

# Societal Impact of Research Funding for Women's Health in Coronary Artery Disease

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## Technical Appendixes

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## Preface

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These technical appendixes accompany the report titled *Societal Impact of Research Funding for Women's Health in Coronary Artery Disease* (Baird et al., 2021) and provide additional information about the data sources and microsimulation model used in that report, which can be found at [www.rand.org/t/RRA708-2](http://www.rand.org/t/RRA708-2).

## Technical Appendix A. Selection of Data Sources

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**Table A.1. Availability of Key Variables Among Potential Data Sources**

	<b>Panel Study of Income Dynamics</b>	<b>National Longitudinal Survey of Youth, 1979</b>	<b>Medical Expenditure Panel Survey</b>
N	24,000 people	12,686 people	30,000 households
Age ranges	Born 1951-present	Born 1957-1964	Range of ages
Received diagnosis of			
Alzheimer's specifically	No (just diagnosis of permanent loss of memory/ mental ability)	No	Yes
Health spending	Yes (aggregated)	No	Yes
Health condition limits activities	Yes	Snapshot	Yes
Extra care needed	Snapshot	No	Yes
Disability insurance participation	Yes	Yes	No
Paid nurse to come to home this year	Yes	No	Yes

Note: "Snapshot" indicates a variable is capture incidentally (e.g. in a single year or at milestone ages) rather than every survey wave (annual/biennial).

## Technical Appendix B. Model

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### Overview of the Model

This microsimulation model is based on a synthetic starting cohort with 1,000,000 individuals aged 25-99. We take the fraction of individuals in each year of age and gender subgroup in the U.S. population from the Census Bureau,<sup>22</sup> and multiply that fraction by 1,000,000 to determine how many individuals in our simulation sample to assign that age and gender at start. Then, conditional on age and gender, individuals in the starting cohort are first sorted into one of two states:

1. Alive without Coronary Artery Disease (CAD)
2. Alive with CAD

The distribution of the two states in the population is determined by the prevalence of CAD conditional on age and gender, which we estimate using Medical Expenditure Panel Survey (MEPS) for individuals age 65 years old or younger and Centers for Medicaid & Medicare Services (CMS) data for those over 65 years old. We identify CAD through ICD-9 (410, 413, 414) and ICD-10 codes (I20, I21, I25) in MEPS, and we further include patients with atherosclerosis (ICD-9 440, ICD-10 I70) and 68% of patients with heart failure (ICD-9 428, ICD-10 I50) to the CAD patient pool (Gheorghiade and Bonow, 1998). In CMS data, ischemic heart disease is one of the selected chronic conditions reported; therefore, we can identify CAD patients through the indicator for ischemic heart disease.

Although there are respondents older than 65 in MEPS, we choose to use CMS data for elderly population due to the advantages of claims dataset, including larger sample sizes and less sampling and recall bias, and because the MEPS data does not include individuals in skilled nursing facilities, such as nursing homes. Insofar as residence in skilled nursing facilities is both more common for older individuals and correlated with CAD diagnoses, using the MEPS for these older individuals would undercount the rate of CAD. We compare the CAD prevalence rates in MEPS with the ones in CMS data for females and males aged 66-75, and generate an inflation ratio (1.32 for males, 1.80 for females) for the CAD prevalence rates among respondents aged 25 to 65 in MEPS. Finally, we fit a flexible monotonic increasing function (logistic function symmetric sigmoid shape, Stata's `nl log3`) to the hybrid CAD prevalence rates of:

1. the inflated prevalence rates from respondents aged 25 to 65 in MEPS
2. the prevalence rates from individuals aged 66 or older in CMS data.

We assign a fraction of individuals in each age and gender subgroup to start with an existing CAD diagnosis based on the fitted prevalence rates from that estimated function.

Having the initial conditions of the representative cohort, there are three steps in this model:

1. Simulating the model for 30 years and assuming the health improvement happens at 10 years out. Predicting the proportion of people diagnosed with CAD, effects on employment, care status, and mortality.
2. Generating aggregate projections of individual-level outcomes, including total non-nursing home health care costs (including formal home care), nursing home costs, productivity loss of the patient and of their informal caregivers, and quality of life loss.
3. Estimating the impact of additional research funding on economic costs, using return on research funding investment.

## Data Sources Used for Estimation

### *Medical Expenditure Panel Survey*

The Medical Expenditure Panel Survey (MEPS), beginning in 1996, is a set of large-scale surveys of individuals and families, their medical providers (doctors, hospitals, pharmacies, etc.), and employment status across the United States.<sup>23</sup> The Household Component (HC) of the MEPS provides data from individual households and their members, which is supplemented by data from their medical providers. The Household Component collects data from a representative sub sample of households drawn from the previous year's National Health Interview Survey (NHIS). Institutionalized population is not included in the MEPS, which implies that we can only use the MEPS to estimate health care costs for the individuals living in communities. Information collected during household interviews includes demographic characteristics, health conditions, health status, use of medical services, and health insurance status. Each year the household survey includes approximately 12,000 households or 34,000 individuals. We estimate expenditures and utilization using 2011-2017 data.

### *Health and Retirement Study*

The Health and Retirement Study (HRS) is a longitudinal panel survey of Americans over the age of 50 occurring every two years (University of Michigan, undated). It's a complex and rich source to explore health transitions relating to aging. We used from the waves 1 (1990) through wave 12 (2014-2016) to estimate the proportion of people being institutionalized. We use the dataset created by RAND (RAND HRS, version Q) as our basis for the analysis. When appropriately weighted, the HRS is representative of U.S. households where at least one member is at least 51 years old.

### *Centers for Medicare & Medicaid Services Data*

The CMS Medicare Beneficiary Summary File (base and chronic conditions components) is used to estimate the age incidence rate, age prevalence rate and mortality hazard of CAD. The master beneficiary summary file (MBSF) base segment includes Medicare enrollment information for the universe of Medicare beneficiaries. It also contains demographic data (date of birth, date of death, sex, race, and ethnicity) and limited socio-economic information

(Medicare/Medicaid dual eligibility status and Part D (drug coverage) cost-sharing status). The MBSF chronic conditions segment contains data on 27 chronic conditions, one of which is Ischemic Heart Disease, and for each condition, it includes the date of first diagnosis as well as indicators for whether the diagnosis is active in the current year. With date of first diagnosis, incident cases can be identified separately from prevalent cases in any year. We use data of these annual files from 2016 and 2017 so we would have one complete year from birthday to birthday for each beneficiary, and from these we identified age-specific incidence rates for CAD. We use the 2017 data to estimate age-specific mortality rates, conditional on CAD status.

## Modeling Health and Economics Statuses

### *Incidence of CAD*

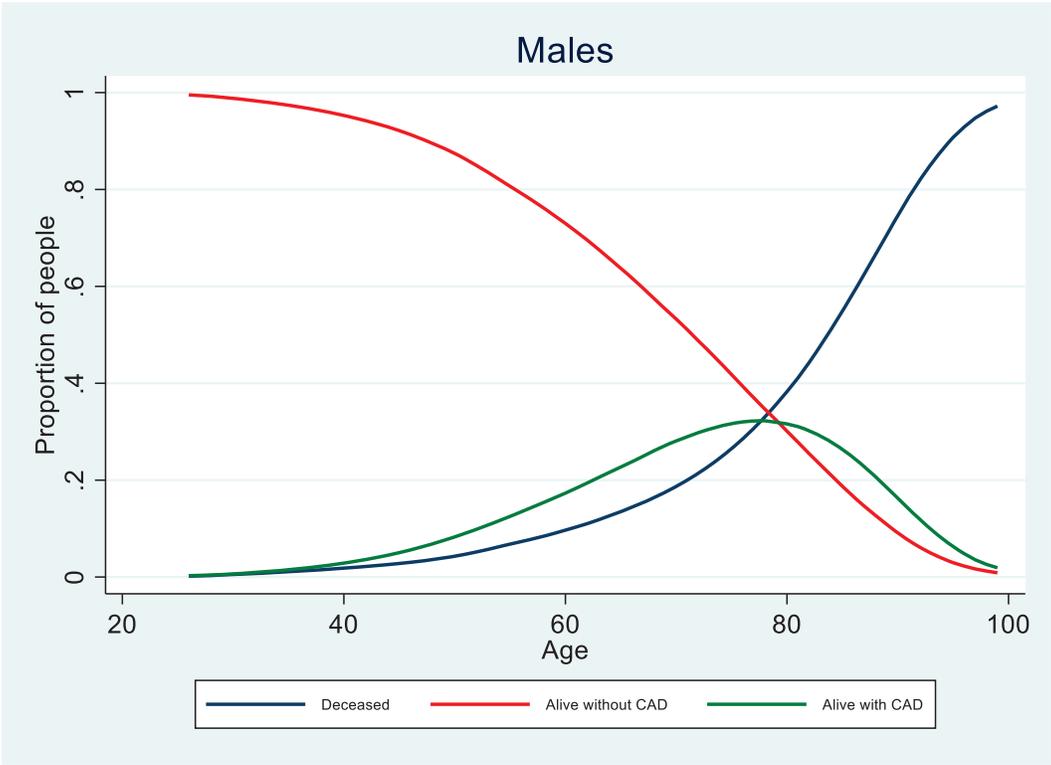
We model the probability of having onset of CAD for each individual. To do so, we estimate the following probability in equation B.1 for each gender  $g$  and age  $t$  using MEPS. Similar to prevalence rates we estimate to construct the starting cohort, we utilize both MEPS and CMS data to get the incidence rates. For population age 65 years old or younger, we use the age of diagnosis collected for CAD patients in MEPS as an estimate of the age of onset of CAD. When patients have multiple age of diagnosis for different CAD diseases, we choose the youngest age as the age of onset of CAD. For example, we expand one cross-sectional observation in MEPS of an individual aged 54 years old who was diagnosed at age 45 to 30 observations, one for each year from age 25 to age 54, and flag age 45 to age 54 as having CAD. This person will only appear in the numerator in the calculation of incidence rate at age 45 (equation B.1). The reason we expand one cross sectional observation to 30 observations in this case is that we underestimate the number of individuals who have lived through age  $t$  (denominator in equation B.1) if we do not include person-years that are CAD free.

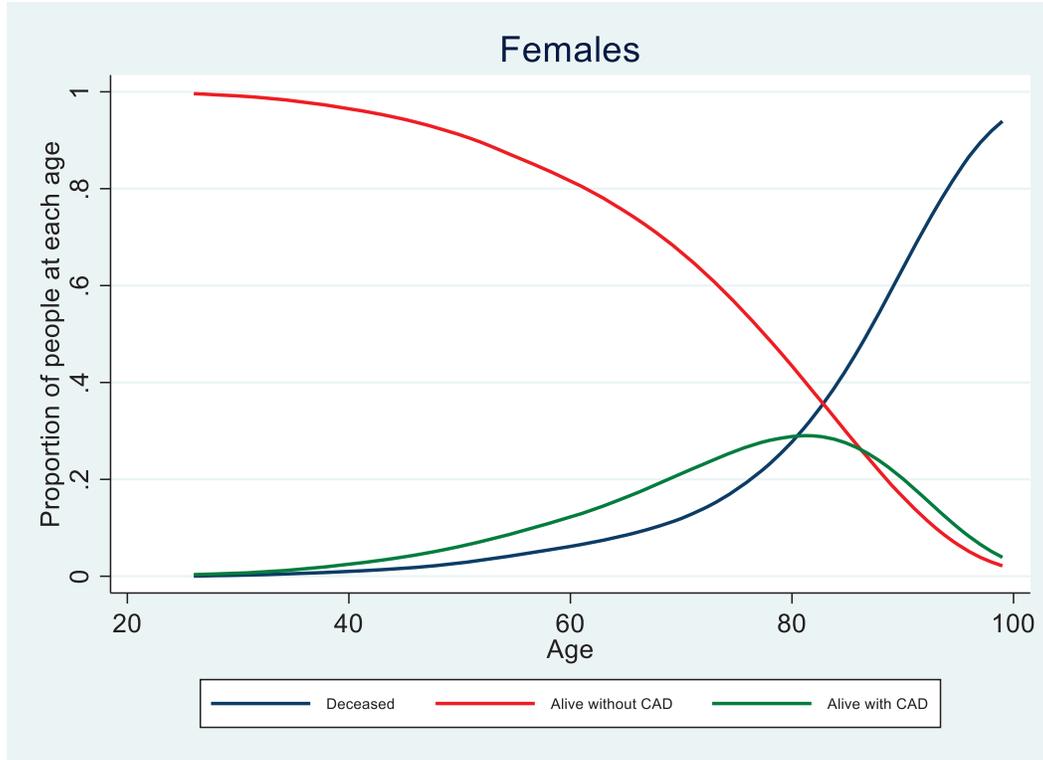
$$\psi_{gt} = \frac{\text{number of individuals who had been newly diagnosed with CAD at age } t \mid \text{gender}=g}{\text{number of individuals who have lived through age } t \mid \text{gender}=g} \quad (\text{B.1})$$

For population age 66 years old or older, we calculate the incidence rates conditional on gender and age from the CMS data using equation B.1. As discussed in the overview section of this appendix, we suspect that MEPS underestimates the incidence rates of CAD across all age groups; therefore, we compare the estimated CAD incidence rates in MEPS with the estimated rates in CMS data for females and males aged 66-75, and generate a inflation ratio (2.70 for males, 3.97 for females) for the incidence rates among respondents aged 25 to 65 in MEPS. Finally, we fit a flexible monotonic increasing function (logistic function symmetric sigmoid shape, Stata's `nl log3`) to hybrid CAD incidence rates of the inflated incidence rates from respondents aged 25 to 65 in MEPS and the rates from individuals aged 66 or older in CMS data. From this, we then predict the incidence rate for each age and gender.

CAD is an absorbing state in our model, which means that once an individual is diagnosed, he/she lives with the condition until death. With the incidence rates estimated for each age and gender, in the microsimulation model we take uniform random draws ( $u_{gt1}$ ) from 0 and 1 for each individual at each age that did not have CAD in the prior year, and model them as having been diagnosed with CAD in that year if the random draw is less than the probability of CAD diagnosis, i.e. if  $u_{gt1} < \psi_{gt}$ . Figure B1 presents our simulated proportion of people at each age in each state of alive with CAD, alive without CAD, and deceased. The fraction of people with CAD peaks shortly after age 80.

Figure B.1. CAD Case Trend in Males and Females





### Probability of Dying

We estimate the probabilities of dying to individuals with and without CAD each year conditional on age and gender using equation B.2 and B.3. We use the United States Life Table in 2017 released by Centers for Disease Control and Prevention (CDC) for the probabilities of dying in the general population in equation B.2,<sup>2</sup> and the CMS data for the mortality hazards of CAD in equation B.3 and B.4. For patients with CAD, probability of dying is the addition of a mortality risk based on age and gender to the baseline probability for individuals without CAD. We calculate the additive mortality hazards of CAD from the CMS data for individuals age 66 years old or older, and fit a monotonic increasing function using Stata command `nl log3`. For individuals younger than 66 years old, we assume they have the same mortality hazard as people age 66 years old. By substituting equation B.3 into B.2, we can derive the probability of dying for individuals without CAD conditional on age and gender using equation B.4.

$$\begin{aligned}
 \Pr(\text{die}|\text{age} = t, \text{gender}) &= \Pr(\text{die}|\text{age} = t, \text{gender}, \text{CAD}) \times \\
 &\Pr(\text{CAD}|\text{age} = t, \text{gender}) + \Pr(\text{die}|\text{age} = t, \text{gender}, \text{no CAD}) \times \\
 &\Pr(\text{no CAD}|\text{age} = t, \text{gender})
 \end{aligned}
 \tag{B.2}$$

$$\Pr(\text{die}|\text{age} = t, \text{gender}, \text{CAD}) = \Pr(\text{die}|\text{age} = t, \text{gender}, \text{noCAD}) +$$

(predicted mortality hazard|age = t, gender)

(B.3)

$$\Pr(\text{die}|\text{age} = t, \text{gender}, \text{noCAD}) = \Pr(\text{die}|\text{age} = t, \text{gender}) -$$

(predicted mortality hazard|age = t, gender) × Pr (CAD|age = t, gender)

(B.4)

### Living in Nursing Homes

We estimated the probabilities of being institutionalized in a nursing home conditional on age using all available waves (through wave 12) of the RAND HRS version Q. We did so separately for women and men by fitting a general, non-linear monotonic increasing function of age on the probability of nursing home entry. Specifically, we used a logistic function (symmetric sigmoid shape) using Stata's nl package with the log4 model (equation B.5).

$$\Pr(\text{NH}|\text{gender}, \text{age}) = b_0 + \frac{b_1}{1 + \exp(-b_2 * (\text{age} - b_3))}$$

(B.5)

Where  $\Pr(\text{NH}|\text{gender}, \text{age})$  is the probability of nursing home entry. We estimated this for individuals age 50-94, and then predicted the smooth line from the estimated parameters to calculate the probability of nursing home entry for the general populations.

We did not find any literature on different probability of nursing home entry for CAD patients and the general population. Therefore, all individuals in our model, with or without CAD, are assigned with probability of nursing home entry solely conditional on their age and gender, independent of CAD status. People younger than 65 years old are assigned zero probability of nursing home entry. Again, we then took random uniform draws between 0 and 1, and if the uniform draw was below the estimated probability of nursing home entry, we assigned that person in the simulation to be institutionalized that year.

Figure B2 and B3 present the simulated care trends.

Figure B.2. Care Trend in Non-CAD Males and Females

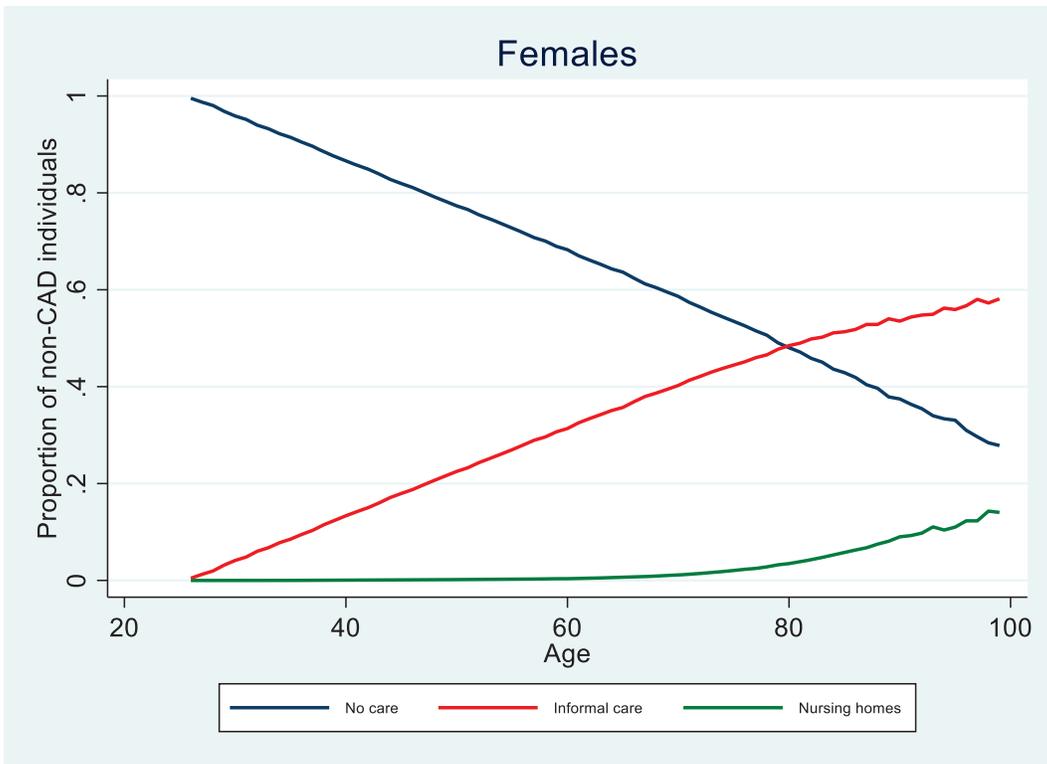
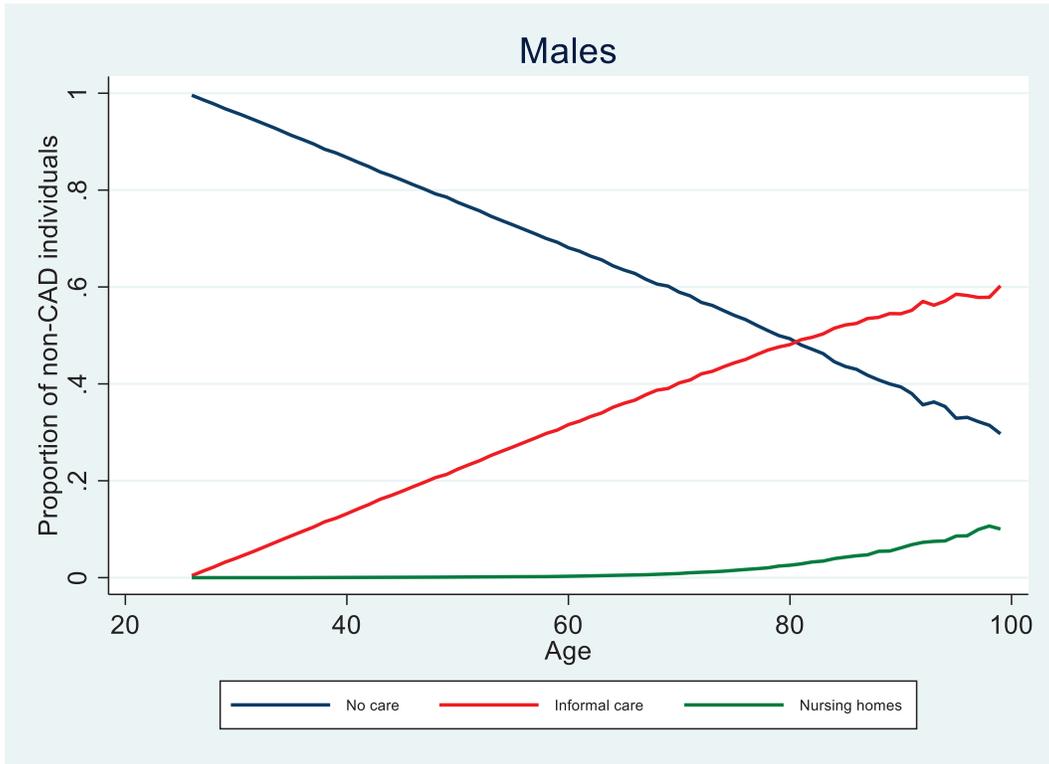
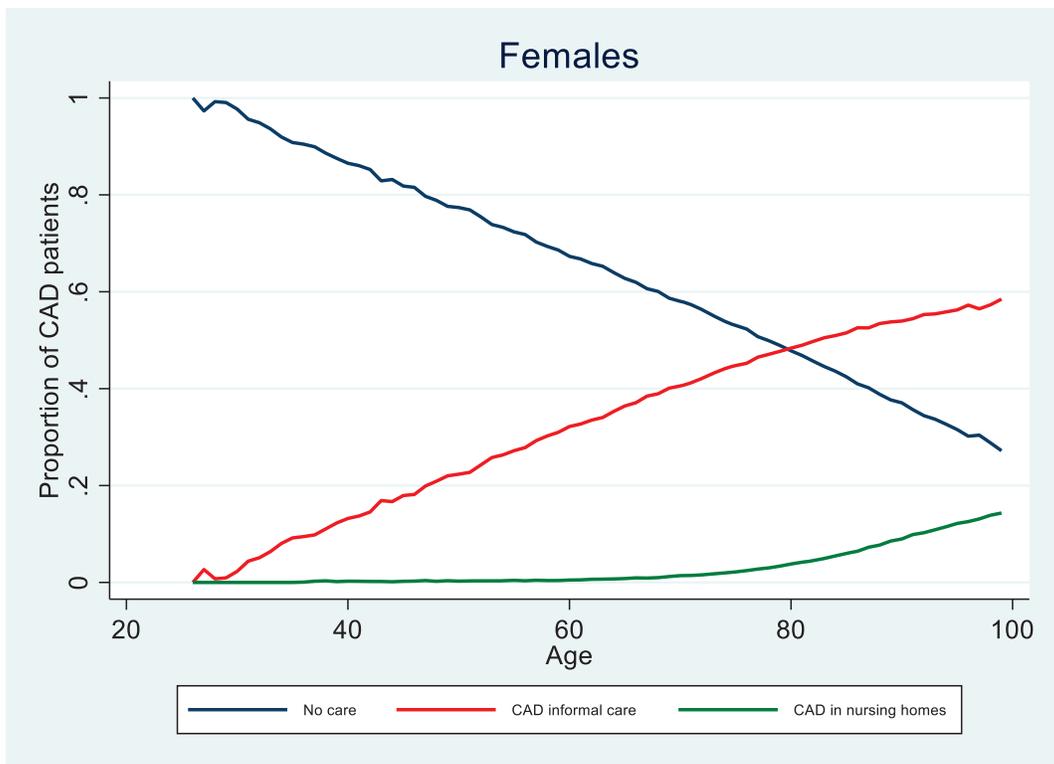


Figure B.3. Care Trend in CAD Males and Females



## Receiving Informal Home Care

To assign the informal home care status for non-CAD and CAD individuals, we use equation B.6 to B.9 below to get the probabilities of receiving informal care and the expected informal care hours conditional on CAD status. We derive the probability of receiving informal care in the general population from Kaye, 2013, exhibit 1 and 2, which show 15% of working-age adults and 45% of individuals older than 65 years old have functional limitations. We then assume all people with functional limitations received informal home care. We fit a linear function of age on the probability of having functional limitations to meet these prevalence rates. We assume the expected informal care hours received by the general population is 65.8 hours per month, according to exhibit 2 from Friedman et al., 2015. Using equation B.6, we can calculate the expected informal care hours in the general population unconditional on receiving care or not.

Next, as we already derive the prevalence of CAD patients in each age and gender group, we know the expected informal care hours conditional on not having CAD will be equal to

$$E(\text{informal care hours}) - (E(\text{informal care hours}|\text{CAD}) - E(\text{informal care hours}|\text{no CAD}) \times \Pr(\text{CAD}))$$

from equation B.7.  $(E(\text{informal care hours}|\text{CAD}) - E(\text{informal care hours}|\text{no CAD}))$  is 0.16 hour/week for males and 0.04 hour/week for females based on Dunbar et al., 2018, and therefore we can calculate out  $E(\text{informal care hours}|\text{CAD})$  for each age and gender group. Once we have estimated  $E(\text{informal care hours}|\text{CAD})$ ,  $E(\text{informal care hours}|\text{no CAD})$  is simply estimated by adding the informal care hours attributable to CAD from Dunbar et al., 2018.

Finally, to estimate the probability of receiving informal home care for CAD and non-CAD individuals, we divide the expected informal care hours conditional on CAD status by the expected informal care hours received conditional on receiving informal care in the general population (equations B.8 and B.9).

$$E(\text{informal care hours}) = E(\text{informal care hours}|\text{receiving care}) \times \Pr(\text{receiving care}) \quad (\text{B.6})$$

$$\begin{aligned} E(\text{informal care hours}) &= (E(\text{informal care hours}|\text{CAD}) + 0.1) \times \Pr(\text{CAD}) \\ &\quad + E(\text{informal care hours}|\text{no CAD}) \times \Pr(\text{no CAD}) \\ \Rightarrow E(\text{informal care hours}|\text{no CAD}) &= E(\text{informal care hours}) - \\ &\quad (E(\text{informal care hours}|\text{CAD}) \times \Pr(\text{CAD})) \end{aligned}$$

(B.7)

$$\Pr(\text{informal care hours}|\text{receiving care, CAD}) = \frac{E(\text{informal care hours}|CAD)}{E(\text{informal care hours}|\text{receiving care,CAD})}$$

(B.8)

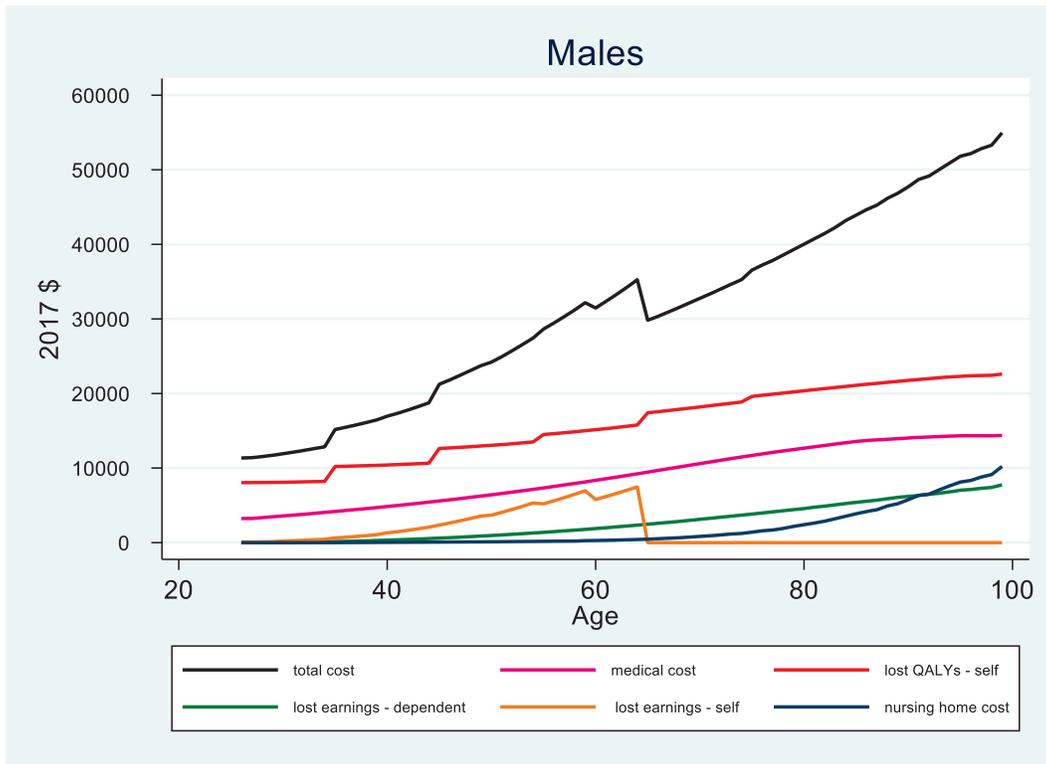
$$\Pr(\text{informal care hours}|\text{receiving care, no CAD}) = \frac{E(\text{informal care hours}|no CAD)}{E(\text{informal care hours}|\text{receiving care,no CAD})} \quad (\text{B.9})$$

As before, we took random uniform draws between 0 and 1, and if the uniform draw was below the estimated probability of receiving informal home care, we assigned that person in the simulation to receive informal home care that year.

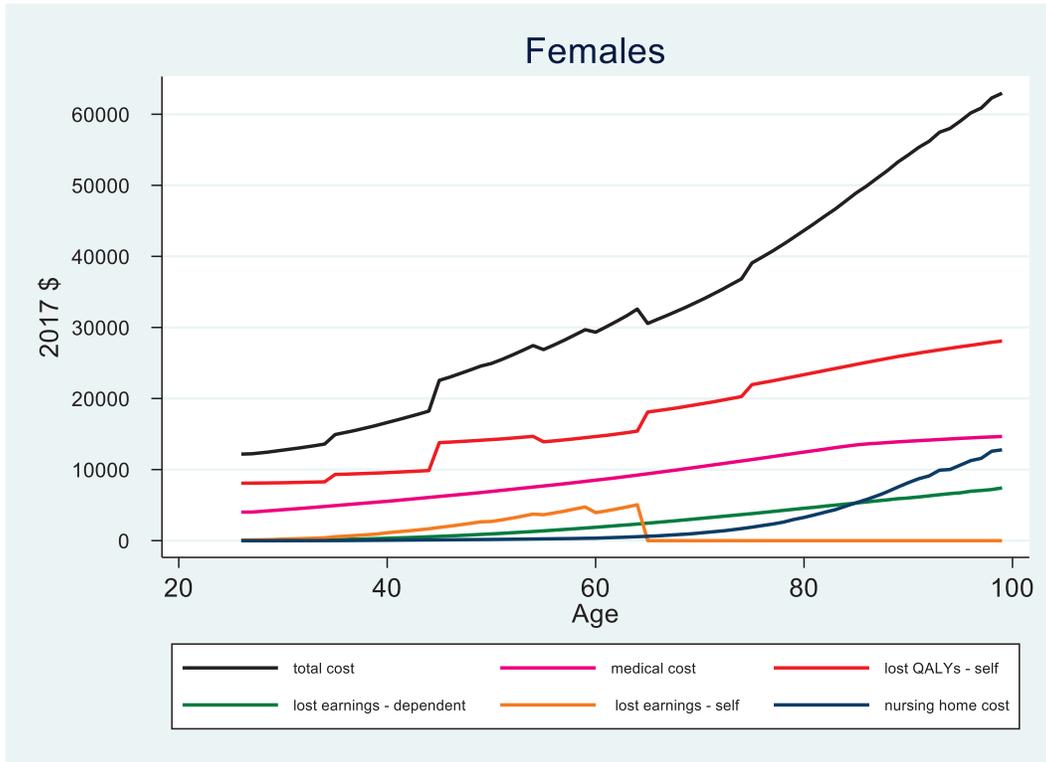
## Cost Model

All costs were projected over 30 years assuming the investment is a one-time cost incurred in 2019. Future medical costs were normalized to 2017 USD using the Personal Consumption Expenditures (PCE) Health index. We adjusted for time preferences and the opportunity cost of investment by discounting future costs and QALYs at an annual rate of 5%. Figures B.4 and B.5 show the average costs—across both CAD and non-CAD patients—by age, based on our simulations. We describe each in turn.

Figure B.4. Average Cost Conditional on Age for Males



**Figure B.5. Average Cost Conditional on Age for Females**



*Health Care Costs*

We estimated the average health care costs (not including nursing home stays) conditional on age and gender using the 2011-2017 MEPS separately for individuals with and without CAD. In view of the impact of insurers on medical spending, we used ordinary least squares regression to estimate total medical spending (medical spending from all payment sources) controlling for year, age, gender, insurer type (Medicaid, Medicare, Tricare and private insurers). Instead of modelling the status of receiving formal home care and assigning formal home health care costs conditionally, we assigned the total health care costs that include formal home care. Informal home health care is not included in the total health care costs from MEPS but estimated using productivity loss of caregivers, as discussed in the following section. Since MEPS is only representative for the US civilian non-institutionalized population, nursing home costs for individuals in nursing homes were estimated separately. However, we chose to assign the same average total health care costs (not including the costs of the nursing home) for institutionalized population on the assumption that their health care costs (not including the costs of the nursing home) do not differ from community-dwelling individuals.

### *Productivity Loss of Self*

We estimate the productivity loss of the patients who have CAD using the MEPS. In addition to decreased earnings due to CAD when patients are alive, we categorize any deaths before the age of 65 as premature deaths (with respect to labor productivity) and calculate the potential earnings until age 65 that would have been earned if they were to live. All earnings are based on those of non-Hispanic white males, to correct for gender and race-based labor market discrimination. We start with estimating the gap of earnings between CAD and non-CAD non-Hispanic White males for each age group  $g$  from the MEPS using equation B.10:

$$\pi_g = E[W|no\ CAD, Age = g] - E[W|CAD, Age = g] \quad (B.10)$$

We do this by estimating the following regression using MEPS data for individuals between ages 25 and 65

$$W = \sum_g \pi_g CAD * 1(Age = g) + \sum_g \delta_g 1(Age = g) \quad (B.11)$$

For CAD patients with premature deaths, we use the wage of non-Hispanic White males not conditional on working (including non-CAD and CAD patients) for each age group  $g$  to construct the expected productivity until age 65. For example, if a CAD patient enters our simulation model at age 45 and dies at age 55, we calculate his/her productivity loss over the 30-year time span of the simulation by accumulating the wage loss for the first ten years of the simulation for having CAD (between ages 45 and 55) and the full productivity loss of wages between ages 55 (when they are estimated to have died) and age 65 (assumed retirement age). This is done by equation B.12.

$$E(\text{Total productivity loss} | CAD\ age\ 45, death\ age\ 55) = \sum_{g=45}^{54} \pi_g 1(Age = g) + \sum_{g=55}^{65} E[W | Age = g] \quad (B.12)$$

### *Productivity Loss of Informal Home Caregivers*

Costs of informal home care are calculated using the productivity (earnings) loss of informal home caregivers, to account for the time they spend providing unpaid, informal care instead of doing paid labor. All informal caregiver earnings are based on those of non-Hispanic white males, to correct for gender and race-based labor market discrimination. The hourly wage for non-Hispanic white males estimated from MEPS is around \$23.86 for workers younger than 65 and \$23.60 for workers older than 65. The steps of calculating the productivity loss are as follows:

1. We assign 30% of caregivers for individuals receiving informal home care to be older than age 65, regardless of patients' CAD status (Spillman et al., 2014).
2. The average hours spent on caretaking is derived in the "Receiving Informal Home Care" section, conditional on patient's age and gender.
3. We multiply the hourly wage of non-Hispanic white males estimated from MEPS with the average informal caregiving hours from step 2 to get productivity loss in a year of informal home caregivers for CAD patients and non-CAD individuals

### *Nursing Home Costs*

The cost of living in nursing homes is set at \$90,520 annually for non-CAD individuals and CAD patients. This rate is based on the reported national average for a private room in the Market Survey of Long-Term Care Costs published by MetLife Mature Market Institute in 2012.<sup>31</sup>

### *Quality of Life Loss*

The value of one quality of life year (QALY) is set between \$50,000 to \$150,000 by the Institute for Clinical and Economic Review, and we choose to use \$100,000 in our model. Although \$50,000 threshold is arguably the "rule of thumb" in cost-effectiveness analysis in health care sector, we believe that this value is an underestimation since it has never been adjusted for advances in technology, increased costs of care, and change in valuations about life over time.

We assign health utilities based on the EuroQol five-dimensions questionnaire (EQ-5D) to the general population conditional on age and gender from Clemens et al., 2014, table 3, and CAD patients conditional on gender based on Xie et al., 2008, table 2.

We calculated lost QALYs for both CAD and non-CAD patients by subtracting their health utilities from 1, i.e. perfect quality of life. If someone is living in a nursing home, an additional 0.1 is added to the lost QALYs.<sup>34</sup> Persons who die in the simulation will have a lost QALY of 1 in the year they die, and for all the subsequent years in the time horizon. Below is an example of the calculation of lost QALYs for a female with CAD not living in a nursing home.

$$1 - 0.68 \text{ (health utilities for female CAD patients)} = 0.32$$

If this female enters a nursing home, the lost QALYs would be:

$$1 - 0.68 \text{ (health utilities for female CAD patients)} + 0.1 = 0.42$$

### **Return on Investment**

Initially the target return on investment was set between 5 and 15%, and parameters were varied to achieve an ROI in this range. This proved a difficult task to calibrate, given small

changes in the parameter could generate small changes in the outcomes (that is, only affecting a few people in our simulation), which when multiplied out to have the one-million person sample scale up to the US adult population, represented large differences. For example, a small change which resulted in one person out of the one million people in our microsimulation having only one fewer year in a nursing home out of the thirty years simulated would represent a large shift in cost savings. With one million people in our sampling frame, and nearly 200 million in the underlying US population, each individual in the microsimulation sample represents nearly 200 people in the US population. Thus, the one fewer year of nursing home for one person, valued at around \$100,000, would represent a cost reduction of \$100,000 times 200, or \$20 million for the economy. Therefore, we instead focused on prechosen health improvements, and evaluated the (typically much larger than 10-15%) ROIs associated with those health improvements, as well as the probability of success necessary for that cost improvement to yield an expected ROI of 15%. These methods are described below.

### *Calculation of Return on Investment*

The return on investment, or ROI, is calculated using the following equation B.13:

$$ROI = 100 * \left( \frac{cost_s - cost_n - Investment}{Investment} - 1 \right) \quad (B.13)$$

Where

- $cost_s$ : US healthcare costs for age 35 and older under *status quo* health
- $cost_n$ : US healthcare costs for age 35 and older with the new health improvement
- $Investment$ : increase in investment

### *Expected ROI Under Uncertain Probability of Success*

The return on investment process described in the previous section assumes that the investment will with certainty yield the health improvement and thus the cost savings. However, this is not a realistic representation of the risky nature of investments into health. We thus additionally frame an investment as a Bernoulli trial, that is, a binary outcome with a probability of success  $P$  achieving the given health improvement (and associated reductions in healthcare costs), or  $(1 - P)$  probability of having no health improvement and remaining at the *status quo* healthcare costs. We write this as follows, where  $cost_i$  is the healthcare cost under investment.

$$E[cost_i] = P * cost_n + (1 - P) * cost_s \quad (B.14)$$

We can combine equation B.12 with the ROI by connecting it to a specific ROI. For example, we can estimate the probability of success that is related to an expected ROI of 15% by

$$15 = E \left[ 100 * \left( \frac{cost_s - cost_i - Investment}{Investment} - 1 \right) \right] \quad (B.15)$$

At the investment decision point, the only uncertainty is what the cost under investment ( $cost_i$ ) will be—either  $cost_n$ , the new healthcare cost under health improvement from the investment, with probability  $P$ , or  $cost_s$ , the *status quo* healthcare cost, with probability  $(1 - P)$ . Solving for the expected cost in the equation, we have

$$E[cost_i] = cost_s - 2.15 * Investment \quad (B.16)$$

Putting the two equations together, we can solve for  $P$  as

$$\begin{aligned} cost_s - 2.15 * Investment &= P * cost_n + (1 - P) * cost_s \\ \Rightarrow P &= \frac{2.15 * Investment}{cost_s - cost_n} \end{aligned}$$

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