REPORT BRIEF

THE WHAM REPORT

Societal Impact of Research Funding for Women's Health

IN CORONARY ARTERY DISEASE

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RAND CORPORATION

Women's Health Access Matters®

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WHAM, whamnow.org, is a 501c3 dedicated to funding women's health research to transform women's lives.

This report was conceived by WHAM in response to the considerable funding gap, historical exclusion, and under representation of women in health research.

As businesswomen, we believed that a focused study showing the impact of accelerating sex and gender-based health research on women, their families and the economy by quantifying costs and economic benefits will be an invaluable accountability index. In other words, if more investment is made in women's health research the plausible assumption is that women would benefit from sex-specific prevention strategies, diagnoses and treatments that reduce their burden of disease and thus improve their wellbeing and hence the wellbeing of society.

WHAM commissioned the RAND Corporation to conduct a data-driven study of the economic impact to society of increasing the investment in women's health research. This first research project comprises three disease modules: Alzheimer's Dementia, Rheumatoid Arthritis as representative of Autoimmune Disease, and Coronary Artery Disease. In the future, we plan to include Lung Cancer and also study different socioeconomic groups to the extent that the data are available and detail the global data which expands this research.

To the best of WHAM's and RAND's knowledge, this is the first analysis of its kind to create and calibrate a microsimulation model of investments in health R&D that examines differences for women's health research investment, and should become a seminal part of the arsenal in advocating for increased investment in women's health research. The research methodology and the microsimulation models have been vetted by a diverse panel of experts convened by RAND.

We are so thankful for the dedicated, invested partnership of the research team at the RAND Corporation who conducted the analysis presented here and brought their findings to life. We encourage other leaders, including advocates, economists, scientists, business leaders, public health experts and policy makers to draw from and act upon the results of this report. Together, we can drive meaningful change.

Carolee Lee
Founder and CEO, WHAM
www.whamnow.org | www.thewhamreport.org

Please find additional infographics and social media toolkits on **www.thewhamreport.org**.

The technical specifications for the models are publicly available. Please visit **www.thewhamreport.org** to learn more about using these data and citing this report.

WHAM's LEAD COLLABORATORS

WHAM's leadership of this research project was encouraged through the generous support and collaboration from the following organizations:

American Heart Association
The American Heart Association is a relentless force for a world of longer, healthier lives dedicated to ensuring equitable health for all—in the United States and around the world. The American Heart Association's signature women's initiative, Go Red for Women® (GRFW), has been the trusted, passionate, relevant force for change to end heart disease and stroke in women all over the world for nearly two decades. Go Red for Women and WHAM will collaborate to directly address the lack of societal-level evidence on the economic cost, benefits, and social impact due to the underrepresentation of women in cardiovascular research.

BrightFocus Foundation
BrightFocus Foundation is a leading source of private research funding to defeat Alzheimer's, macular degeneration and glaucoma. Supporting scientists early in their careers to kick-start promising ideas, BrightFocus addresses a full and diverse range of approaches from better understanding the root causes of the diseases and improving early detection and diagnosis, to developing new drugs and treatments. The nonprofit has a longstanding commitment to funding pioneering, sex-based research in Alzheimer's and related dementias. BrightFocus currently manages a global portfolio of over 275 scientific projects, a $60 million investment, and shares the latest research findings and best practices to empower families impacted by these diseases of mind and sight.

The Connors Center for Women's Health and Gender Biology at Brigham and Women's Hospital/Harvard Medical School is a leading local and national force in advancing the health of women, with a rich history and strong foundation of women's health and sex-differences discovery, clinical care, and advocacy for equity in the health of women and is the Premier Partner and the Lead Scientific Research Partner of the WHAM Collaborative for Women's Health Research. The Connors Center shares the bold vision of improving the health of women and a commitment to joining forces to advance scientific discovery for the benefit of all women.

La Jolla Institute for Immunology
La Jolla Institute (LJI) is one of the top five research institutes in the world focused on the study of the immune system. LJI is home to three research centers that harness the efforts of collaborative groups of researchers on defined areas of inquiry, to accelerate progress toward the development of new treatments and vaccines to prevent and cure autoimmune conditions, cancer and infectious disease. Together, LJI and WHAM will create a framework for researchers to re-analyze existing data with sex as a biological variable, to work together to spark new projects, to hire new faculty to build key research areas, to communicate via the WHAM Report, and to establish an ignition point for new leadership in the scientific field.

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WHAM convenes thought leaders, researchers, and scientists to work together to identify problems and devise solutions. Our members include:

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RAND convened advisory panels to help guide the work and elicit insights on the target case study areas of autoimmune and immune disease, cardiovascular disease, and Alzheimer's disease. Central to RAND's work was the creation of health economic models in each case study area. RAND is committed to creating final products with immediate relevance for use by funders, advocacy organizations, researchers, and other stakeholders.

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Executive Summary

The impact of limited knowledge about women's health relative to men's is far-reaching. Without information on the potential return on investment (ROI) for women's health research, research funders, policymakers, and business leaders lack a basis for altering research investments to improve knowledge of women's health.

Using microsimulation analyses, we examined the societal cost impact of increasing research funding in coronary artery disease (CAD). We quantified the potential impact of increasing funding for women's health on health outcomes and the ultimate societal costs, including health care expenditures, labor productivity, and quality-adjusted life years (QALYs). We calculated impacts across 30 years of doubling the proportion of the National Institutes of Health (NIH) extra-mural CAD portfolio devoted to women's health.

Key Takeaways

Large returns result from very small health improvements. Assuming health improvements of 0.01 percent or less in terms of age incidence, mortality, and quality of life yields the following results:

- For the U.S. population age 25 and older, more than 53,000 years with CAD can be saved across 30 years, with substantial gains in health-related quality of life.
- Almost 12,000 more years (and $236 million) can be saved in terms of labor productivity, both from higher labor and earnings from having fewer years of CAD and more years alive.

- The ROI is 9,500 percent for doubled investment in women's health research, even with only 0.01 percent improvement in health outcomes.

Investing in women's health research for CAD yields benefits similar to investing in general research, with improved health-related quality of life for women from women-focused research.

The results establish the potential for investment in women's health research on CAD to realize gains beyond additional general research investment and point the way to a concrete, actionable research and funding agenda.

Implications

Large societal gains may be possible by increasing investment in women's health research on CAD. The potential to recognize societal gains is greater for research devoted to women's health relative to general research, according to the assumptions used here.

We recommend the following policy actions based on this research to inform decisions about research funding allocations:

- Expand the research agenda to address
  - the unknown interactions of sex and gender with cardiovascular disease antecedents and disease progression to inform treatment and prevention research
  - understudied interactions of gender and race with cardiovascular disease risk, health care, and disease progression; in particular, examine obstacles to access to and use of medical provider visits, prescription drugs, and relevant devices
  - differences by sex and gender in dietary impacts on disease and adherence to dietary recommendations
  - differences in disease course and outcomes by sex and gender based on different patterns of use of formal and informal caregiving
  - health-related quality of life of women with CAD and the potential for earlier detection to positively affect health and quality of life outcomes.

By raising awareness of the current state of funding directed toward women's health in CAD and the potential for such funding to yield societal benefits, researchers and other communities can pursue information that is relevant for improving funding allocation decisions. Specific ways to connect other communities to the relevant issues include the following:

- Raise awareness of differences between the CAD course for women and men and the potential for investment to improve disease outcomes.
- Raise awareness among the business community of the potential ROI for women in the workforce from investment in women's health research.

Introduction

Because women have been underrepresented in health research, what we know about women's health is limited. Even today, the value of research investment on women's health is not widely accepted. The impact of this oversight is far-reaching.

Also unknown is the potential impact of accelerating and increasing funding for women's health research. What difference would doing so make in the health and well-being of everyone? Understanding this impact would provide vital information to funders, researchers, and policymakers to help them plan investments that can yield the greatest public health benefits.

As part of an initiative of the Women's Health Access Matters (WHAM) nonprofit foundation, RAND Corporation researchers examined the impact of increasing funding for women's health. WHAM has four pillar areas of focus: heart health, brain health, oncology, and autoimmune diseases. We reviewed disorders to use as case examples within each of these areas, comparing them in terms of overall prevalence; prevalence by gender; societal impact in terms of morbidity, mortality, and overall cost burden; and feasibility of obtaining data for constructing models. Within heart health, CAD was chosen as an important case study that could meaningfully inform funding policy.

We invited an expert advisory group to two meetings, in late summer and early fall 2020, about the project to provide input into model structure and assumptions. Members included health economists, health researchers and funders (including women's health experts), patient advocates, and representatives from health insurers and from the elder care business community. The advisers' input enabled us to finalize key assumptions and the model structure.

Why Focus on Coronary Artery Disease?

Physiological differences between men and women affect factors that relate to the development and progression of cardiovascular disease. For example, hormonal status influences renal sodium and water retention, with subsequent differences in blood pressure, and changes in blood pressure in response to changes in sodium intake are greater for women than men (Morrison and Ness, 2011). Evidence suggests that dietary changes may impact mortality differentially for women and men (Morrison and Ness, 2011). Differences extend to access and use of health services. More women than men are prescribed diuretics, and more men than women are prescribed aspirin, statins, and angiotensin-converting enzyme (ACE) inhibitors (Zhao et al., 2020). Incidence of death is higher for women than men during disease follow-up, despite more health care visits and prescription fills (Nichols et al., 2010).

Differences between men and women are also evident in the availability of informal caregivers for patients with CAD. More men than women CAD patients have informal caregivers, and having a caregiver is associated with better attainment of treatment goals (Hammond et al., 2012; Mondesir et al., 2018). Still mostly unexplored are the complex interactions of gender-based biology, individual physiology, and cultural factors in terms of cardiovascular disease risks and disease course (Barber et al., 2016; Tibuakuu et al., 2018).

Given these known differences and the potential for unknown differences to affect morbidity and mortality, investment in women's health could be expected to yield a favorable return for society.

The lack of societal-level evidence on the economic costs, benefits, and social impacts of attention to sex and gender in health research is a major obstacle to moving from policies of passive inclusion to an active focus on the medical gender gap. Research on CAD to date has yielded some benefits, but lagging attention to women leaves a knowledge gap.

Quantifying the impact of research funding investment is a relatively new area of inquiry (Adam et al., 2018). Microsimulation modeling can help address the gap in knowledge about investment in women's health research on CAD and examine the impacts of additional investments (see, for example, Grant and Buxton, 2018). Impacts can be quantified in economic terms. By understanding the impact of CAD and potential disease mitigation on health-related quality of life (as well as other health outcomes), we can ensure that outcomes beyond those that are readily monetized are appropriately considered and included.

We present the results of microsimulation modeling used to explore the potential for enhanced investment in women's health research, in terms of the economic well-being of women and for the U.S. population. Few studies have employed models stratified by sex or gender to test the sex and gender differences of CAD. In a review of the literature on gender differences for Alzheimer's disease, CAD, and rheumatoid arthritis in 2020, RAND researchers determined that the majority of studies use sex and gender as a population variable, descriptive variable, or control variable. *Women's health research* as used in this report refers both to analyses that address sex and/or gender within general sample or population studies and to research focusing on women specifically.[1] Our microsimulation model approach contributes to the existing body of literature by allowing us to project

Microsimulation modeling can help address the gap in knowledge about investment in women's health research on CAD and examine the impacts of additional investments

[1] We follow terminology guidance from the NIH, which states the following:

- "Sex" refers to biological factors and processes (e.g., sex chromosomes, endogenous hormonal profiles) related to differentiation between males (who generally have XY chromosomes) and females (who generally have XX chromosomes). "Gender" refers to culturally- and socially-defined roles for people, sometimes but not always along the lines of a gender binary (girls and women, boys and men).
- "Gender" incorporates individuals' self-perceptions (gender identity); the perceptions, attitudes, and expectations of others (gender norms); and social interactions (gender relations) (NIH, 2020a).

For the purposes of these analyses, we refer to sex and/or gender research generally; assumptions are about sex and/or research focused on women.

the future impact of funding on health outcomes and changes in societal burden from CAD.

Determining the Research Investment

We used current levels of funding from the NIH as the base case, with comparisons to doubling the level of research funding invested in women-focused research. We assumed that the impacts of increased funding occur through innovations that reduce the age incidence of disease and disease mortality and improve health-related quality of life. We quantified the innovations through costs of informal and paid caregiving, work productivity for informal caregivers, and healthy life years gained or lost.

In the United States, the universe of funding for research on cardiovascular disease extends beyond NIH and includes other major funders and advocacy organizations, such as the American Heart Association, the biopharmaceutical industry, and philanthropic organizations (American Heart Association, undated). The NIH's share of CAD research investment is large, however, and provides a starting

point for understanding investments in health research generally and women's health research in particular.

The goal of the analyses is to serve as a foundation for developing a concrete, actionable research and funding agenda. The analyses are intended to demonstrate the potential impacts of increased funding for research on women's health and thereby inform the prioritization of research funding allocations for funders, legislators, and the business community.

Methods

We used microsimulation models to address the impact of funding for women's health research on CAD. The models followed a cohort representing the U.S. population of individuals age 25 and older who have or could develop CAD. The youngest age of 25 reflects the fact that CAD affects adults and captures the working-age population and older. The model assumed 100 percent mortality at age 99.

The model simulated the progression of each person's health in the sample over a 30-year time horizon. We generated a model to first reflect the status quo of the disease and then re-simulated the model under the assumption that increased investment improves health outcomes and thus lowers costs (see Figure 1).[2]

Coronary Artery Disease Model

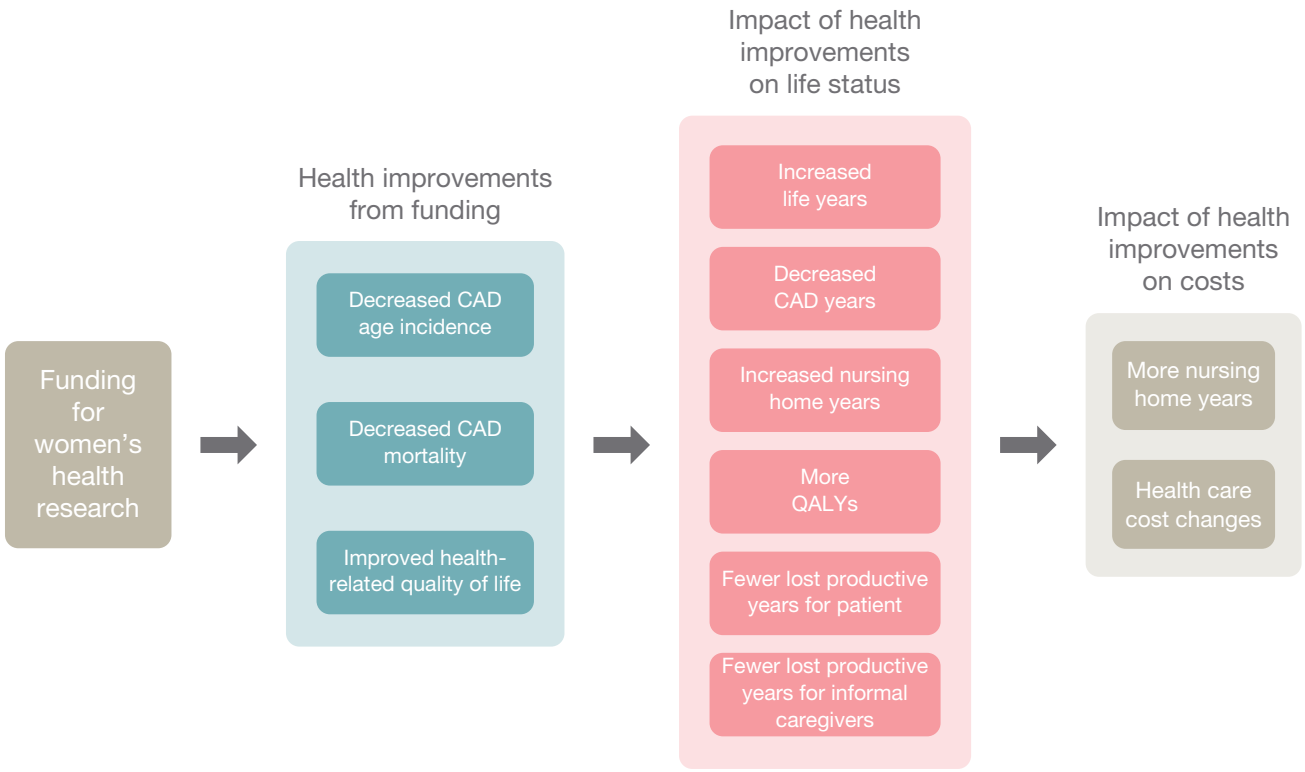
By tying different funding scenarios to societal burden, the microsimulation model quantifies how funding amounts affect the societal burden of CAD in terms of health expenditures, productivity loss, caregiver time loss, and lost life years. The model provides an estimate of impact on QALYs, not just on absolute lost life years. The QALY is one way in which monetary value can be assigned to disease impact and has been used as a metric for disease impact and impact of health innovation, incorporating length of life with the quality of life (Grant and Buxton, 2018).

The model assumes improved health as a result of increased funding for women's health research: specifically, because of decreased

[2] For a detailed technical appendix describing the specifics of the microsimulation model, please visit www.rand.org/t/RRA708-2.

FIGURE 1

Model of Research Funding Impacts for CAD



age incidence of CAD, decreased mortality, and improved health-related quality of life.

We used the Medical Expenditure Panel Survey because of its large sample and range of ages, clear diagnosis indicators, detailed data on medical expenditures, and detailed employment and income data. We also used data from the Centers for Medicaid & Medicare Services Medicare Beneficiary Summary File to estimate age-specific incidence and mortality rates for patients.

A Key Contribution: Addressing Future Earnings Equality

In the United States, earnings for white males exceed those of Black and Latino males and exceeds those for all women. Rather than use race and ethnicity and gender to adjust earnings for the hypothetical cohort, we chose to base earnings calculations for everyone on the earnings of non-Hispanic white males. This avoids the gender- and

race-based labor market discrimination that is inherent in the different (and lower) earnings for women and non-Hispanic white males.

Time Horizon

The representative cohort of around 1 million lives was moved through a 30-year time horizon, with the impact of investment expected ten years from initiation. The cohort was created as a representative sample of the United States, following age and gender distributions for individuals age 25 and older and using existing disease rates by age and gender.

We chose a ten-year investment impact using existing research on the time from investment to health care impacts (Cruz Rivera et al., 2017; Hansen et al., 2013; Scott et al., 2014). The 30-year model time horizon permits accrual of impacts for the 20 subsequent years, within the lifespan of the majority of the cohort.

We used prior research on funding investment return as a basis for assumptions on return on research investment: that is, the impact of funding levels on health outcomes (Grant and Buxton, 2018). The return on research investment calculation was a function of the following specific health outcomes: age incidence of disease, improved detection rates and earlier detection in the disease course, and reduced mortality due to disease. Following analyses in which the return on research investment was permitted to vary, we constrained the model to determine inputs that would yield an expected ROI of 15 percent, in line with findings from several therapeutic areas (Committee on Family Caregiving for Older Adults, 2016).

Taken together, these components enabled us to simulate the effects of increasing funding for health research on women in terms of economic outcomes. These economic outcomes included the monetary value of workers being able to stay in the labor force longer as a result of decreased caregiving burden.

Investment Impacts on Health Improvements

The model provides information on the ROI associated with multiple innovation impacts. Models address each of the following health improvement impacts separately and then address all three impacts occurring together:

1. decreased age incidence of disease (probability of onset at a given age)
2. decreased mortality rates for CAD patients, given age and gender
3. improvements in health-related quality of life, with the assumption that reduction in symptoms and more functional independence would account for more QALYs.

How Much Health Improvement?

Given the uncertainty regarding overall health improvements that investment in research can produce, we examined three levels of improvement: 0.01 percent, 0.02 percent, and 1 percent improvement. That is, we estimated the reduced disease incidence, reduced mortality, and improved quality of life together were estimated to sum to an overall health improvement at these three levels.

Who Benefits?

The main model assumption was that health improvements for women were three times that of men for a targeted investment in women's CAD research. Investment in women's health research can be expected to benefit women, but some of the innovation will benefit everyone.

For comparison purposes, we examined results assuming equal health innovation impacts on men and women: i.e., assuming research investments in general research rather than research on women's health specifically. Given the relative lack of attention to women even within gender-neutral research, this assumption likely overestimates the impact on women's health.

Thus, when considering an average health improvement of 1 percent, the equal impact assumes that both women and men realize a 1 percent improvement, whereas the three-times model assumes that women realize a 1.5 percent improvement and men realize a 0.5 percent improvement

Value of Investing in Women's Health Research

To further understand investment impact, we also examined the probability of success of research investment levels. We calculated the minimum probability of success of the investment to generate a target of 15 percent ROI for a given health improvement. Results are presented for the doubling investment scenario.

Baseline Investment in Women's Health Research

To estimate the baseline level of research funding for women's health in CAD, we retrieved all titles and abstracts in this research portfolio using NIH RePORTER, the publicly available interface of funded extramural NIH projects (NIH, 2020b). The terms used to search the retrieved titles and abstracts to determine the total number of women-focused projects were "women," "sex," "gender," and "female." Projects without these terms in the title or abstract were excluded from the women-focused research set examined (N = 56,612). The RePORTER search identified 10,685 CAD projects from 2008 to 2019; 4.5 percent of the total dollar amount of the portfolio was women-focused. The 4.5 percent increment was added to the 2019 amount to double the level of investment in women's health research by $20.1 million to $40.2 million. All costs are presented in 2017 U.S. dollars.

Results

We present the health and economic improvements and resulting impact on costs for the primary specification, scenario 1: a 0.01 percent average health improvement, with three times the impact for women as for men. Different funding scenarios are compared to provide context for these results. Finally, we present the resulting ROIs and probability of success necessary to have an expected ROI of 15 percent. Complete results are provided in the technical report (Baird et al., 2021).

Impact of Increased Funding of Women's Health on Health and Economic Outcomes

Figure 2 presents results in terms of health and economic outcomes and the resulting impact on costs, using the model cohort and then scaled up to the U.S. population, age 25 and older. This represents approximately 225 million people, of which about 24 million people had CAD at baseline.

Increased Life Expectancy

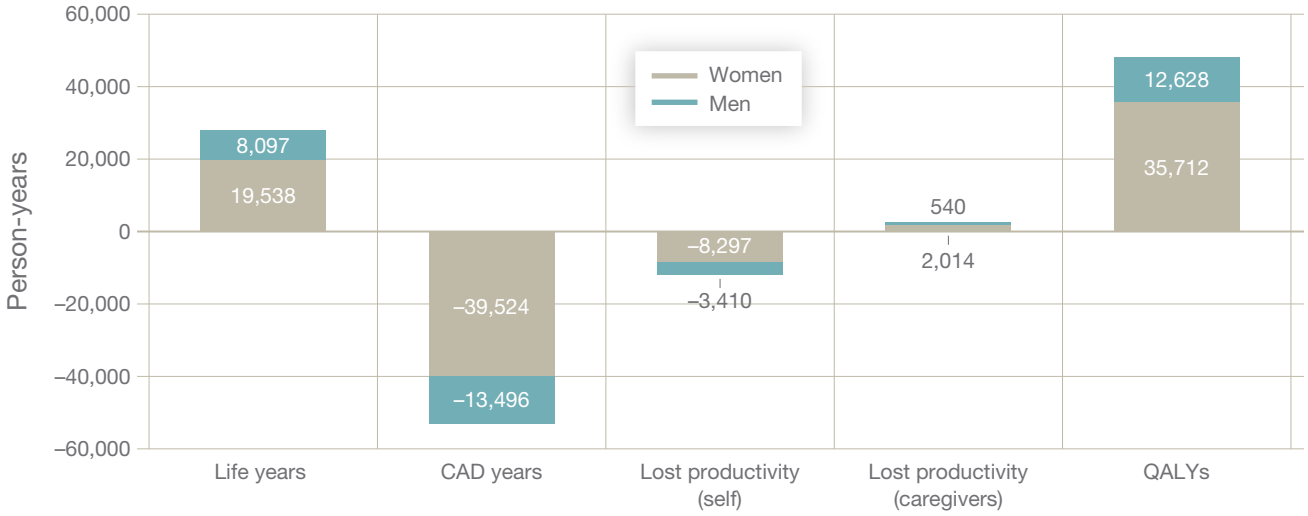
We found that women realize almost 20,000 more life years from innovations, while men realize more than 8,000 additional life years from innovations, for a total of almost 28,000 more life years.

Decreased Disease Burden

Innovations generated a reduction in CAD burden in terms of life years with CAD because of shorter disease duration and a reduction in age incidence. Women have nearly 40,000 fewer life years with CAD, and men have more than 13,000 fewer life years with CAD.

FIGURE 2

Health and Economic Improvements of Increased Investment in Women's CAD Research



NOTE: Figure represents the U.S. population age 25 and older of about 225 million and shows a 0.01 percent impact, which is three times larger for women than men.

Lost Productivity for People with Coronary Artery Disease

Health improvements increase employment and earnings of the CAD population in two ways. Fewer years of CAD create less lost earnings, and more years of life allows for more years of work. This yields around 8,000 more years of work for women and 3,000 more for men.

Caregiver Productivity

Of interest is that caregiver productivity drops by around 2,000 years for women and 500 years for men. Innovations result in more years of life for patients, leading to an added burden in terms of informal caregiving.

Increased Quality of Life

Delayed onset reduces the years of CAD burden, which increases quality of life. Decreased mortality rates lead to more years alive, which increases quality of life. Finally, we directly decreased the reduction in quality of life for CAD patients because of the health improvements, which represent potential innovations that, while not changing the onset or severity of the disease, decrease the burden of the disease. For these reasons, the QALYs represent a large effect, with about 48,000 more life-year equivalents of a fully-healthy adult. Of these full life-year equivalents, approximately 74 percent are from women patients, and 26 percent are from men.

Impact on Cost Outcomes

Costs associated with the 0.01 percent health improvement vary by sector examined (see Figure 3).

The overall reduction in costs was about $1.9 billion over 30 years, in 2017 dollars. About 73 percent of the costs are from female patients, and 27 percent are from male patients. Nursing home costs, direct health care costs, and lost productivity of caregivers are small relative to the impact on fewer lost QALYs and fewer lost years of workforce productivity.

What Is the Return on Investment for Funding Women's Health Research?

According to the model assumptions (doubling the investment in women's health research within the CAD portfolio and assuming the small 0.01 percent health improvement), the ROI is very large: 9,500 percent. This result suggests that modest increases in funding for women's health research have the potential to yield very large gains.

FIGURE 3

Change in Costs with Increased Funding for Women's Health Research

NOTE: Figure shows a 0.01 percent impact, which is three times larger for women than men.

Discussion

Small investments in CAD are likely to yield large societal gains. The very high ROI from assumptions of relatively small overall health improvement support the potential for gains from research on women. The overall magnitude of impact is greater than similar research on the impact of research investment (Luce et al., 2006). The results can help establish the value of new interventions by addressing which stakeholders and which societal payers are affected (El-Hayek et al., 2019).

These results assumed that dollars invested in women's health research would yield greater benefits for women than for men but that all people would recognize health benefits from the investment. We made comparisons between an "equal" impact on women and men and a differential impact on women. The status quo investment stance for general research disadvantages women, given the historical use of men as research standards and women as special cases. That is, gender-neutral or gender-inclusive research yields results that are less applicable to women than to men. Assuming that women benefit from women-focused research investment at a rate of three to one compared with men may underestimate actual benefit to women.

Estimates for the time from investment to a discernible impact of investment for health research are about 13 to 25 years (Cruz Rivera et al., 2017; Hansen et al., 2013; Scott et al., 2014). Future research may accelerate that timeline. The speed with which treatments and vaccines are being developed to address the coronavirus disease 2019 (COVID-19) pandemic may be a bellwether for research time horizons, demonstrating the potential for shorter timelines for peer review and publication of research results. These models assume a single cohort without replacement. Although impacts were scaled up to the U.S. population, cumulative impacts of health improvements may be greater than presented here, given the movement of individuals over 30 years.

The very high ROI from assumptions of relatively small health improvement support the potential for gains from research on women.

One key consideration when modeling using labor force participation and earnings is selection of earnings profiles. We chose to apply the earnings of non-Hispanic white males for all races and ethnicities and genders in the informal caregiving population. This has the advantage of avoiding assumed ongoing bias but represents a departure from the strict matching of other economic modeling studies.

Health research investments affect society through many pathways. The models examined here focused on a small but important subset of potential impacts on population health using investment in women's health research. Although a cure and/or preventive intervention may be possible for CAD over the coming decades, these analyses assume relatively small health impacts from research investment. More-optimistic scenarios are not unreasonable.

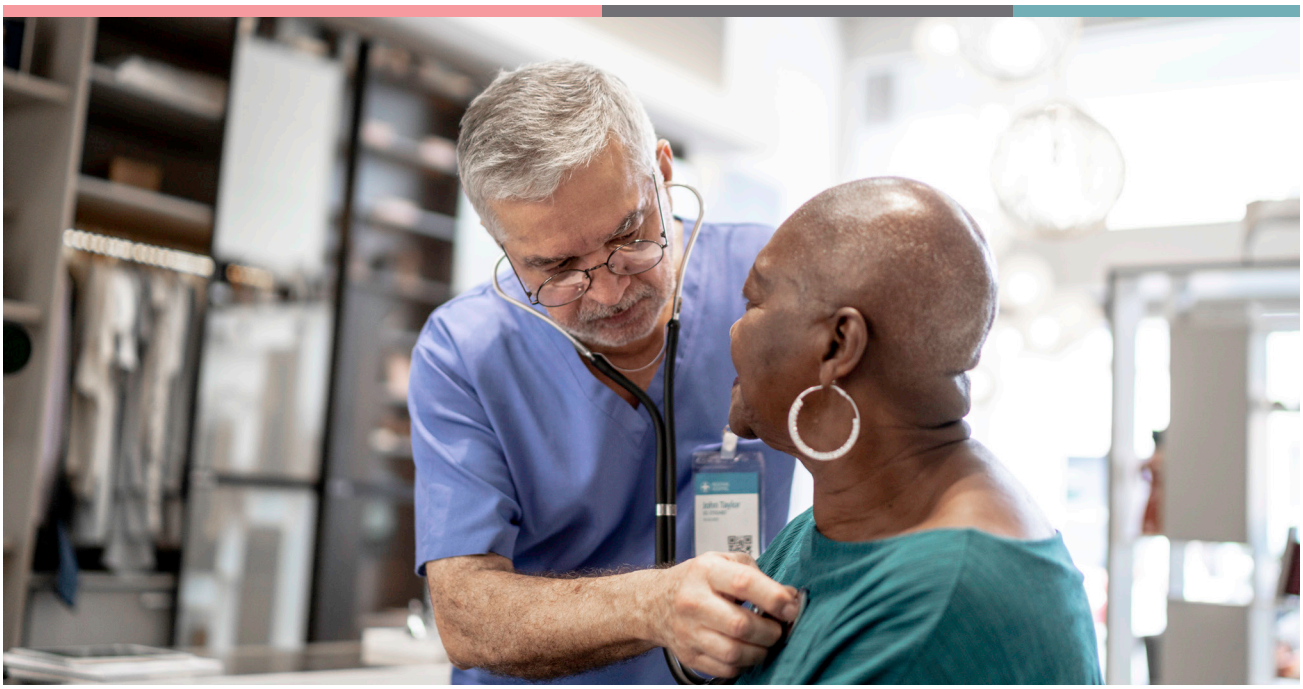
Limitations

All models involve assumptions, by design. The assumptions made for the models reported here were (in general) selected to return more-conservative results: that is, results that bound the lower end of possibilities for investment in women's health research. The potential impact of health improvements on patient functioning may lead to workforce productivity loss for informal caregivers, underscoring the importance of identifying policy scenarios that address possible transitions between informal caregiving and formal long-term care if innovations extend time in functionally impaired stages. The analyses here do not reference transgender or other sex and gender identities. This is not to deemphasize the importance of a wider consideration of sex and gender identities, but the focus here is on a first view of the underresourced area of women's health.

Policy Implications

The results of these analyses suggest several policy actions to inform decisionmaking about research funding allocations. Specifically, the following are likely fruitful areas for expanding the research agenda on sex and gender and CAD:

- the unknown interactions of sex and gender with cardiovascular disease antecedents and disease progression to inform treatment and prevention research
- understudied interactions of gender and race with cardiovascular disease risk, health care, and disease progression (in particular,



examining obstacles to access to and use of medical provider visits, prescription drugs, and relevant devices)
- differences by sex and gender in dietary impacts on disease and adherence to dietary recommendations
- differences in disease course and outcomes by sex and gender according to different patterns of use of formal and informal caregiving.

Further study of the relationship between earlier detection for women and improved disease management, in terms of the impact on health and quality of life outcomes, can aid with tracking investment impacts in the future, given the findings here of the potential for impact on health-related quality of life of women with CAD. The following recommendations can provide a foundation to support research funding allocation decisions:

- Raise awareness of differences between the CAD course for women and men, as well as the potential for investment to improve disease outcomes and societal impact.
- Raise awareness among the business community of the potential ROI for women's health research, particularly for women in the workforce.

Conclusion

Understanding the full range of societal impacts from health research investment requires consideration of multiple factors and, given the uncertainty of the future, requires assumptions. Differences in etiology, detection, care access, and treatment by sex and gender are well-documented in CAD and can provide specifics to inform an agenda for research on women's health (Gulati et al., 2009; Merz et al., 2006; Quyyumi, 2006). In conjunction with detailing the research agenda, the financial investment needed to realize the goals of that agenda requires planning. Investing more in research on women's health is likely to deliver net positive societal impacts. A clear understanding of the potential for investment can improve decisions about where and how to invest in order to recognize positive impacts for women and for society as a whole.

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Social and Behavioral Policy Program

RAND Social and Economic Well-Being is a division of the RAND Corporation that seeks to actively improve the health and social and economic well-being of populations and communities throughout the world. This research was conducted in the Social and Behavioral Policy Program within RAND Social and Economic Well-Being. The program focuses on such topics as risk factors and prevention programs, social safety net programs and other social supports, poverty, aging, disability, child and youth health and well-being, and quality of life, as well as other policy concerns that are influenced by social and behavioral actions and systems that affect well-being. For more information, email sbp@rand.org.

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RAND SOCIAL AND ECONOMIC WELL-BEING

Women's health has suffered from insufficient research addressing women. The research community has not widely embraced the value of this research, and the impact of limited knowledge about women's health relative to men's is far-reaching. Without information on the potential return on investment for women's health research, research funders, policymakers, and business leaders lack a basis for altering research investments to improve knowledge of women's health.

As part of an initiative of the Women's Health Access Matters (WHAM) nonprofit foundation, RAND Corporation researchers examined the impact of increasing funding for women's health research on coronary artery disease (CAD). CAD was chosen partly because physiological differences between men and women affect factors that relate to the development and progression of cardiovascular disease. In this report, the authors present the results of microsimulation models used to explore the potential for enhanced investment in women's health research, in terms of the economic well-being of women and for the U.S. population.

The RAND Corporation is a research organization that develops solutions to public policy challenges to help make communities throughout the world safer and more secure, healthier and more prosperous. RAND is nonprofit, nonpartisan, and committed to the public interest.

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Societal Impact of Research Funding for Women's Health

IN CORONARY ARTERY DISEASE

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RAND CORPORATION

Women's Health Access Matters®

THE WHAM REPORT

WHAM, whamnow.org, is a 501c3 dedicated to funding women's health research to transform women's lives.

This report was conceived by WHAM in response to the considerable funding gap, historical exclusion, and under representation of women in health research.

As businesswomen, we believed that a focused study showing the impact of accelerating sex and gender-based health research on women, their families and the economy through a study quantifying costs and economic benefits would be an invaluable accountability index. In other words, if more investment is made in women's health research the plausible assumption is that women would benefit from sex-specific prevention strategies, diagnoses and treatments that reduce their burden of disease and thus improve their wellbeing and hence of society.

WHAM commissioned the RAND Corporation to conduct a data-driven study of the economic impact to society of increasing the investment in women's health research. This first research project comprises three disease modules: Alzheimer's Dementia, Rheumatoid Arthritis as representative of Autoimmune Disease, and Cardiovascular Disease. In the future, we plan to include Lung Cancer and also study different socioeconomic groups to the extent that the data are available and detail the global data which expands this research.

To the best of WHAM's and RAND's knowledge, this is the first analysis of its kind to create and calibrate a microsimulation model of investments in health R&D that examines differences for women's health research investment, and should become a seminal part of the arsenal in advocating for increased investment in women's health research. The research methodology and the microsimulation models have been vetted by a diverse panel of experts convened by RAND.

We are so thankful for the dedicated, invested partnership of the research team at the RAND Corporation who conducted the analysis presented here and brought their findings to life. We encourage other leaders, including advocates, economists, scientists, business leaders, public health experts and policy makers to draw from and act upon the results of this report. Together, we can drive meaningful change.

Carolee Lee
Founder and CEO, WHAM
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Please find additional infographics and social media toolkits on **www.thewhamreport.org**.

The technical specifications for the models are publicly available. Please visit **www.thewhamreport.org** to learn more about using these data and citing this report.

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WHAM's leadership of this research project was encouraged through the generous support and collaboration from the following partners:

American Heart Association
The Association is a relentless force for a world of longer, healthier lives dedicated to ensuring equitable health for all – in the U.S. and around the world. The Go Red for Women® movement is the trusted, passionate, relevant force for change to end heart disease and stroke in women all over the world.

GRFW and WHAM will collaborate to directly address the lack of societal-level evidence on the economic cost, benefits and social impact due to the underrepresentation of women in cardiovascular research.

BrightFocus Foundation
BrightFocus Foundation is a leading source of private research funding to defeat Alzheimer's, macular degeneration and glaucoma. Supporting scientists early in their careers to kick-start promising ideas, BrightFocus addresses a full and diverse range of approaches from better understanding the root causes of the diseases and improving early detection and diagnosis, to developing new drugs and treatments. The nonprofit has a longstanding commitment to funding pioneering, sex-based research in Alzheimer's and related dementias. BrightFocus currently manages a global portfolio of over 275 scientific projects, a $60 million investment, and shares the latest research findings and best practices to empower families impacted by these diseases of mind and sight.

The Connors Center for Women's Health and Gender Biology at Brigham and Women's Hospital/Harvard Medical School is a leading local and national force in advancing the health of women, with a rich history and strong foundation of women's health and sex-differences discovery, clinical care, and advocacy for equity in the health of women and is the Premier Partner and the Lead Scientific Research Partner of the WHAM Collaborative for Women's Health Research. The Connors Center shares the bold vision of improving the health of women and a commitment to joining forces to advance scientific discovery for the benefit of all women.

La Jolla Institute for Immunology
La Jolla Institute (LJI) is one of the top five research institutes in the world focused on the study of the immune system. LJI is home to three research centers that harness the efforts of collaborative groups of researchers on defined areas of inquiry, to accelerate progress toward the development of new treatments and vaccines to prevent and cure autoimmune conditions, cancer and infectious disease. Together, LJI and WHAM will create a framework for researchers to re-analyze existing data with sex as a biological variable, to work together to spark new projects, to hire new faculty to build key research areas, to communicate via the WHAM Report, and to establish an ignition point for new leadership in the scientific field.

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RESEARCH ADVISORY PANEL

RAND convened an advisory panel to help guide the work and elicit insights on the target case study areas of Autoimmune/Immune Disease, Cardiovascular Disease, and Alzheimer's Disease. Central to RAND's work was the creation of health economic models in each case study area. RAND is committed to creating final products with immediate relevance for use by funders, advocacy organizations, researchers, and other stakeholders.

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Executive Summary

The impact of limited knowledge about women's health relative to men's is far-reaching. Without information on the potential return on investment (ROI) for women's health research, research funders, policymakers, and business leaders lack a basis for altering research investments to improve knowledge of women's health.

Using microsimulation analyses, we examined the societal cost impact of increasing research funding in coronary artery disease (CAD). We quantified the potential impact of increasing funding for women's health on health outcomes and the ultimate societal costs, including health care expenditures, labor productivity, and quality-adjusted life years (QALYs). We calculated impacts across 30 years of doubling the proportion of the National Institutes of Health (NIH) extra-mural CAD portfolio devoted to women's health.

Key Takeaways

Large returns result from very small health improvements. Assuming health improvements of 0.01 percent or less in terms of age incidence, mortality, and quality of life yields the following results:

- For the U.S. population age 25 and older, more than 53,000 years with CAD can be saved across 30 years, with substantial gains in health-related quality of life.
- Almost 12,000 more years (and $236 million) can be saved in terms of labor productivity, both from higher labor and earnings from having fewer years of CAD and more years alive.

- The ROI is 9,500 percent for doubled investment in women's health research, even with only 0.01 percent improvement in health outcomes.

Investing in women's health research for CAD yields benefits similar to investing in general research, with improved health-related quality of life for women from women-focused research.

The results establish the potential for investment in women's health research on CAD to realize gains beyond additional general research investment and point the way to a concrete, actionable research and funding agenda.

Implications

Large societal gains may be possible by increasing investment in women's health research on CAD. The potential to recognize societal gains is greater for research devoted to women's health relative to general research, according to the assumptions used here.

We recommend the following policy actions based on this research to inform decisions about research funding allocations:

- Expand the research agenda to address
  - the unknown interactions of sex and gender with cardiovascular disease antecedents and disease progression to inform treatment and prevention research
  - understudied interactions of gender and race with cardiovascular disease risk, health care, and disease progression; in particular, examine obstacles to access to and use of medical provider visits, prescription drugs, and relevant devices
  - differences by sex and gender in dietary impacts on disease and adherence to dietary recommendations
  - differences in disease course and outcomes by sex and gender based on different patterns of use of formal and informal caregiving
  - health-related quality of life of women with CAD and the potential for earlier detection to positively affect health and quality of life outcomes.

By raising awareness of the current state of funding directed toward women's health in CAD and the potential for such funding to yield societal benefits, researchers and other communities can pursue information that is relevant for improving funding allocation decisions. Specific ways to connect other communities to the relevant issues include the following:

- Raise awareness of differences between the CAD course for women and men and the potential for investment to improve disease outcomes.
- Raise awareness among the business community of the potential ROI for women in the workforce from investment in women's health research.

Introduction

Because women have been underrepresented in health research, what we know about women's health is limited. Even today, the value of research investment on women's health is not widely accepted. The impact of this oversight is far-reaching.

Also unknown is the potential impact of accelerating and increasing funding for women's health research. What difference would doing so make in the health and well-being of everyone? Understanding this impact would provide vital information to funders, researchers, and policymakers to help them plan investments that can yield the greatest public health benefits.

As part of an initiative of the Women's Health Access Matters (WHAM) nonprofit foundation, RAND Corporation researchers examined the impact of increasing funding for women's health. WHAM has four pillar areas of focus: heart health, brain health, oncology, and autoimmune diseases. We reviewed disorders to use as case examples within each of these areas, comparing them in terms of overall prevalence; prevalence by gender; societal impact in terms of morbidity, mortality, and overall cost burden; and feasibility of obtaining data for constructing models. Within heart health, CAD was chosen as an important case study that could meaningfully inform funding policy.

We invited an expert advisory group to two meetings, in late summer and early fall 2020, about the project to provide input into model structure and assumptions. Members included health economists, health researchers and funders (including women's health experts), patient advocates, and representatives from health insurers and from the elder care business community. The advisers' input enabled us to finalize key assumptions and the model structure.

Why Focus on Coronary Artery Disease?

Physiological differences between men and women affect factors that relate to the development and progression of cardiovascular disease. For example, hormonal status influences renal sodium and water retention, with subsequent differences in blood pressure, and changes in blood pressure in response to changes in sodium intake are greater for women than men (Morrison and Ness, 2011). Evidence suggests that dietary changes may impact mortality differentially for women and men (Morrison and Ness, 2011). Differences extend to access and use of health services. More women than men are prescribed diuretics, and more men than women are prescribed aspirin, statins, and angiotensin-converting enzyme (ACE) inhibitors (Zhao et al., 2020). Incidence of death is higher for women than men during disease follow-up, despite more health care visits and prescription fills (Nichols et al., 2010).

Differences between men and women are also evident in the availability of informal caregivers for patients with CAD. More men than women CAD patients have informal caregivers, and having a caregiver is associated with better attainment of treatment goals (Hammond et al., 2012; Mondesir et al., 2018). Still mostly unexplored are the complex interactions of gender-based biology, individual physiology, and cultural factors in terms of cardiovascular disease risks and disease course (Barber et al., 2016; Tibuakuu et al., 2018).

Given these known differences and the potential for unknown differences to affect morbidity and mortality, investment in women's health could be expected to yield a favorable return for society.

The lack of societal-level evidence on the economic costs, benefits, and social impacts of attention to sex and gender in health research is a major obstacle to moving from policies of passive inclusion to an active focus on the medical gender gap. Research on CAD to date has yielded some benefits, but lagging attention to women leaves a knowledge gap.

Quantifying the impact of research funding investment is a relatively new area of inquiry (Adam et al., 2018). Microsimulation modeling can help address the gap in knowledge about investment in women's health research on CAD and examine the impacts of additional investments (see, for example, Grant and Buxton, 2018). Impacts can be quantified in economic terms. By understanding the impact of CAD and potential disease mitigation on health-related quality of life (as well as other health outcomes), we can ensure that outcomes beyond those that are readily monetized are appropriately considered and included.

We present the results of microsimulation modeling used to explore the potential for enhanced investment in women's health research, in terms of the economic well-being of women and for the U.S. population. Few studies have employed models stratified by sex or gender to test the sex and gender differences of CAD. In a review of the literature on gender differences for Alzheimer's disease, CAD, and rheumatoid arthritis in 2020, RAND researchers determined that the majority of studies use sex and gender as a population variable, descriptive variable, or control variable. *Women's health research* as used in this report refers both to analyses that address sex and/or gender within general sample or population studies and to research focusing on women specifically.[1] Our microsimulation model approach contributes to the existing body of literature by allowing us to project

Microsimulation modeling can help address the gap in knowledge about investment in women's health research on CAD and examine the impacts of additional investments

[1] We follow terminology guidance from the NIH, which states the following:

- "Sex" refers to biological factors and processes (e.g., sex chromosomes, endogenous hormonal profiles) related to differentiation between males (who generally have XY chromosomes) and females (who generally have XX chromosomes). "Gender" refers to culturally- and socially-defined roles for people, sometimes but not always along the lines of a gender binary (girls and women, boys and men).
- "Gender" incorporates individuals' self-perceptions (gender identity); the perceptions, attitudes, and expectations of others (gender norms); and social interactions (gender relations) (NIH, 2020a).

For the purposes of these analyses, we refer to sex and/or gender research generally; assumptions are about sex and/or research focused on women.

the future impact of funding on health outcomes and changes in societal burden from CAD.

Determining the Research Investment

We used current levels of funding from the NIH as the base case, with comparisons to doubling the level of research funding invested in women-focused research. We assumed that the impacts of increased funding occur through innovations that reduce the age incidence of disease and disease mortality and improve health-related quality of life. We quantified the innovations through costs of informal and paid caregiving, work productivity for informal caregivers, and healthy life years gained or lost.

In the United States, the universe of funding for research on cardiovascular disease extends beyond NIH and includes other major funders and advocacy organizations, such as the American Heart Association, the biopharmaceutical industry, and philanthropic organizations (American Heart Association, undated). The NIH's share of CAD research investment is large, however, and provides a starting

point for understanding investments in health research generally and women's health research in particular.

The goal of the analyses is to serve as a foundation for developing a concrete, actionable research and funding agenda. The analyses are intended to demonstrate the potential impacts of increased funding for research on women's health and thereby inform the prioritization of research funding allocations for funders, legislators, and the business community.

Methods

We used microsimulation models to address the impact of funding for women's health research on CAD. The models followed a cohort representing the U.S. population of individuals age 25 and older who have or could develop CAD. The youngest age of 25 reflects the fact that CAD affects adults and captures the working-age population and older. The model assumed 100 percent mortality at age 99.

The model simulated the progression of each person's health in the sample over a 30-year time horizon. We generated a model to first reflect the status quo of the disease and then re-simulated the model under the assumption that increased investment improves health outcomes and thus lowers costs (see Figure 1).[2]

Coronary Artery Disease Model

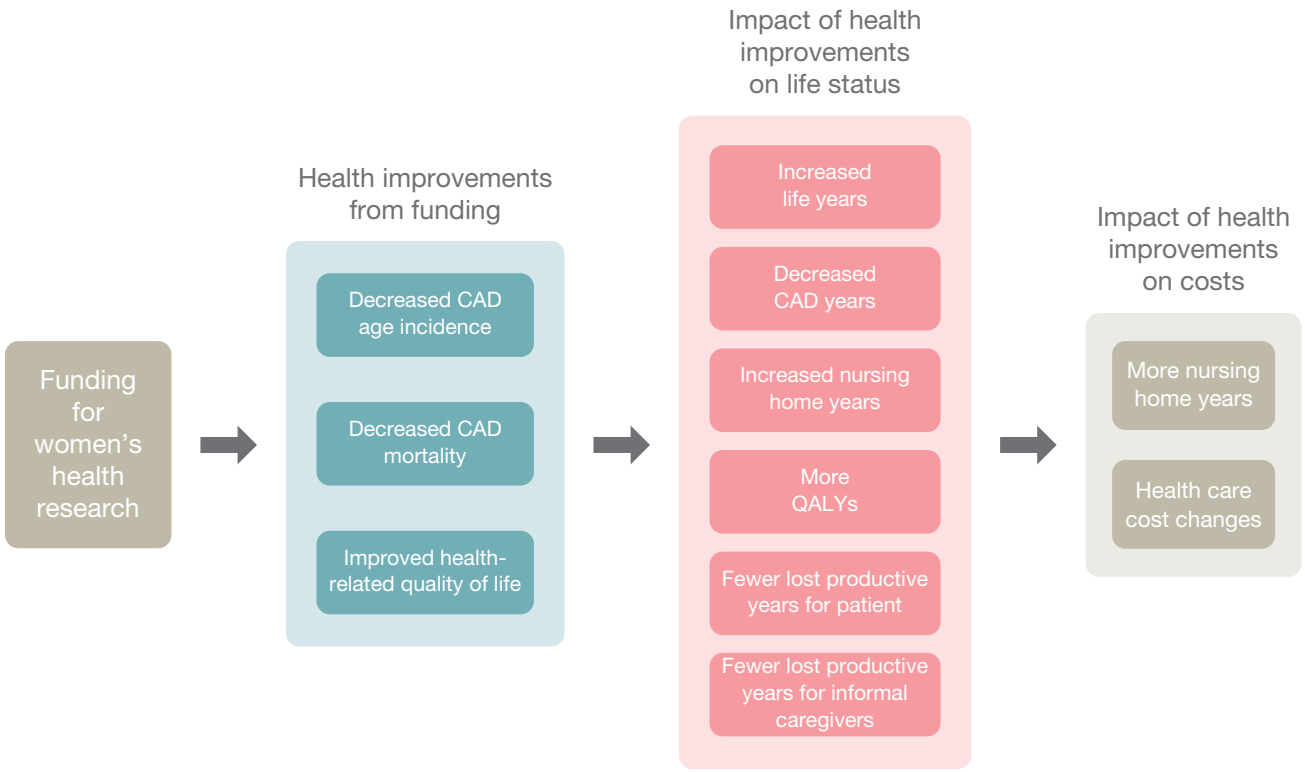
By tying different funding scenarios to societal burden, the microsimulation model quantifies how funding amounts affect the societal burden of CAD in terms of health expenditures, productivity loss, caregiver time loss, and lost life years. The model provides an estimate of impact on QALYs, not just on absolute lost life years. The QALY is one way in which monetary value can be assigned to disease impact and has been used as a metric for disease impact and impact of health innovation, incorporating length of life with the quality of life (Grant and Buxton, 2018).

The model assumes improved health as a result of increased funding for women's health research: specifically, because of decreased

[2] For a detailed technical appendix describing the specifics of the microsimulation model, please visit www.rand.org/t/RRA708-2.

FIGURE 1

Model of Research Funding Impacts for CAD



age incidence of CAD, decreased mortality, and improved health-related quality of life.

We used the Medical Expenditure Panel Survey because of its large sample and range of ages, clear diagnosis indicators, detailed data on medical expenditures, and detailed employment and income data. We also used data from the Centers for Medicaid & Medicare Services Medicare Beneficiary Summary File to estimate age-specific incidence and mortality rates for patients.

A Key Contribution: Addressing Future Earnings Equality

In the United States, earnings for white males exceed those of Black and Latino males and exceeds those for all women. Rather than use race and ethnicity and gender to adjust earnings for the hypothetical cohort, we chose to base earnings calculations for everyone on the earnings of non-Hispanic white males. This avoids the gender- and

race-based labor market discrimination that is inherent in the different (and lower) earnings for women and non-Hispanic white males.

Time Horizon

The representative cohort of around 1 million lives was moved through a 30-year time horizon, with the impact of investment expected ten years from initiation. The cohort was created as a representative sample of the United States, following age and gender distributions for individuals age 25 and older and using existing disease rates by age and gender.

We chose a ten-year investment impact using existing research on the time from investment to health care impacts (Cruz Rivera et al., 2017; Hansen et al., 2013; Scott et al., 2014). The 30-year model time horizon permits accrual of impacts for the 20 subsequent years, within the lifespan of the majority of the cohort.

We used prior research on funding investment return as a basis for assumptions on return on research investment: that is, the impact of funding levels on health outcomes (Grant and Buxton, 2018). The return on research investment calculation was a function of the following specific health outcomes: age incidence of disease, improved detection rates and earlier detection in the disease course, and reduced mortality due to disease. Following analyses in which the return on research investment was permitted to vary, we constrained the model to determine inputs that would yield an expected ROI of 15 percent, in line with findings from several therapeutic areas (Committee on Family Caregiving for Older Adults, 2016).

Taken together, these components enabled us to simulate the effects of increasing funding for health research on women in terms of economic outcomes. These economic outcomes included the monetary value of workers being able to stay in the labor force longer as a result of decreased caregiving burden.

Investment Impacts on Health Improvements

The model provides information on the ROI associated with multiple innovation impacts. Models address each of the following health improvement impacts separately and then address all three impacts occurring together:

1. decreased age incidence of disease (probability of onset at a given age)
2. decreased mortality rates for CAD patients, given age and gender
3. improvements in health-related quality of life, with the assumption that reduction in symptoms and more functional independence would account for more QALYs.

How Much Health Improvement?

Given the uncertainty regarding overall health improvements that investment in research can produce, we examined three levels of improvement: 0.01 percent, 0.02 percent, and 1 percent improvement. That is, we estimated the reduced disease incidence, reduced mortality, and improved quality of life together were estimated to sum to an overall health improvement at these three levels.

Who Benefits?

The main model assumption was that health improvements for women were three times that of men for a targeted investment in women's CAD research. Investment in women's health research can be expected to benefit women, but some of the innovation will benefit everyone.

For comparison purposes, we examined results assuming equal health innovation impacts on men and women: i.e., assuming research investments in general research rather than research on women's health specifically. Given the relative lack of attention to women even within gender-neutral research, this assumption likely overestimates the impact on women's health.

Thus, when considering an average health improvement of 1 percent, the equal impact assumes that both women and men realize a 1 percent improvement, whereas the three-times model assumes that women realize a 1.5 percent improvement and men realize a 0.5 percent improvement

Value of Investing in Women's Health Research

To further understand investment impact, we also examined the probability of success of research investment levels. We calculated the minimum probability of success of the investment to generate a target of 15 percent ROI for a given health improvement. Results are presented for the doubling investment scenario.

Baseline Investment in Women's Health Research

To estimate the baseline level of research funding for women's health in CAD, we retrieved all titles and abstracts in this research portfolio using NIH RePORTER, the publicly available interface of funded extramural NIH projects (NIH, 2020b). The terms used to search the retrieved titles and abstracts to determine the total number of women-focused projects were "women," "sex," "gender," and "female." Projects without these terms in the title or abstract were excluded from the women-focused research set examined (N = 56,612). The RePORTER search identified 10,685 CAD projects from 2008 to 2019; 4.5 percent of the total dollar amount of the portfolio was women-focused. The 4.5 percent increment was added to the 2019 amount to double the level of investment in women's health research by $20.1 million to $40.2 million. All costs are presented in 2017 U.S. dollars.

Results

We present the health and economic improvements and resulting impact on costs for the primary specification, scenario 1: a 0.01 percent average health improvement, with three times the impact for women as for men. Different funding scenarios are compared to provide context for these results. Finally, we present the resulting ROIs and probability of success necessary to have an expected ROI of 15 percent. Complete results are provided in the technical report (Baird et al., 2021).

Impact of Increased Funding of Women's Health on Health and Economic Outcomes

Figure 2 presents results in terms of health and economic outcomes and the resulting impact on costs, using the model cohort and then scaled up to the U.S. population, age 25 and older. This represents approximately 225 million people, of which about 24 million people had CAD at baseline.

Increased Life Expectancy

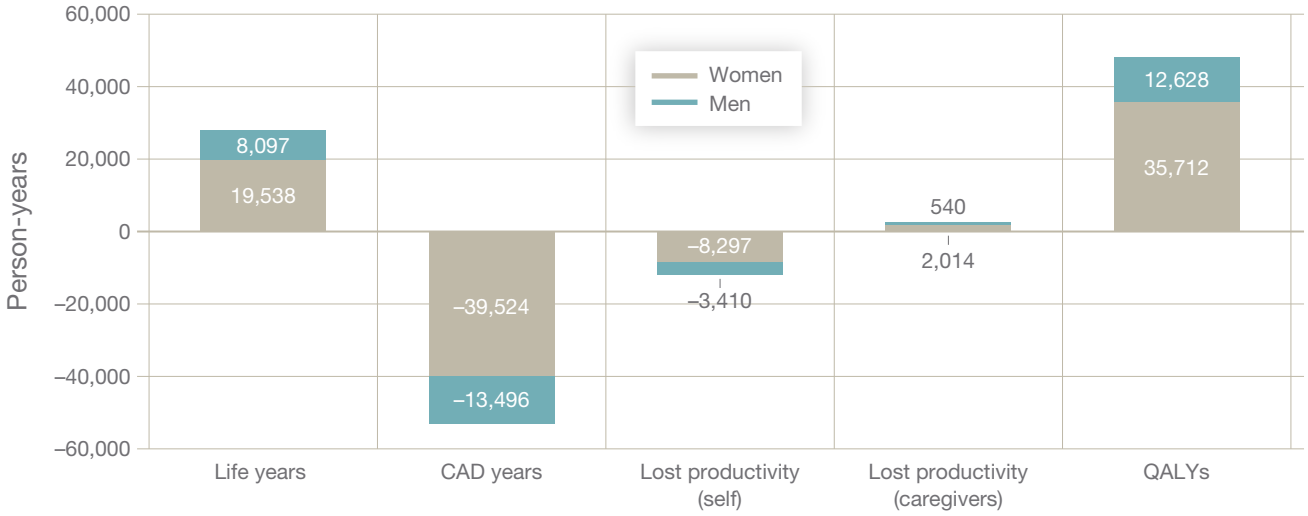
We found that women realize almost 20,000 more life years from innovations, while men realize more than 8,000 additional life years from innovations, for a total of almost 28,000 more life years.

Decreased Disease Burden

Innovations generated a reduction in CAD burden in terms of life years with CAD because of shorter disease duration and a reduction in age incidence. Women have nearly 40,000 fewer life years with CAD, and men have more than 13,000 fewer life years with CAD.

FIGURE 2

Health and Economic Improvements of Increased Investment in Women's CAD Research



NOTE: Figure represents the U.S. population age 25 and older of about 225 million and shows a 0.01 percent impact, which is three times larger for women than men.

Lost Productivity for People with Coronary Artery Disease

Health improvements increase employment and earnings of the CAD population in two ways. Fewer years of CAD create less lost earnings, and more years of life allows for more years of work. This yields around 8,000 more years of work for women and 3,000 more for men.

Caregiver Productivity

Of interest is that caregiver productivity drops by around 2,000 years for women and 500 years for men. Innovations result in more years of life for patients, leading to an added burden in terms of informal caregiving.

Increased Quality of Life

Delayed onset reduces the years of CAD burden, which increases quality of life. Decreased mortality rates lead to more years alive, which increases quality of life. Finally, we directly decreased the reduction in quality of life for CAD patients because of the health improvements, which represent potential innovations that, while not changing the onset or severity of the disease, decrease the burden of the disease. For these reasons, the QALYs represent a large effect, with about 48,000 more life-year equivalents of a fully-healthy adult. Of these full life-year equivalents, approximately 74 percent are from women patients, and 26 percent are from men.

Impact on Cost Outcomes

Costs associated with the 0.01 percent health improvement vary by sector examined (see Figure 3).

The overall reduction in costs was about $1.9 billion over 30 years, in 2017 dollars. About 73 percent of the costs are from female patients, and 27 percent are from male patients. Nursing home costs, direct health care costs, and lost productivity of caregivers are small relative to the impact on fewer lost QALYs and fewer lost years of workforce productivity.

What Is the Return on Investment for Funding Women's Health Research?

According to the model assumptions (doubling the investment in women's health research within the CAD portfolio and assuming the small 0.01 percent health improvement), the ROI is very large: 9,500 percent. This result suggests that modest increases in funding for women's health research have the potential to yield very large gains.

FIGURE 3

Change in Costs with Increased Funding for Women's Health Research

NOTE: Figure shows a 0.01 percent impact, which is three times larger for women than men.

Discussion

Small investments in CAD are likely to yield large societal gains. The very high ROI from assumptions of relatively small overall health improvement support the potential for gains from research on women. The overall magnitude of impact is greater than similar research on the impact of research investment (Luce et al., 2006). The results can help establish the value of new interventions by addressing which stakeholders and which societal payers are affected (El-Hayek et al., 2019).

These results assumed that dollars invested in women's health research would yield greater benefits for women than for men but that all people would recognize health benefits from the investment. We made comparisons between an "equal" impact on women and men and a differential impact on women. The status quo investment stance for general research disadvantages women, given the historical use of men as research standards and women as special cases. That is, gender-neutral or gender-inclusive research yields results that are less applicable to women than to men. Assuming that women benefit from women-focused research investment at a rate of three to one compared with men may underestimate actual benefit to women.

Estimates for the time from investment to a discernible impact of investment for health research are about 13 to 25 years (Cruz Rivera et al., 2017; Hansen et al., 2013; Scott et al., 2014). Future research may accelerate that timeline. The speed with which treatments and vaccines are being developed to address the coronavirus disease 2019 (COVID-19) pandemic may be a bellwether for research time horizons, demonstrating the potential for shorter timelines for peer review and publication of research results. These models assume a single cohort without replacement. Although impacts were scaled up to the U.S. population, cumulative impacts of health improvements may be greater than presented here, given the movement of individuals over 30 years.

The very high ROI from assumptions of relatively small health improvement support the potential for gains from research on women.

One key consideration when modeling using labor force participation and earnings is selection of earnings profiles. We chose to apply the earnings of non-Hispanic white males for all races and ethnicities and genders in the informal caregiving population. This has the advantage of avoiding assumed ongoing bias but represents a departure from the strict matching of other economic modeling studies.

Health research investments affect society through many pathways. The models examined here focused on a small but important subset of potential impacts on population health using investment in women's health research. Although a cure and/or preventive intervention may be possible for CAD over the coming decades, these analyses assume relatively small health impacts from research investment. More-optimistic scenarios are not unreasonable.

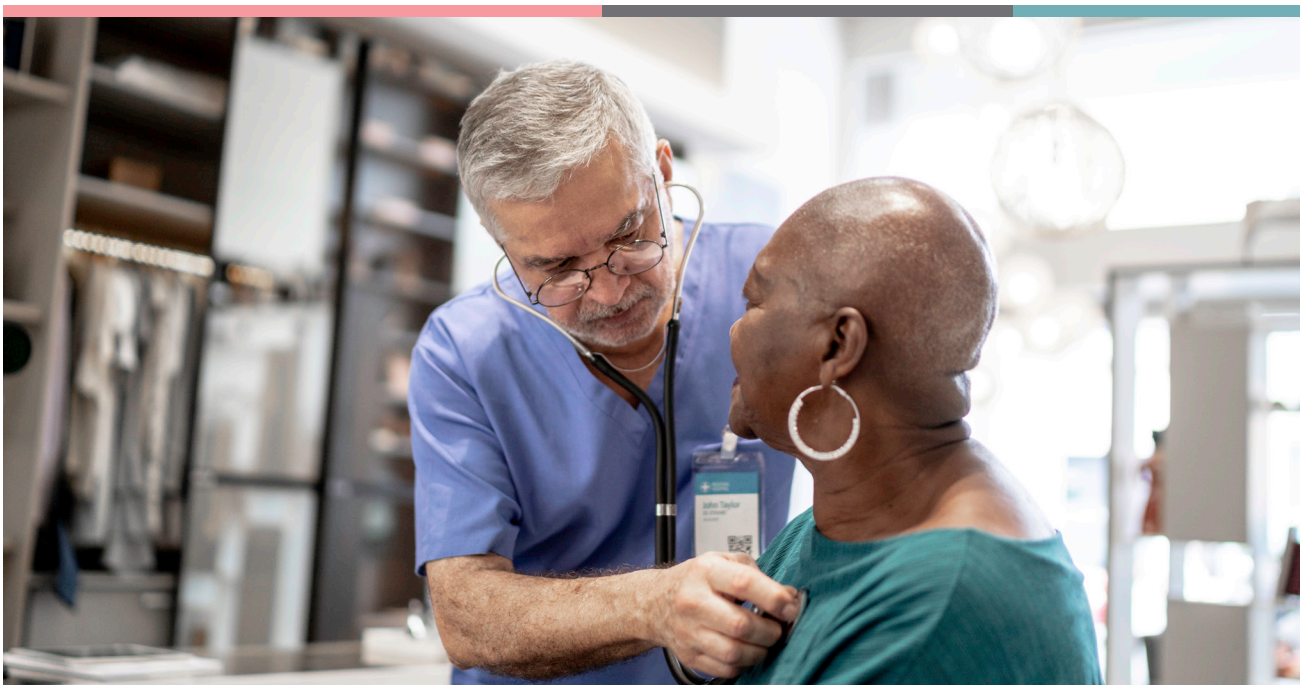
Limitations

All models involve assumptions, by design. The assumptions made for the models reported here were (in general) selected to return more-conservative results: that is, results that bound the lower end of possibilities for investment in women's health research. The potential impact of health improvements on patient functioning may lead to workforce productivity loss for informal caregivers, underscoring the importance of identifying policy scenarios that address possible transitions between informal caregiving and formal long-term care if innovations extend time in functionally impaired stages. The analyses here do not reference transgender or other sex and gender identities. This is not to deemphasize the importance of a wider consideration of sex and gender identities, but the focus here is on a first view of the underresourced area of women's health.

Policy Implications

The results of these analyses suggest several policy actions to inform decisionmaking about research funding allocations. Specifically, the following are likely fruitful areas for expanding the research agenda on sex and gender and CAD:

- the unknown interactions of sex and gender with cardiovascular disease antecedents and disease progression to inform treatment and prevention research
- understudied interactions of gender and race with cardiovascular disease risk, health care, and disease progression (in particular,



examining obstacles to access to and use of medical provider visits, prescription drugs, and relevant devices)
- differences by sex and gender in dietary impacts on disease and adherence to dietary recommendations
- differences in disease course and outcomes by sex and gender according to different patterns of use of formal and informal caregiving.

Further study of the relationship between earlier detection for women and improved disease management, in terms of the impact on health and quality of life outcomes, can aid with tracking investment impacts in the future, given the findings here of the potential for impact on health-related quality of life of women with CAD. The following recommendations can provide a foundation to support research funding allocation decisions:

- Raise awareness of differences between the CAD course for women and men, as well as the potential for investment to improve disease outcomes and societal impact.
- Raise awareness among the business community of the potential ROI for women's health research, particularly for women in the workforce.

Conclusion

Understanding the full range of societal impacts from health research investment requires consideration of multiple factors and, given the uncertainty of the future, requires assumptions. Differences in etiology, detection, care access, and treatment by sex and gender are well-documented in CAD and can provide specifics to inform an agenda for research on women's health (Gulati et al., 2009; Merz et al., 2006; Quyyumi, 2006). In conjunction with detailing the research agenda, the financial investment needed to realize the goals of that agenda requires planning. Investing more in research on women's health is likely to deliver net positive societal impacts. A clear understanding of the potential for investment can improve decisions about where and how to invest in order to recognize positive impacts for women and for society as a whole.

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Social and Behavioral Policy Program

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RAND SOCIAL AND ECONOMIC WELL-BEING

Women's health has suffered from insufficient research addressing women. The research community has not widely embraced the value of this research, and the impact of limited knowledge about women's health relative to men's is far-reaching. Without information on the potential return on investment for women's health research, research funders, policymakers, and business leaders lack a basis for altering research investments to improve knowledge of women's health.

As part of an initiative of the Women's Health Access Matters (WHAM) nonprofit foundation, RAND Corporation researchers examined the impact of increasing funding for women's health research on coronary artery disease (CAD). CAD was chosen partly because physiological differences between men and women affect factors that relate to the development and progression of cardiovascular disease. In this report, the authors present the results of microsimulation models used to explore the potential for enhanced investment in women's health research, in terms of the economic well-being of women and for the U.S. population.

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