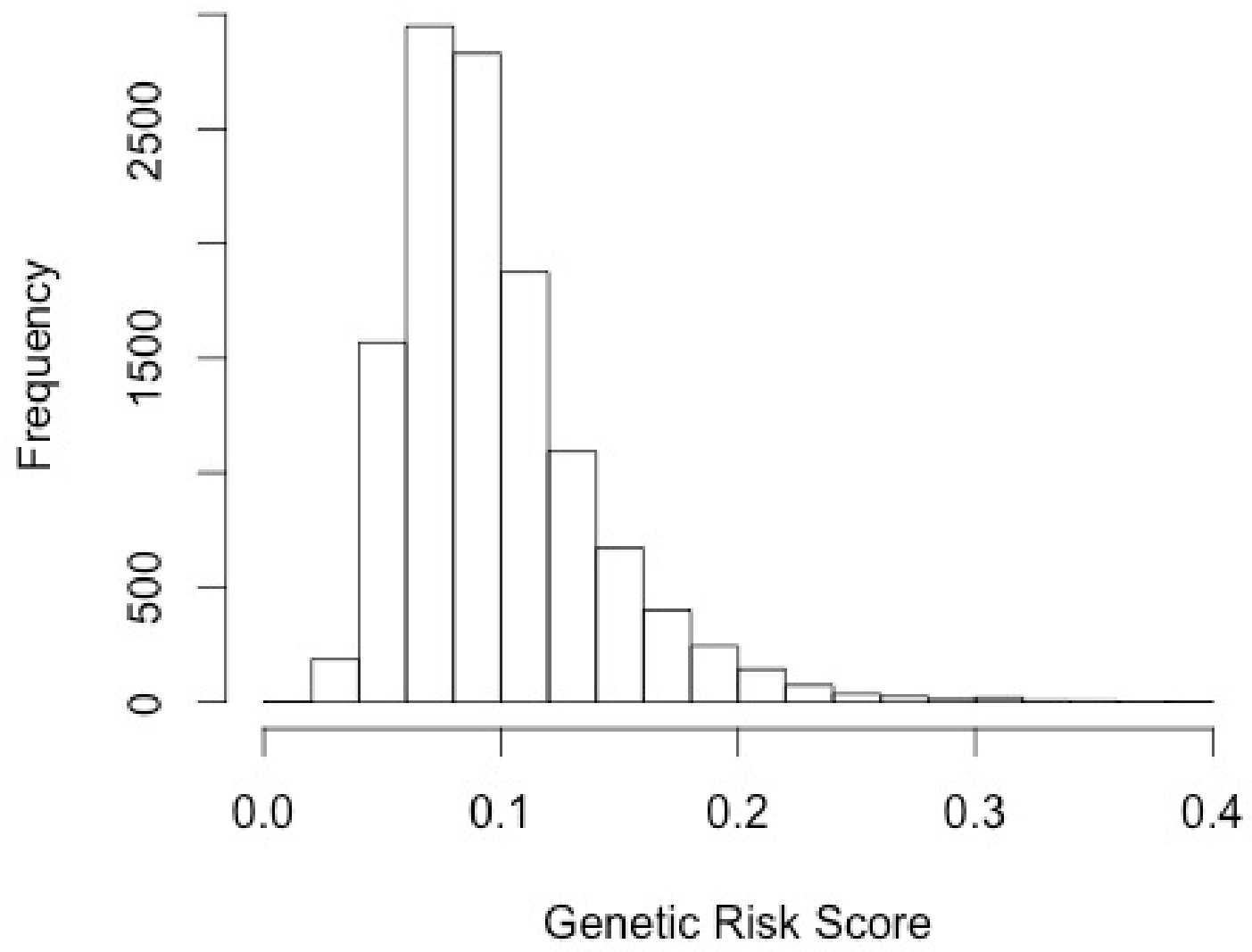
# The Instrument: Genetic Risk Score (GSR)

- Compilation of 19 SNPs that are associated with cognitive decline and memory loss, including APOE.
- Risk Score is created for each individual by creating a weighted sum of risk alleles (Lambert et al., 2013)
- Demonstrated to be associated with memory loss in the HRS population (Marden et al., 2016)

# Genes included in instrument (GRS)

- APOE(rs429358 & rs7412)
- BIN1 (rs4663105)
- CLU (rs9331896)
- ABCA7 (rs3764650)
- CR1 (rs6656401)
- PICALM (rs10792832)
- MS4A6A (rs983392)
- CD33 (rs3865444)
- CD2AP (rs10948363)
- EPHA1 (rs11771145)
- HLA-DRB5—HLA-DRB1 (rs111418223)
- PTK2B (rs28834970)
- SORL1 (rs11218343)
- SLC24A4 RIN3 (rs10498633)
- DSG2 (rs8093731)
- INPP5D (rs35349669)
- MEF2C (rs190982)

# Histogram of Genetic Risk Score



# Assumptions for Mendelian Randomization

Assumption 1 (Non-zero effect of the instrument):

Instrument must be associated with exposure

Assumption 2 (Independence):

Instrument must not differ systematically with respect to confounders

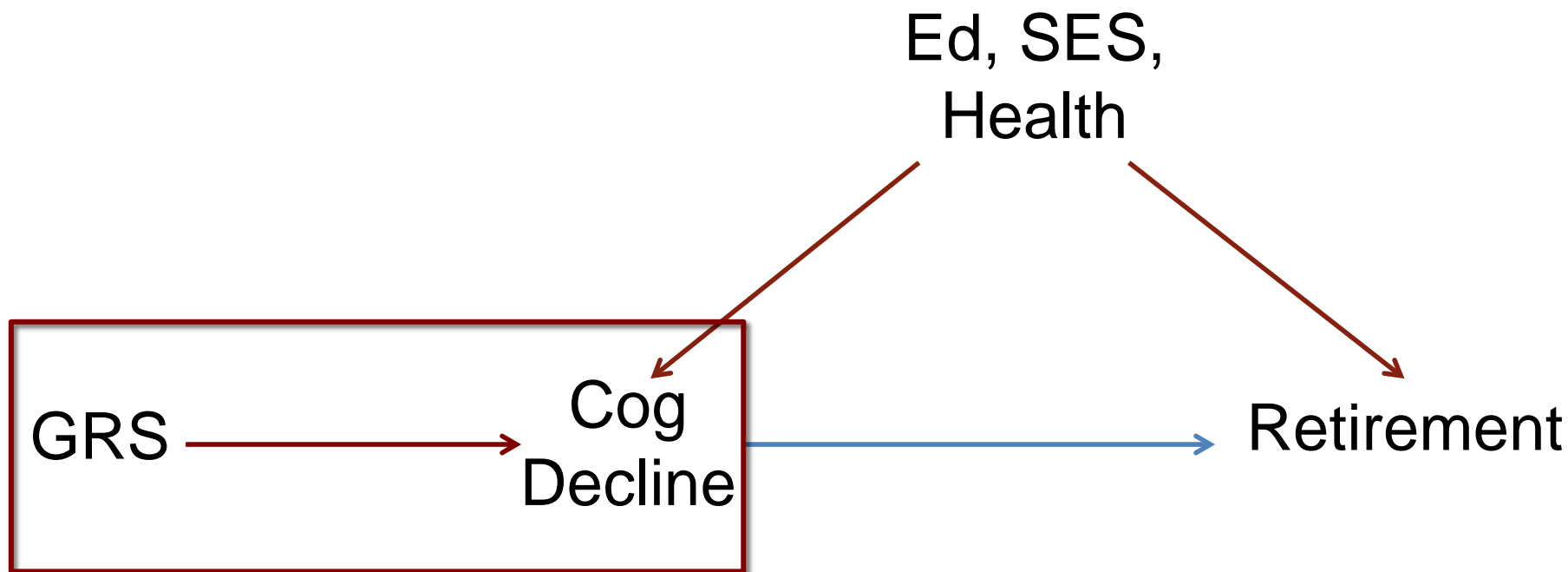
Assumption 3 (Exclusion):

Instrument not associated with outcome except through exposure

Assumption 4 ( :

# Assumption 1:

Instrument must be associated with exposure



# Satisfying Assumption 1

$$\text{Cognitive Age} = b_0 + b_1 \text{ GRS} + e$$

	Estimate	Std. Error	T value	Pr(> t )
Intercept	0.41904	.03515	11.922	< 2e-16 ***
Genetic Risk Score	.06378	.01334	-4.78	6.22e-05 ***

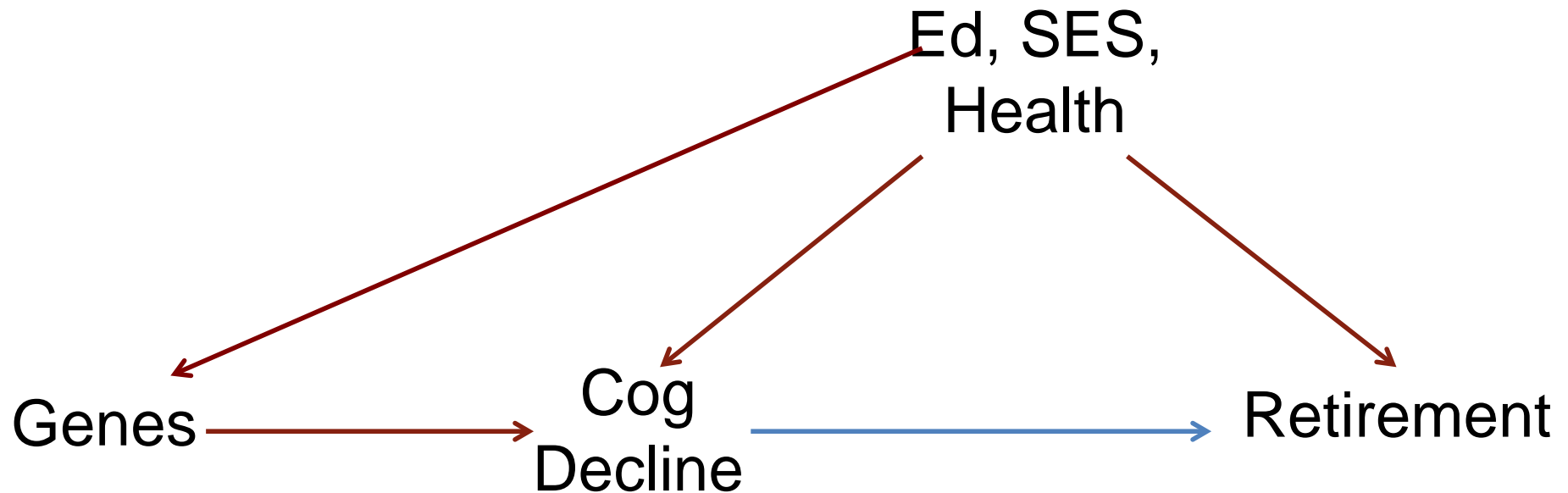
F-statistic: 22.85

Controlling for 5 principal components



## Assumption 2:

Instrument must not differ systematically with respect to confounders



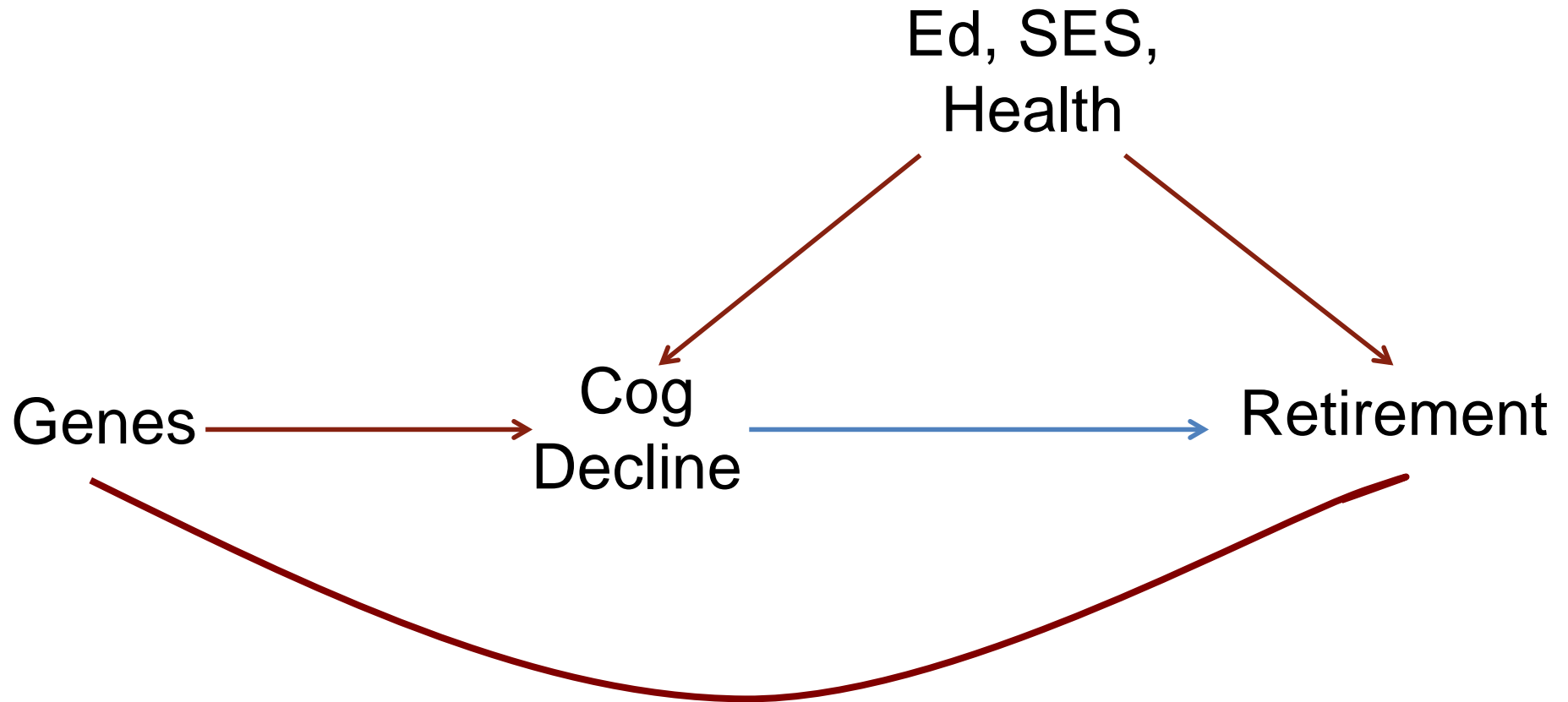
# Testing associations with confounders

No systematic differences by genotype with:

- Education
- Age
- Heart Disease
- Stroke
- Blood Pressure
- Income
- Wealth

# Assumption 3:

Instrument not associated with outcome



# Genetic Pleiotropy

- Genes may act on retirement through other biological pathways
- 19 SNPs are relatively well-documented to have no other biological causes that we can't account for
- Testing individual biological pathways

# Results

## Association of Cognitive Age on Retirement Age

	Estimate	Std. Error	Pr(> t )
Cognitive Age: Naïve Estimate	0.116	.0284	6.97e-13 ***
Cognitive Age: Genetic Risk Score Instrument	-0.663	3.9091	0.8713

# Preliminary Conclusions

- The Genetic Risk Score appears to satisfy the assumptions necessary to be a valid instrument
- Using a Mendelian Randomization method, there is no statistically significant evidence that cognitive decline impacts retirement age
- Consider 2-sample IV to increase power

# Thank you!

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# Discussion of “The Role of Cognitive Decline in Retirement Decisions”

Kathleen J. Mullen, RAND

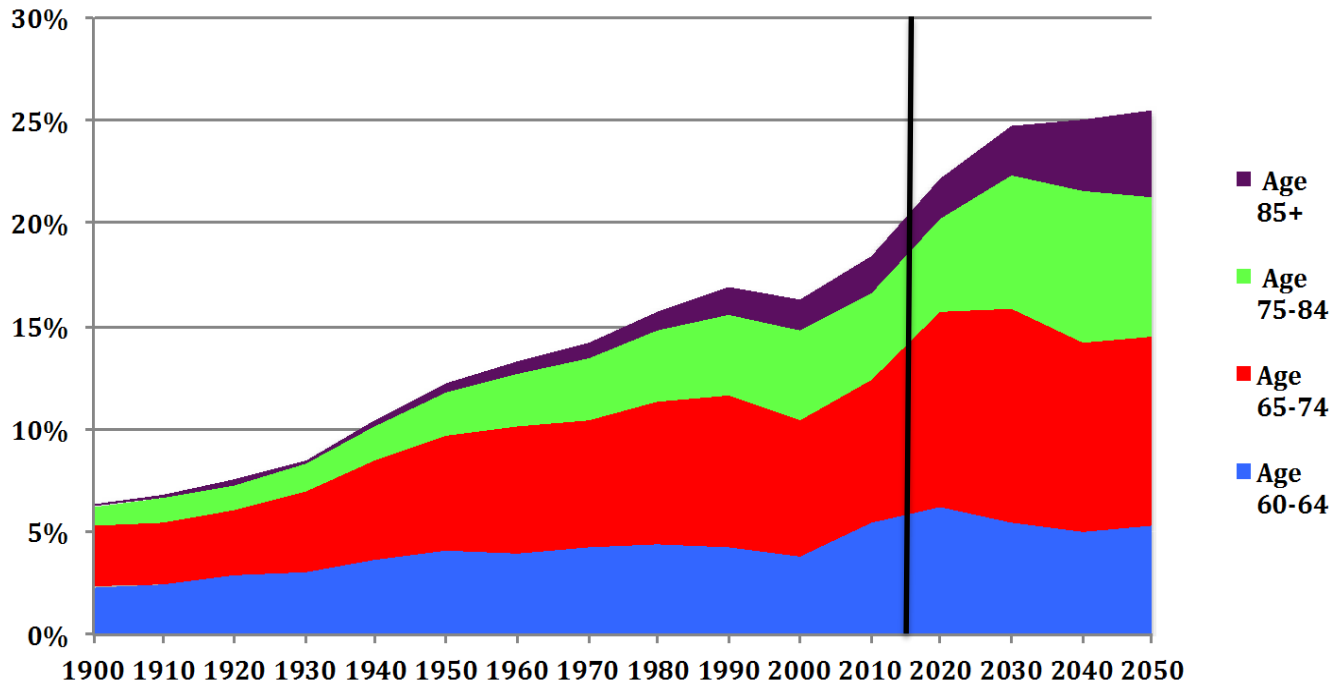
RRC Annual Meeting

August 2016



# Population Aging in the United States

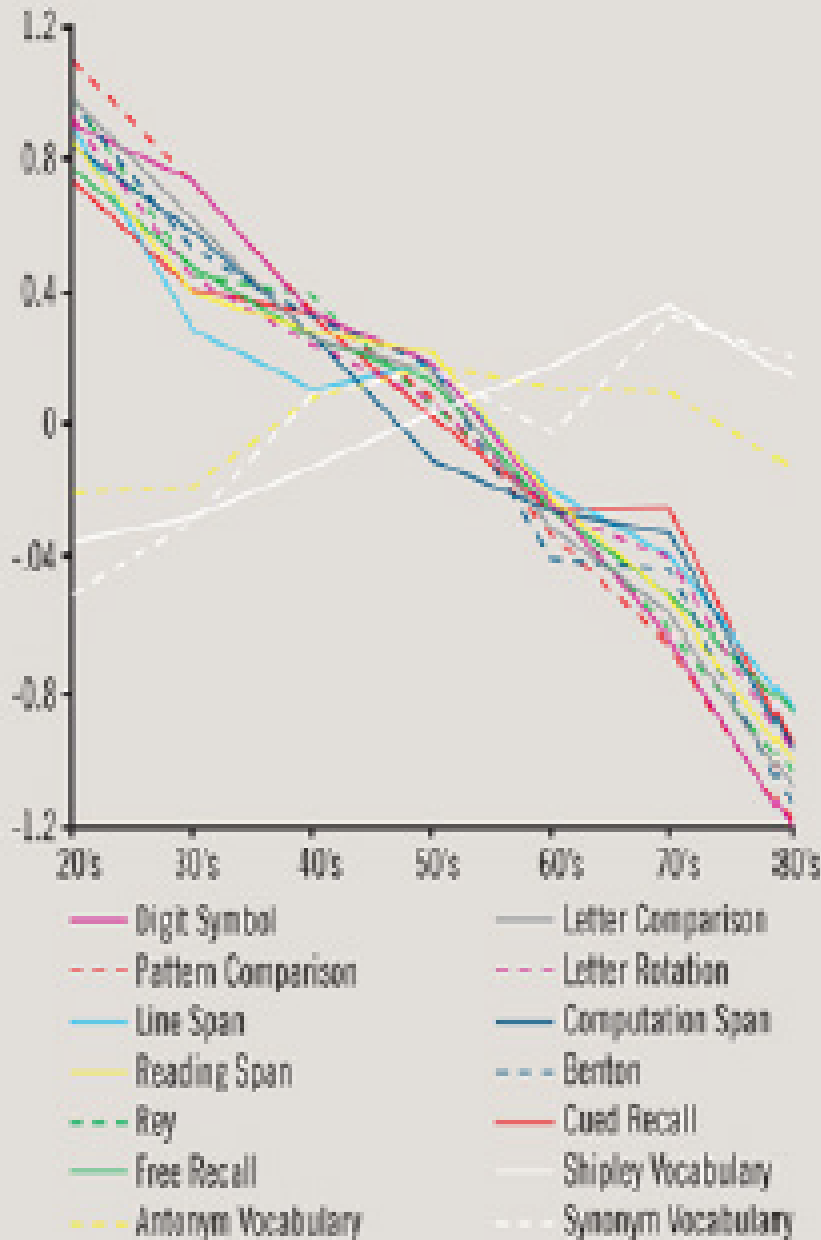
Percent of U.S. Population Age 60+ 1990-2050  
Actual and Projected



Source: U.S. Census Bureau, compiled by U.S. Administration on Aging

**The percent of the U.S. population aged 60+ is projected to increase by 21% between 2010 and 2020, and by 39% between 2010 and 2050.**

## Normal Aging and Cognitive Test Performance<sup>1</sup>



Decreases in mechanics (speed) may be compensated with increases in other areas (e.g., vocabulary, experience)

Source: Park et al. (2002) from Levenson, 2016, RAND Summer Institute presentation

# Three heartening trends

- Decline of cognitive mechanics starting later
- Increases in intellectual functioning across cohorts
  - Dementia prevalence declining across generations (Matthews et al, 2013, Lancet; Wu et al, 2015, Lancet Neurology; Satizabal et al, 2016, NEJM)
- Evidence that “training” interventions can slow decline in mechanics

# What this paper tries to do

- Goal is to estimate role of cognitive decline on retirement timing
- Problem: people experiencing cognitive declines might have retired earlier anyway
- Authors' solution: find an instrument that exogenously pushes people into earlier cognitive decline and see how that affects retirement
  - IV = Genetic risk score

# 4 assumptions for validity of IV

- Independence
  - “As good as random” assignment
- Exclusion restriction
  - Single causal channel
- First stage
  - Genetic risk score affects cognitive decline
- Monotonicity
  - Genetic risk score increases cog decline for everyone (need for LATE, i.e., IV = weighted avg of underlying heterogeneous causal effects)

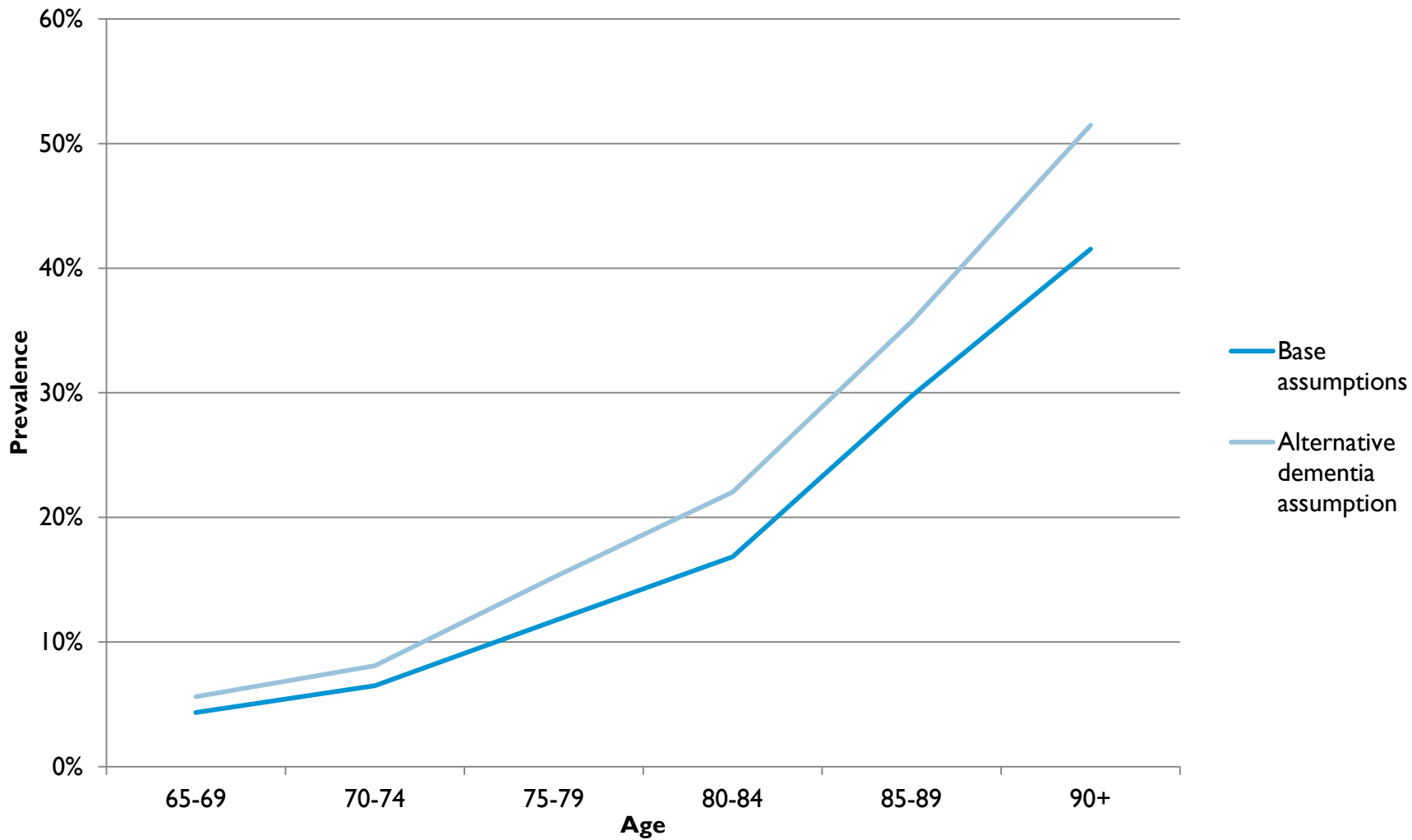


AUGUST 4, 2016

*Melissa M. Favreault and Richard W. Johnson*  
*Urban Institute*

# Our goals

- Understand late-life disability risk
- Examine how out-of-pocket expenses for health care and long-term services and supports (LTSS) vary by individual characteristics, combinations
- Compare ***stylized***, roughly cost-equivalent policy options that address heavy out-of-pocket cost burdens for people with late-life disability
  - Social Security
  - Medicare cost sharing
  - Medicaid LTSS cost sharing
  - New LTSS insurance options
- Look across program silos on a level-playing





# Our findings

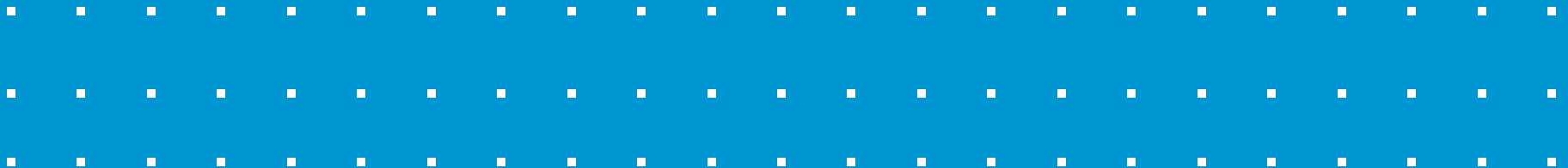
- Out-of-pocket spending burdens fall heavily on those with long-term disabilities
  - Risk of ever experiencing a long-term disability is significant
    - Longer you live, the greater chance you will become disabled
  - For those with long-term disabilities, costs are potentially impoverishing
- Benefits for all the interventions we examine flow disproportionately to older adults with disabilities
  - Targeting differs can be refined with further policy development work



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# Context



# Costs of late-life disability

- LTSS literature

- *Risks*: Kemper, Komisar, Alekcih (2005/2006); Stallard (2011); Favreault and Dey (2015); *Policy options*: Rivlin and Wiener (1988), Wiener, Illston, and Hanley (1994); Tumlinson, Hammelman, Stair, and Wiener (2013); Favreault, Gleckman, and Johnson (2015)

- Literature on costs of cognitive impairment

- Alzheimer's Association (2015), Hurd, Martorell, Delavande, et al. 2013; Yang, Zhang, Lin, et al. (2012); cross-nationally: Wimo, Jönsson, Bond, et al. (2013)

- Literature on out-of-pocket health care risk

- Fronstin, Salisbury, and VanDerhei (2015); Hatfield, Favreault, Chernew, McGuire (2016); Schoen, Buttorff, Andersen, and Davis (2015); Zuckerman, Shang, and Waidmann (2012)

- Combined financial risks

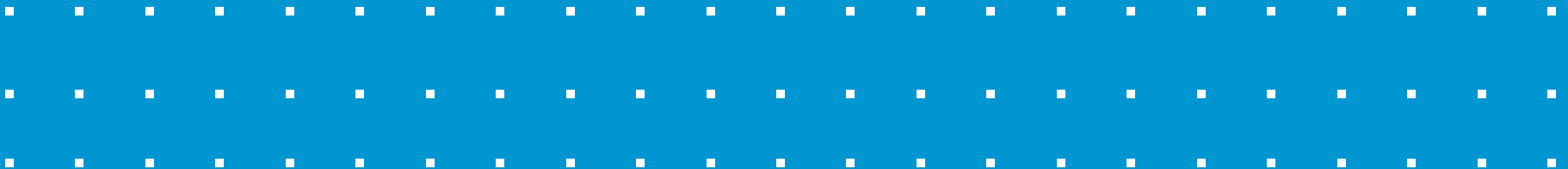
- Spillman and Lusitzi (2000) E



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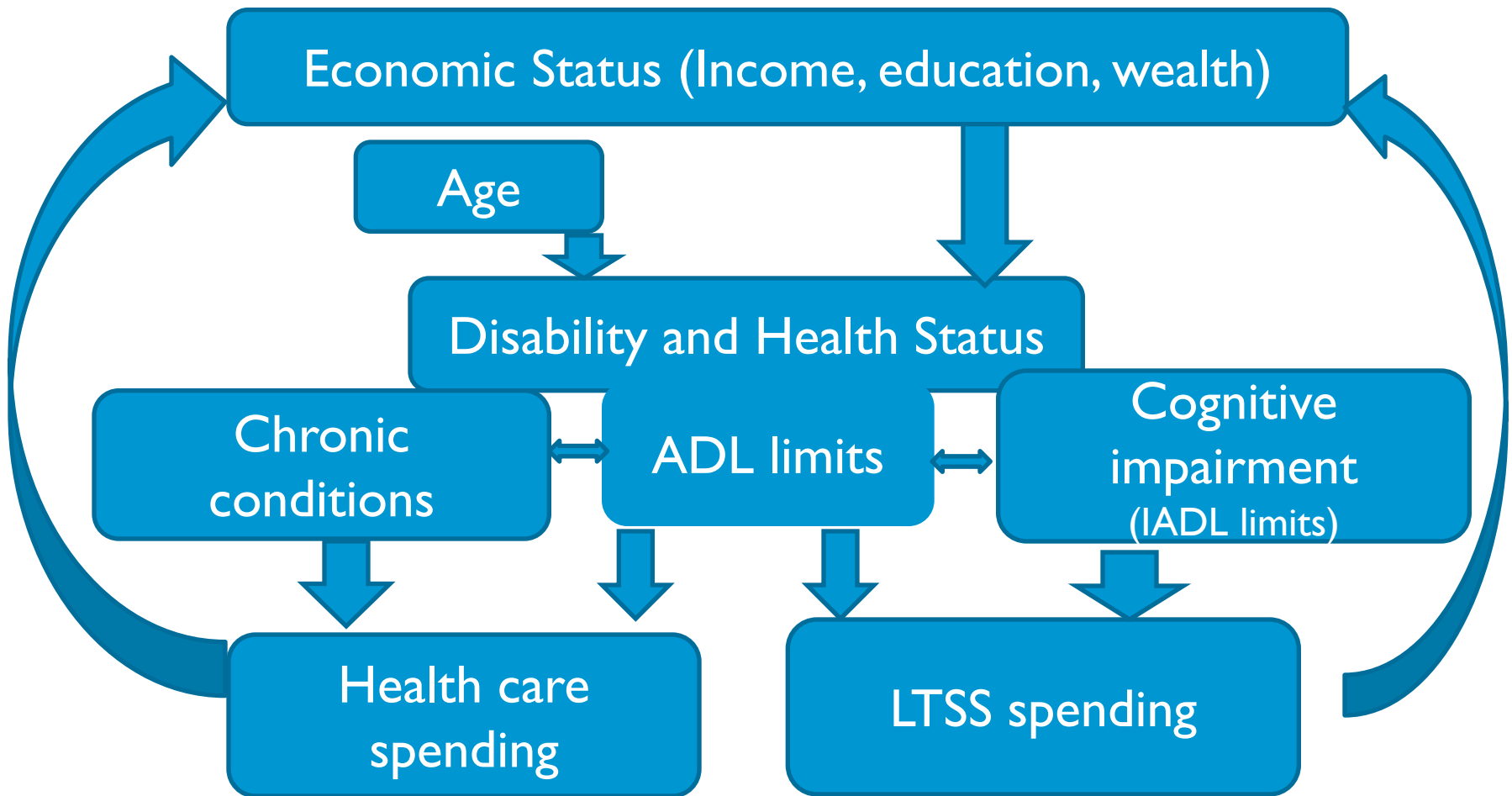
# Methods



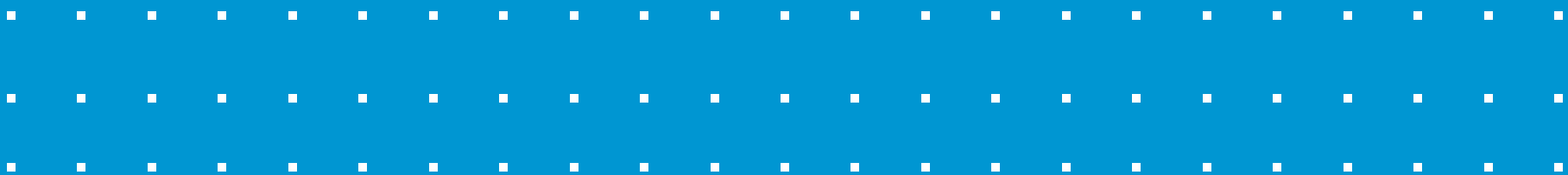
# Our approach

- Take an existing, well-validated model: DYNASIM3
  - SIPP-based starting file
  - Projects for 75 years
- Add in disability, LTSS, and health care spending modules using HRS, MCBS, and NHATS data
  - Prevalence, intensity, costs, payers
- Calibrate to OASDI and HI TR assumptions
- Validate cost and projections against aggregates, academic literature
  - “Black box”/“Nate Silver-ize”
  - Sensitive to projections about the future, especially morbidity improvement and spending growth
    - Use advisory boards to vet assumptions & choices
- Simulate alternatives

# Modeling challenges: Interrelationships over the life course



# Baseline Risk and Spending Estimates

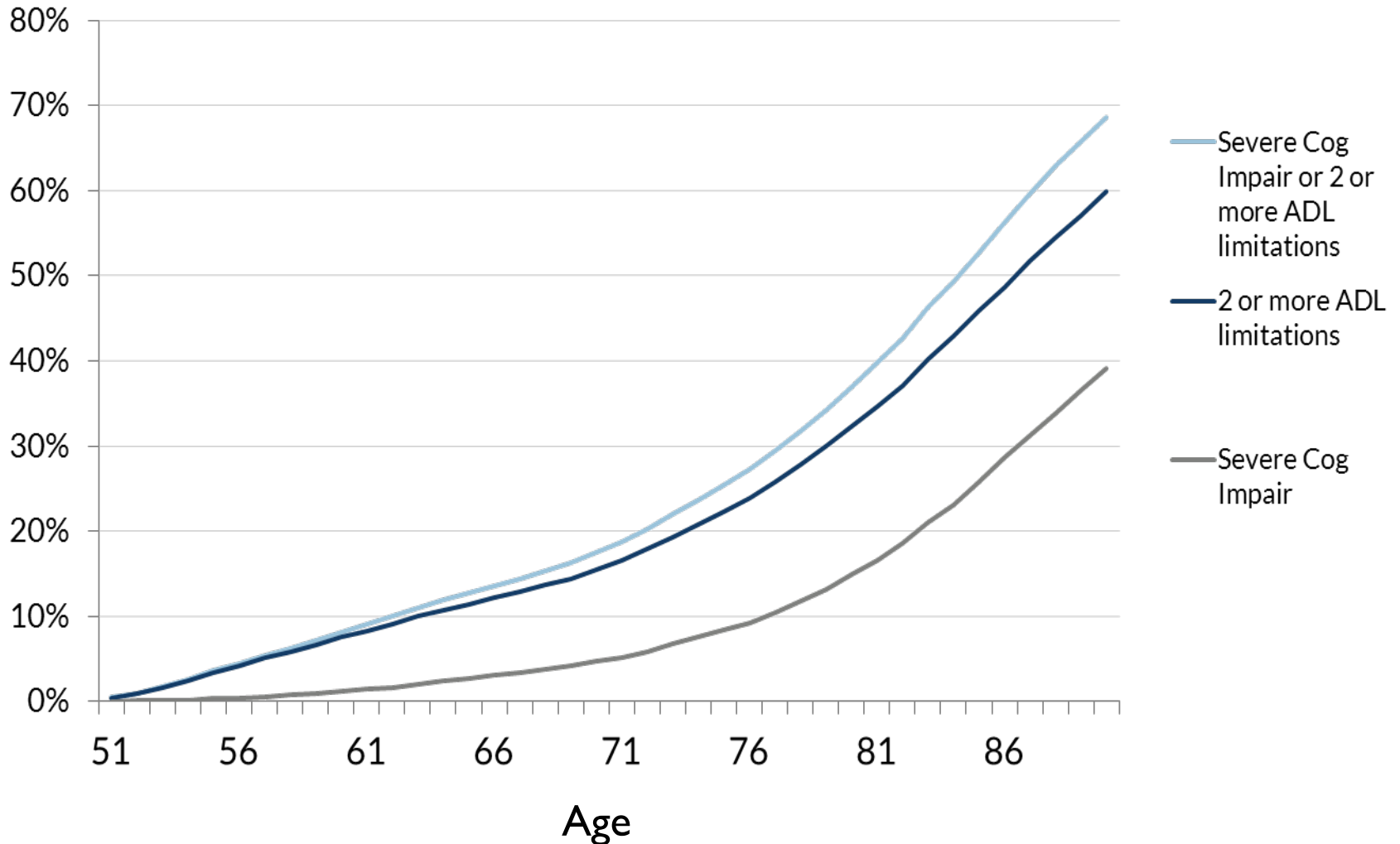


# Our analytic focus

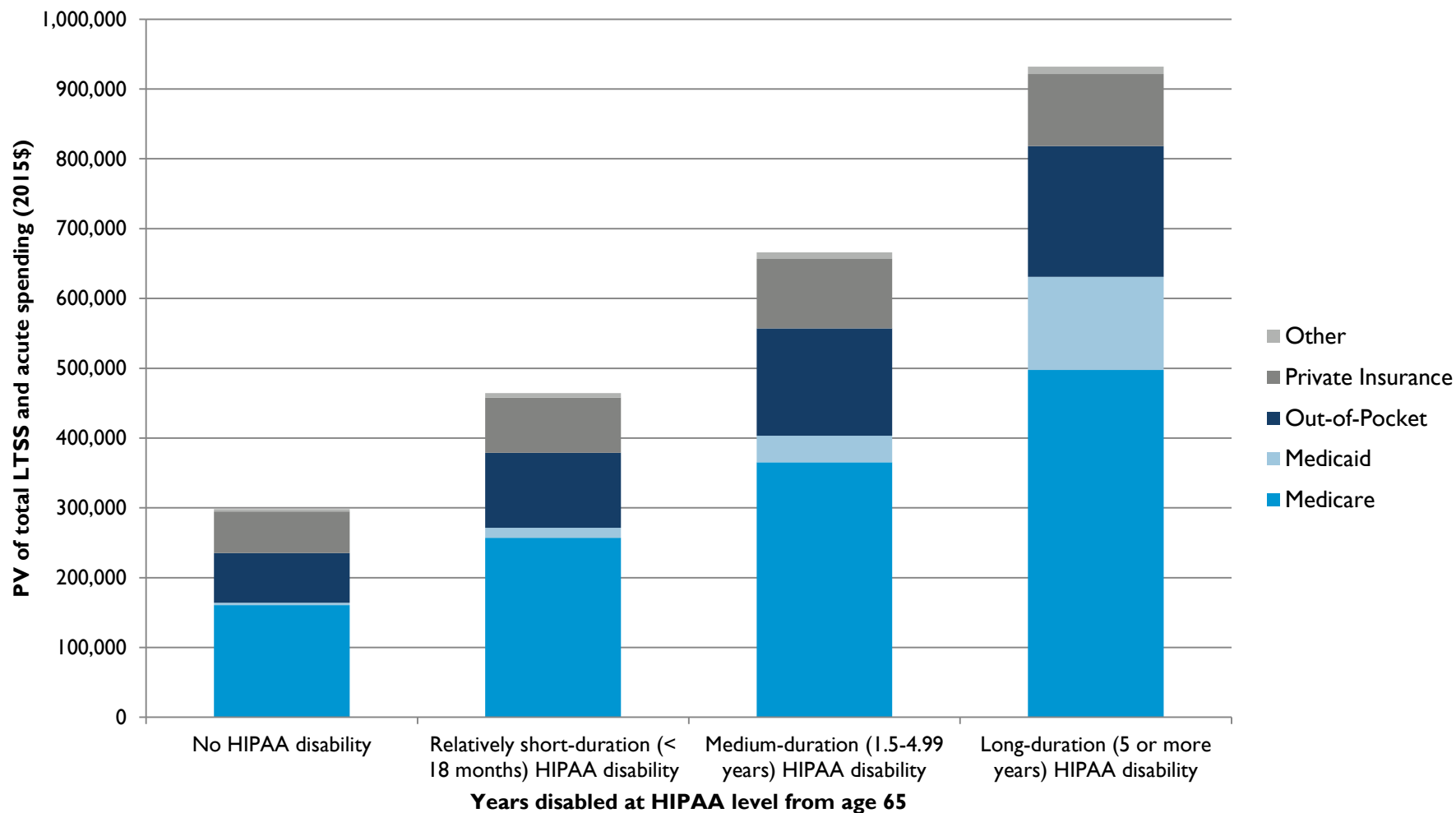
- Adults ages 65 and older
  - Focus on costs from age 65 through death
  - Paper also shows cross-section burdens
  - Present discounted values, real \$2016, 2.7% discount rate
- Acute care costs, including premiums (Medicare, Medigap) and point-of-care cost shares
- Formal LTSS, which including nursing home care, paid home care, residential care
  - Informal care huge part of LTSS, but not in this draft
- Focus on severe disability
  - HIPAA definition for qualifying plans: 2 or more ADL limits or severe cognitive impairment



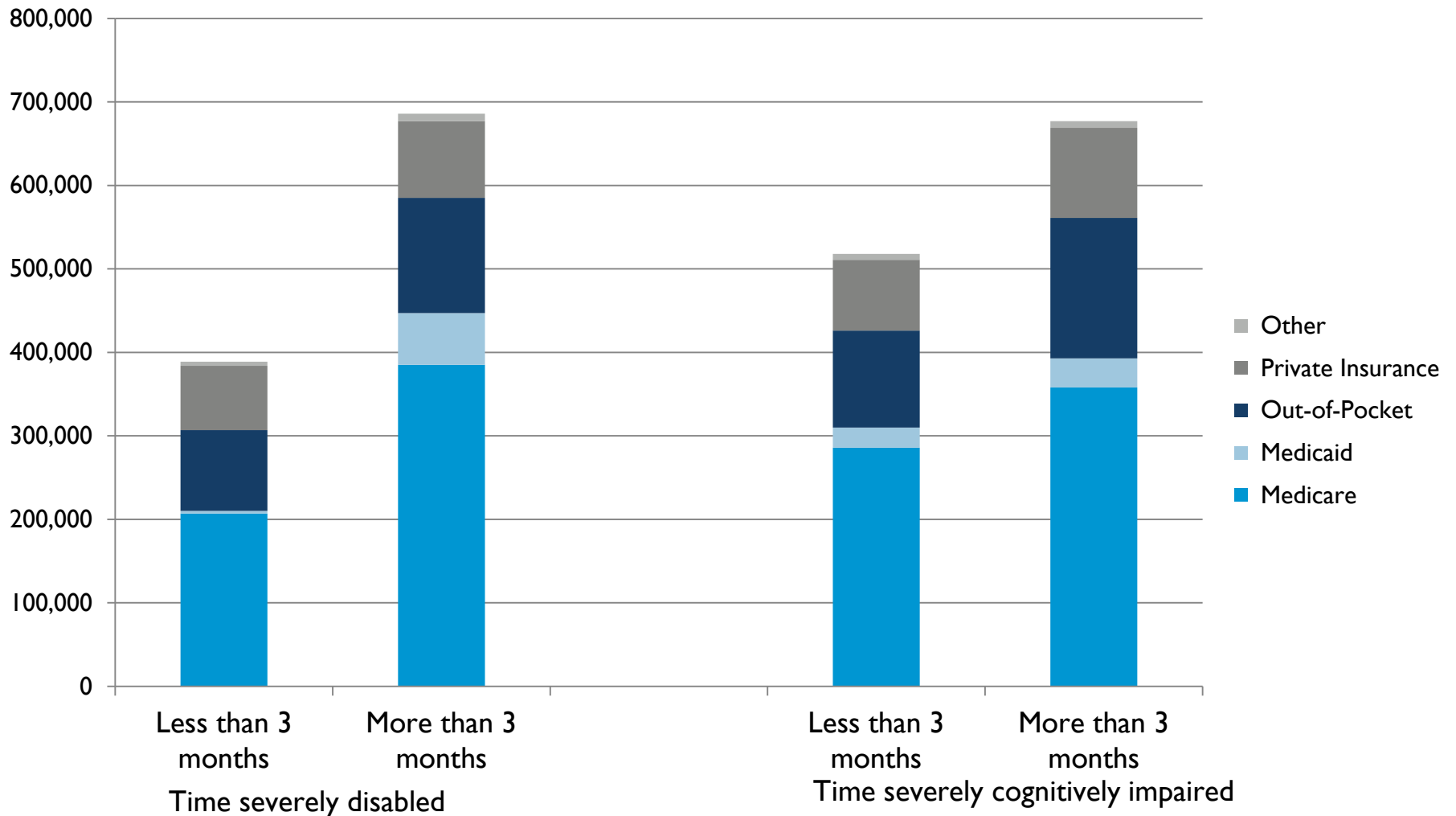
# Chances of ever having severe disabilities increases with age



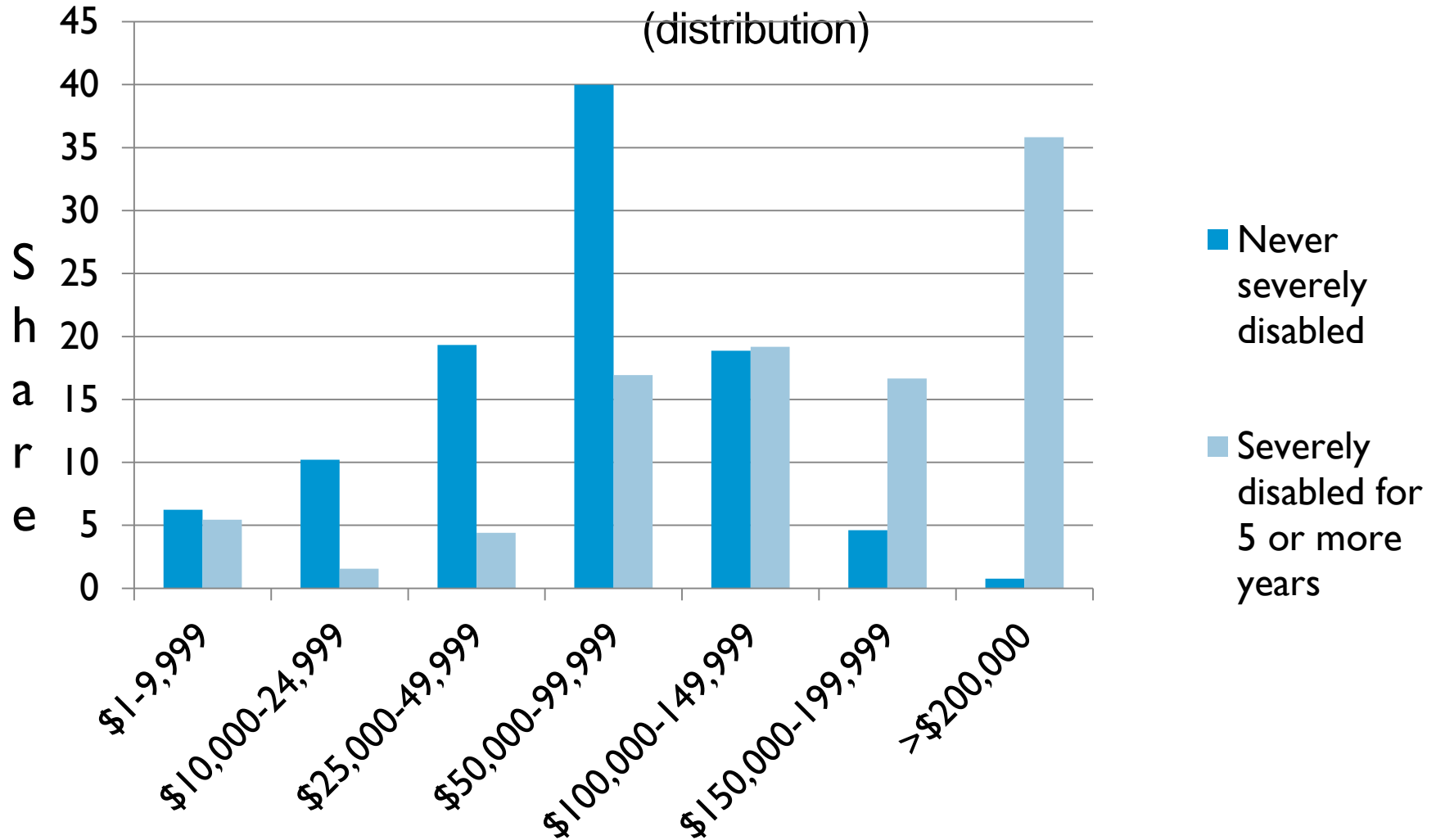
Authors' calculations from HRS



Source: Authors' tabulations from DYNASIM.

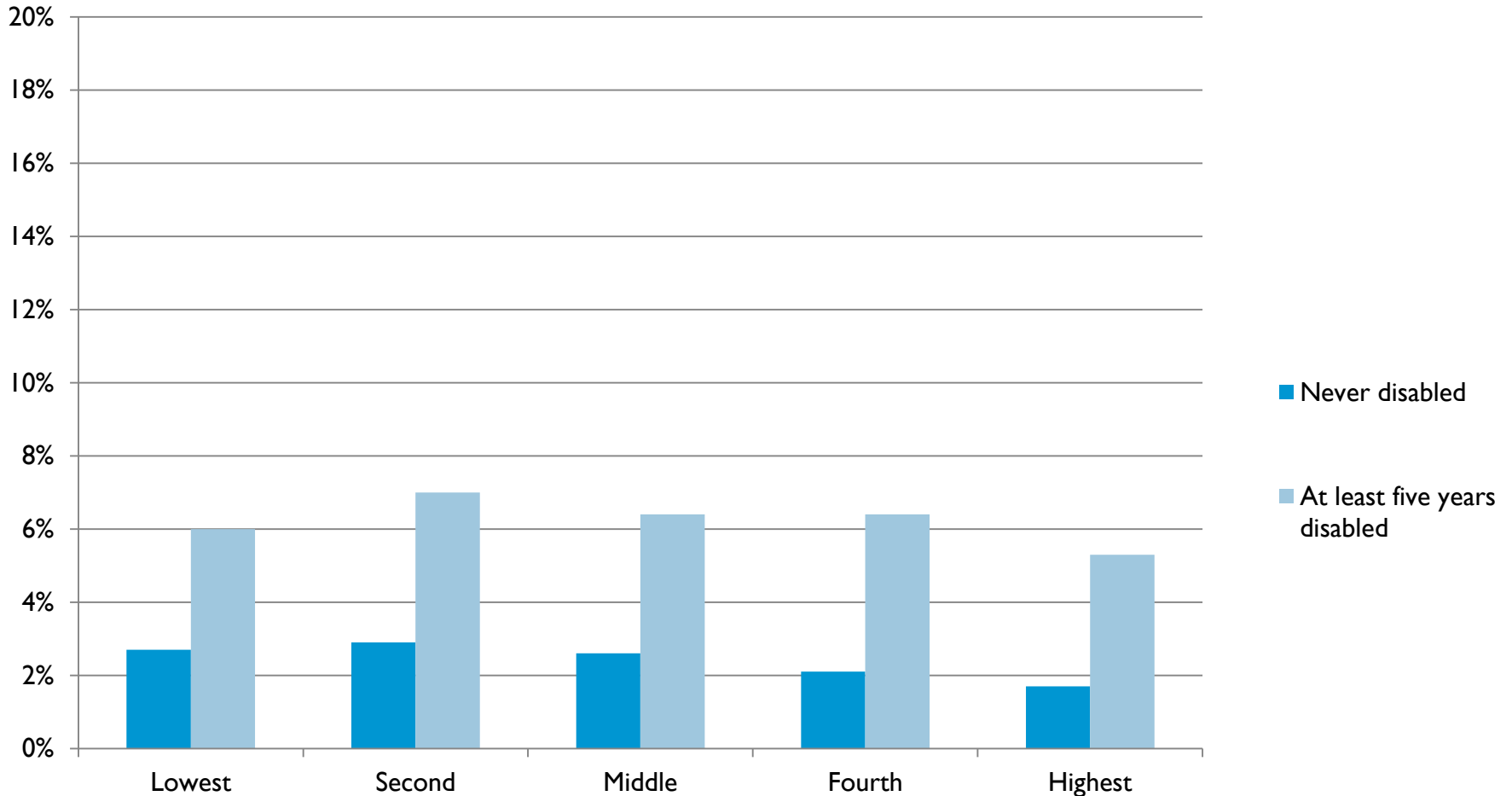


# Mean spending masks important variation: Total acute-care and LTSS out-of-pocket costs



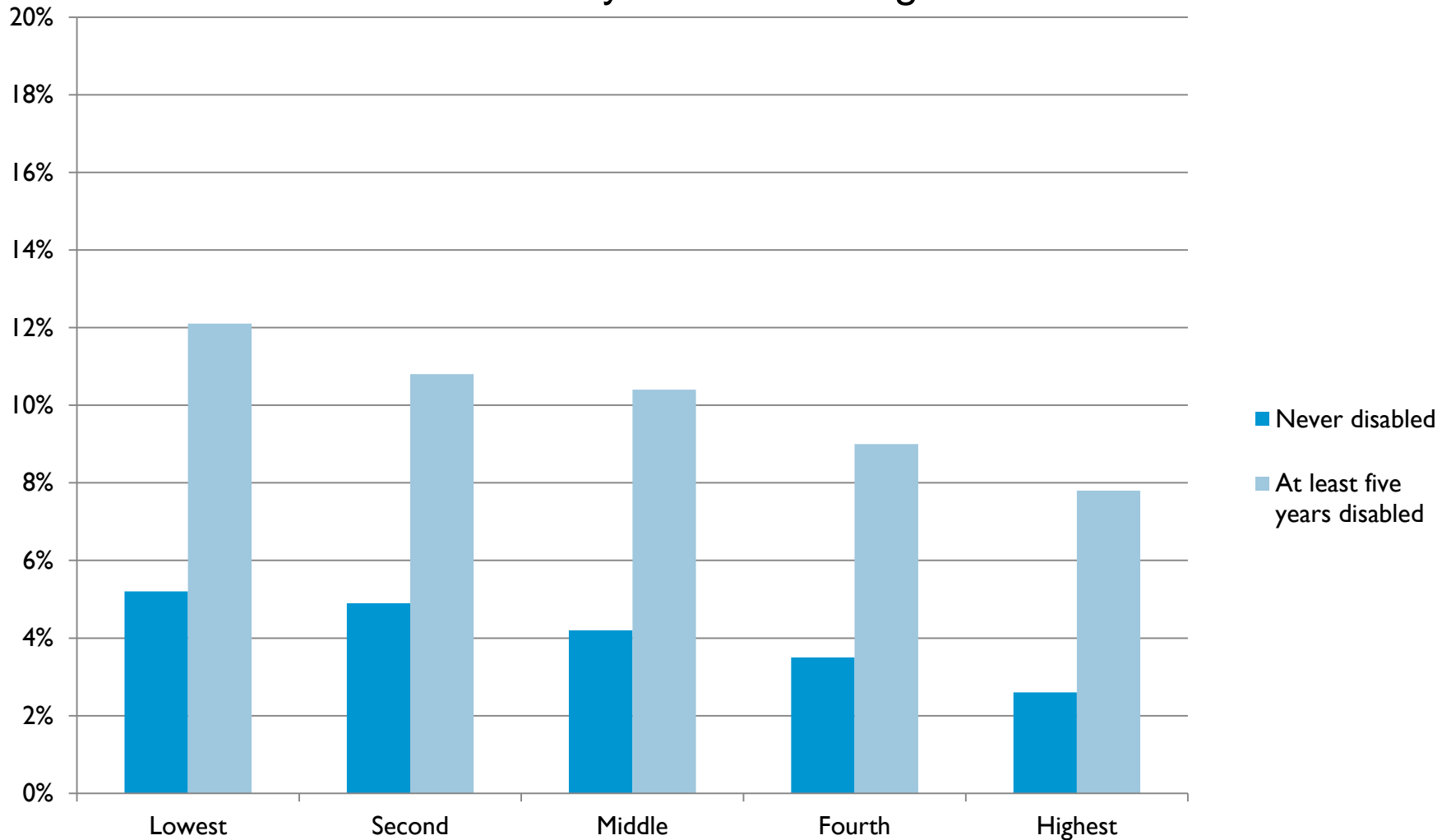
# Spending burdens vary by lifetime income:

**Median** total acute-care and LTSS out-of-pocket costs as a percent of family lifetime earnings



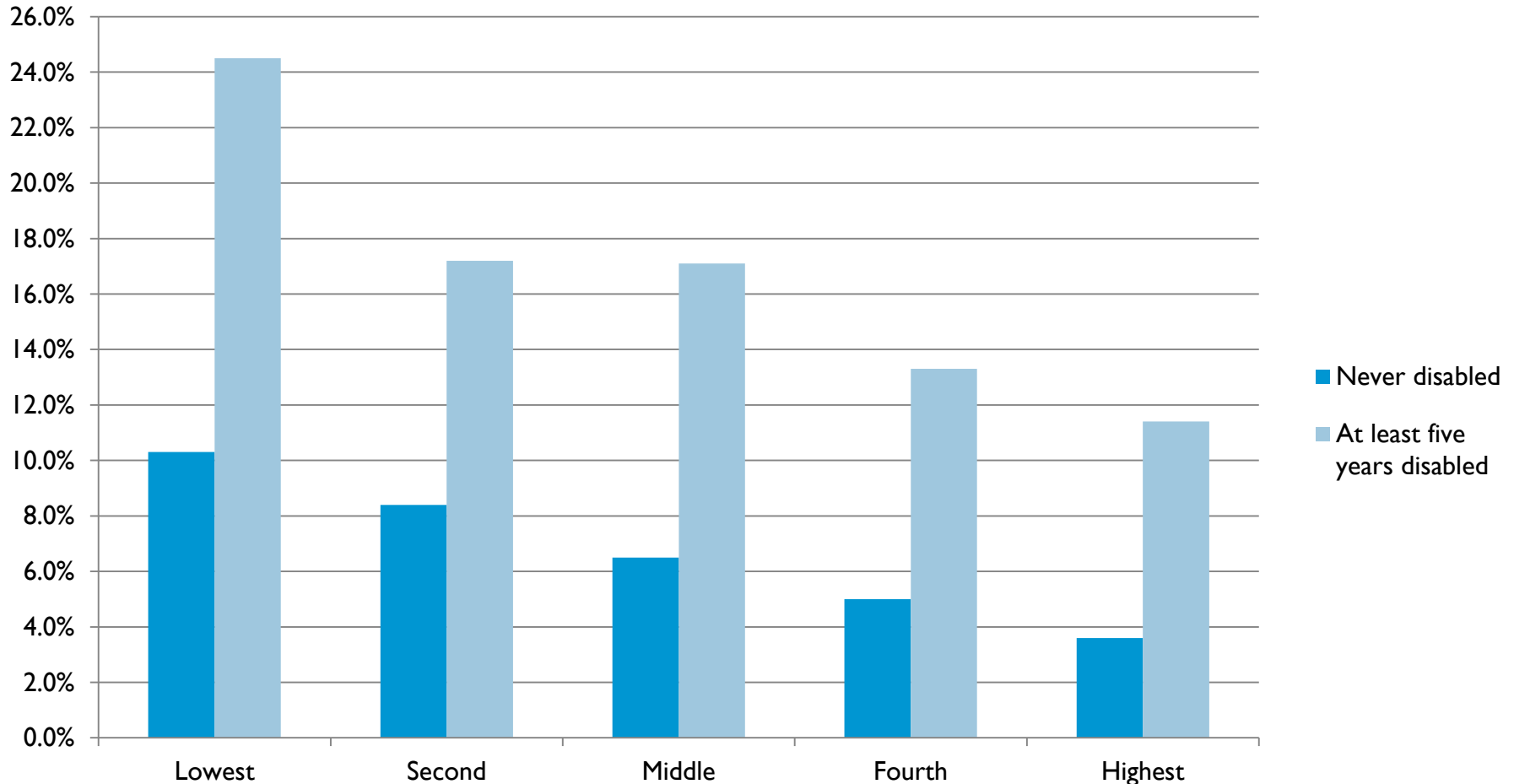
# Spending burdens vary by lifetime income:

**75<sup>th</sup> percentile** of total acute-care and LTSS out-of-pocket costs as a percent of family lifetime earnings



# Spending burdens vary by lifetime income:

**90th percentile** of total acute-care and LTSS out-of-pocket costs as a percent of family lifetime earnings

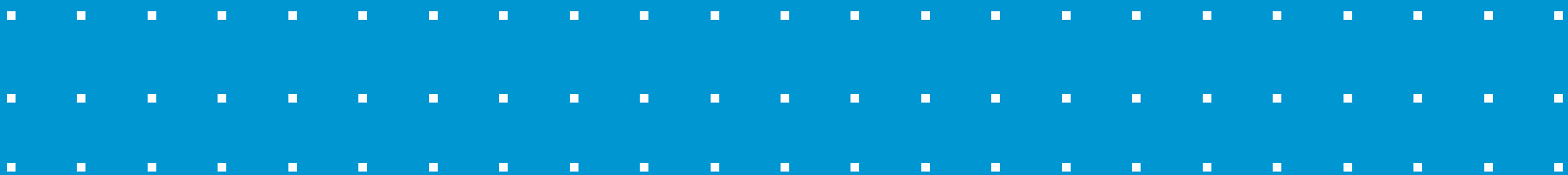




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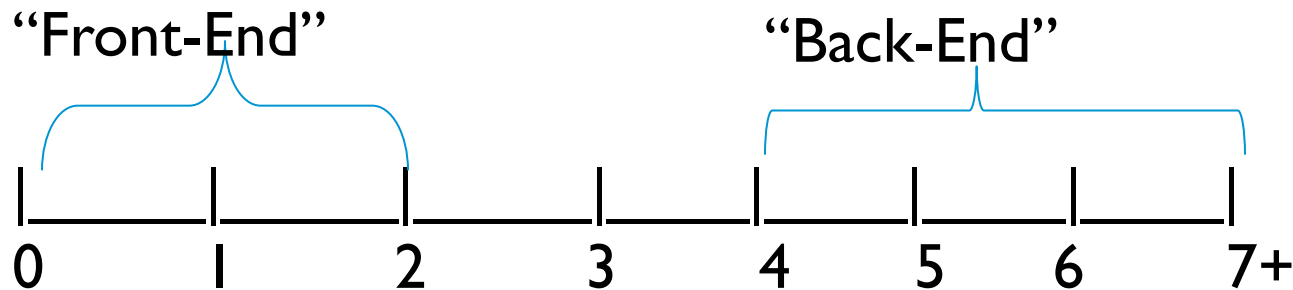
# Federal Policy Options





# Alternate policy options for addressing out-of-pocket risk from late-life disability

- Social Security
  - Benefit increases at ages 81-85 or 86-90
- Medicare point-of service cost sharing
  - Targeted to a.) **all** or b.) **high spenders**
- New LTSS insurance



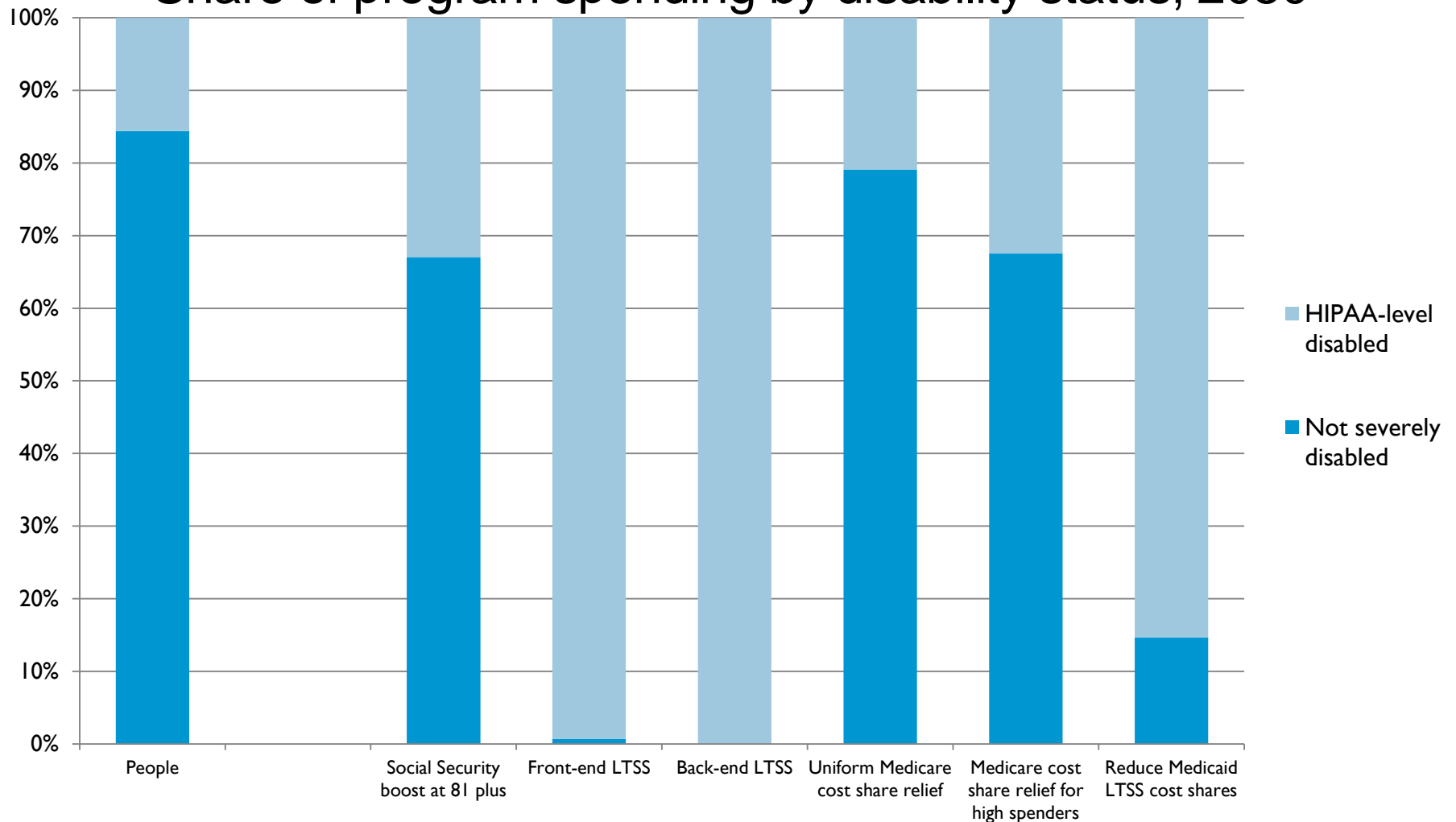
- Reduce Medicaid LTSS cost-sharing

# Options modeled

- All cost about the same amount
  - Agnostic to financing the benefits
- Examine at a point when fully phased in
  - An issue for the LTSS insurance options if they were to be funded like OASDI with prefunding
- Consider effects per dollar spent for groups
- Vary generosity and eligibility

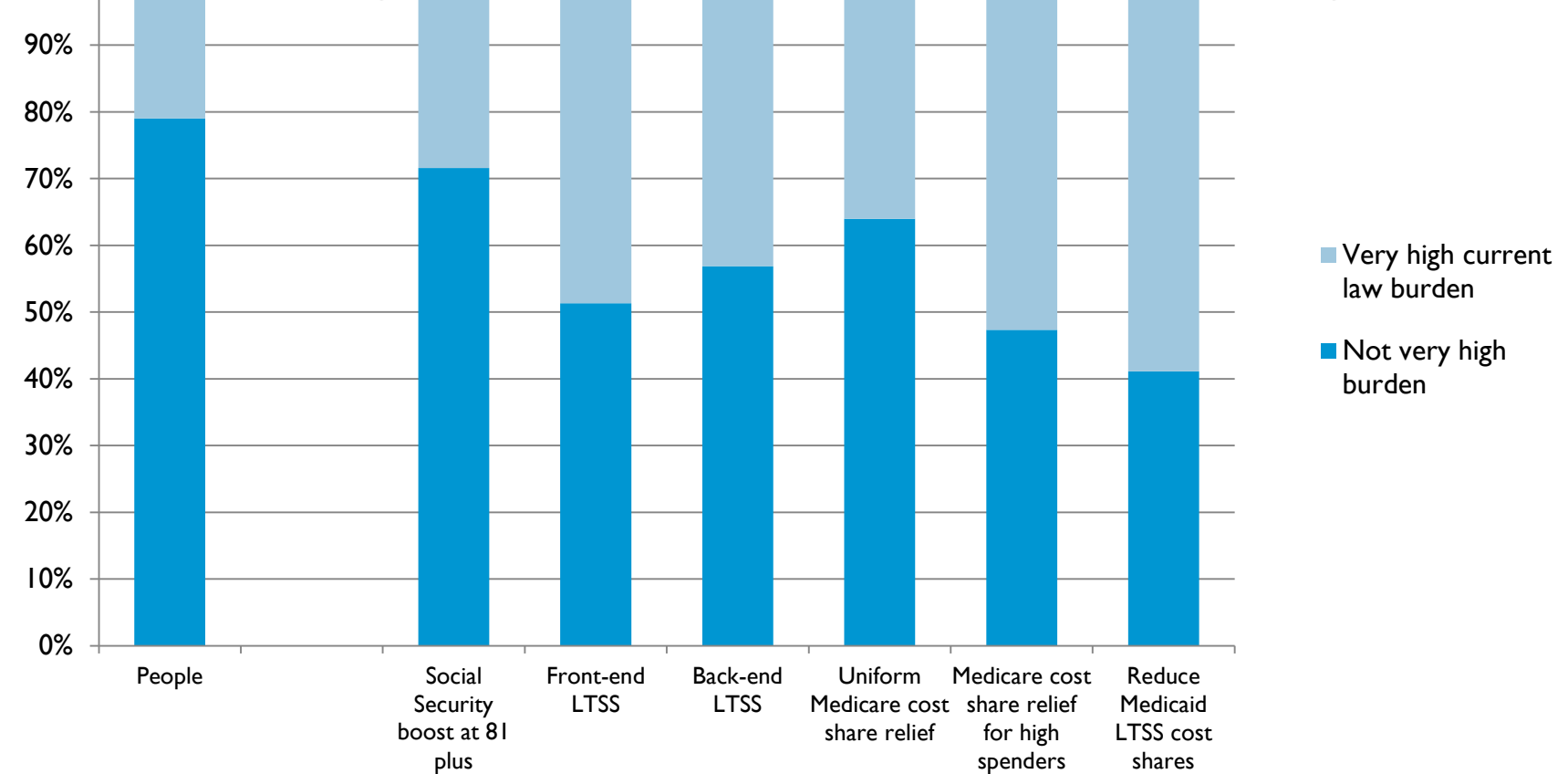
# All Options Target Disabled Adults: LTSS and Medicaid Options More So

Share of program spending by disability status, 2050



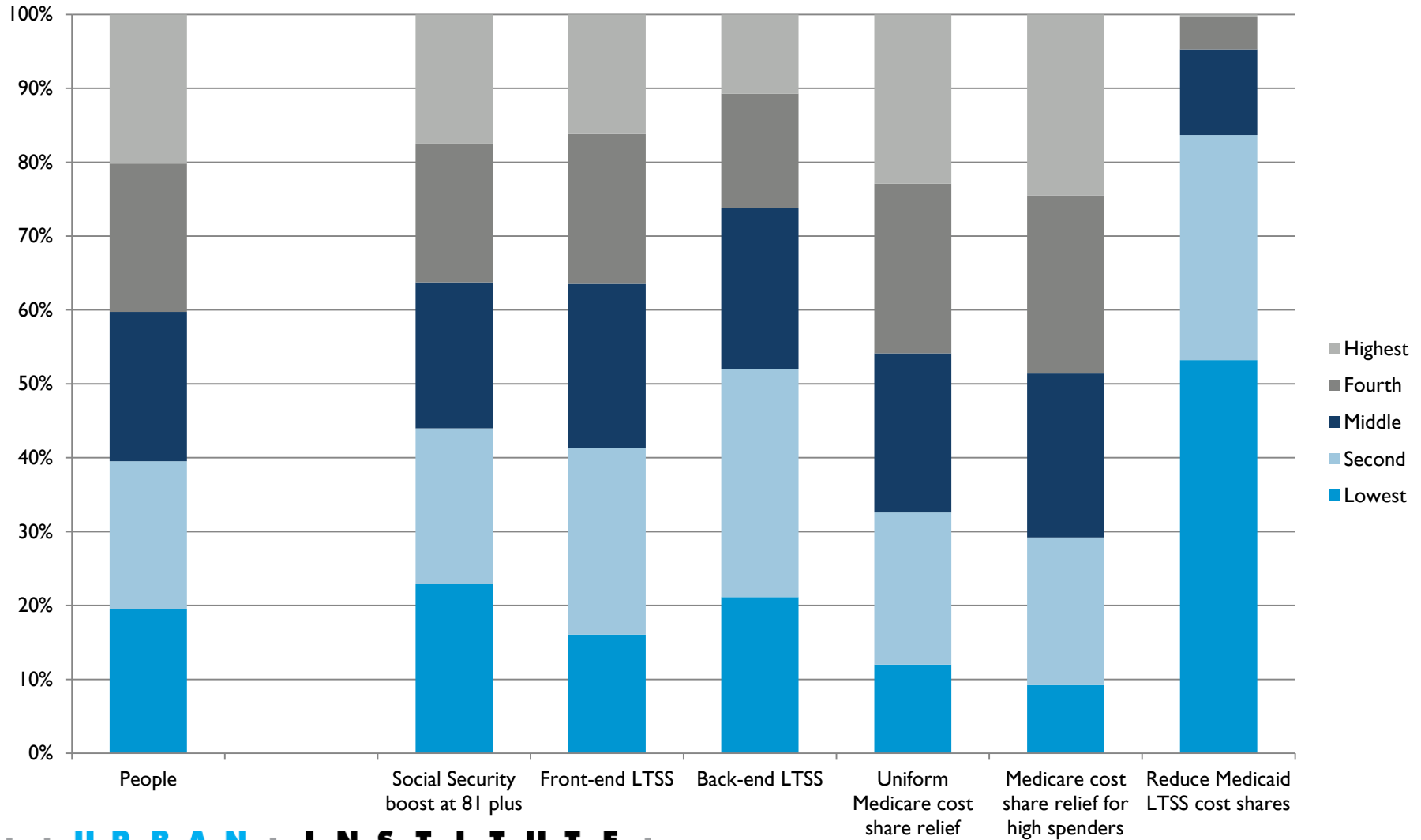
# All Options Target High Spenders: LTSS, Targeted Medicare, and Medicaid Options

Share of program spending by current law spending, 2050

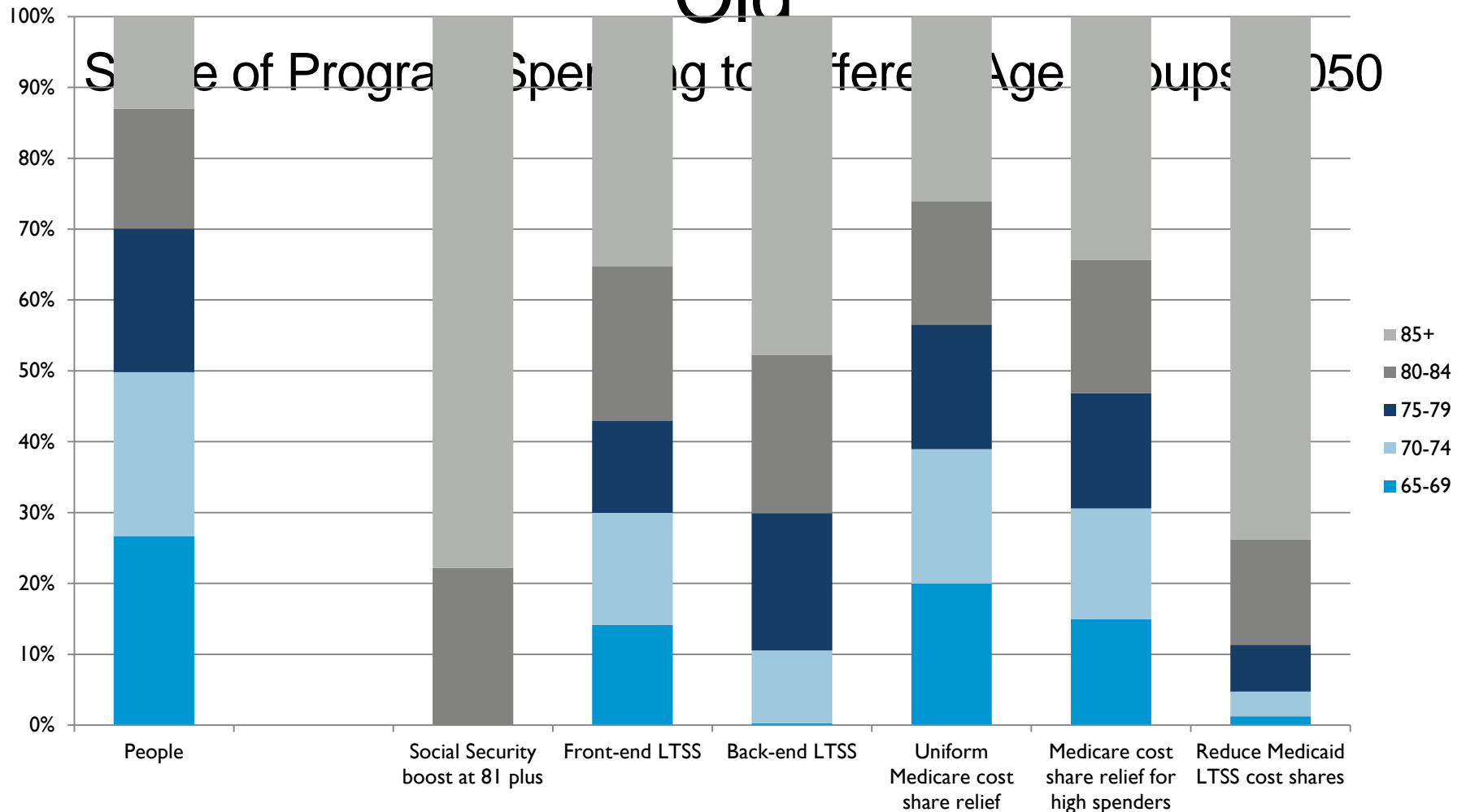


# Options Vary in Income Targeting: Medicaid Options Most Progressive

Share of program spending by current law income, 2050



# All Options Target Older Adults: OASDI, Back-end LTSS, and Medicaid Most to Old



# Caveats

- These projections depend on many assumptions, some controversial
  - Where to draw the line on disability?
  - What qualifies as LTSS (residential care)?
  - Spending growth for health care/LTSS
- Policies are highly stylized, illustrative
  - Each could be targeted better
    - Tradeoff: more people vs. high spenders
  - Important considerations besides targeting
    - Political viability / universality
    - Fairness
    - Cost of administration

# Further policy ideas to compare

- SSI options
- Medicaid package of benefits
- Medicare package of benefits
- Asset tests
  - Medicaid and SSI
- Targeted relief based on health care and LTSS expenses as a share of income
  - Premiums and not just point-of-service cost shares
  - MSPs (QMB, SLMB, QI)
  - Income tested deductibles in LTSS



# Thank you

All estimates in this paper are preliminary. Please consult the website of the Center for Retirement Research at Boston College in the fall for final results.

Views expressed are my own and not those of SSA, the Center for Retirement Research, or the Urban Institute.

**No slides from discussant Paul Van de Water**