THE WHAM REPORT

The Case To Fund Women's Health Research

AN ECONOMIC AND SOCIETAL IMPACT ANALYSIS

Matthew D. Baird
Melanie A. Zaber
Annie Chen
Andrew W. Dick
Chloe E. Bird
Molly Waymouth
Grace Gahlon
Denise D. Quigley
Hamad Al-Ibrahim
Lori Frank

RAND CORPORATION

Women's Health Access Matters®

The Case To Fund Women's Health Research

AN ECONOMIC AND SOCIETAL IMPACT ANALYSIS

Matthew D. Baird
Melanie A. Zaber
Annie Chen
Andrew W. Dick
Chloe E. Bird
Molly Waymouth
Grace Gahlon
Denise D. Quigley
Hamad Al-Ibrahim
Lori Frank

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 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.

WHAM REPORT PARTNERS

THE WHAM BOARD

Carolee Lee, Chair

Meryl Comer, Vice Chair

Anula Jayasuriya, Vice Chair

Dr. Dale Atkins, Psychologist; Author

Joanne Bauer, Global Corporate Executive and Board Member; retired President of Kimberly-Clark's Global Health Care Business

Nelly Bly, Vice Chair, The Center for Discovery Board of Directors; Trustee, Dwight-Englewood School; Author

Marilyn Chinitz, Litigator and Partner, Blank Rome LLP

Maria Chrin, Partner, Circle Wealth Management

Meryl Comer, Vice Chair and Global Chair, WHAM; Co-Founder, UsAgainstAlzheimers/ WomenAgainstAlzheimers; Chair, Global Alliance on Women's Brain Health

Gina Diez Barroso, President and CEO, Grupo Diarq; Founder, DaliaEmpower

Chaz Ebert, President of the Roger and Chaz Ebert Foundation

Vicki Escarra, Senior Advisor, The Boston Consulting Group; former CCO & CMO, Delta Airlines

Michele Fabrizi, Board Portfolio career; former, CEO & President of National Ad agency

Mary Foss-Skiftesvik, Board Member & Investor; MBA

Anula Jayasuriya, Vice Chair and Chief Scientific Officer, WHAM; Founder and Managing Director at EXXclaim Capital; MD, PhD, MBA

Ann Kaplan Partner, Circle Wealth Management

Susan King, Board Member, Private Investor, CMO, Advisor, and Advocate

Carolee Lee, Founder, CEO, and Chair, WHAM; Founder and CEO, AccessCircles; Founder and former CEO of CAROLEE

Sharon Love, CEO, TPN

Susan Morrison, Founding Board Director, Women Moving Millions

Anne Lim O'Brien, Vice Chairman, Heidrick & Struggles

Ekta Singh-Bushell, Global Chair/Chief Operating Officer; Board Member; Non-Executive Director; Public, Private, & Startup Advisor

Elisa Spungen Bildner, Former CEO food company; Lawyer/Journalism Professor; Cookbook Author and Food Writer

Lynn Tetrault, Chairwoman of the Board, NeoGenomics; Non-Executive Director, Rhythm Pharmaceuticals; former Executive Vice President of AstraZeneca PLC; JD

Donna Van Eekeren, President and CEO, Springboard Arts Chicago

Celia Weatherhead, Philanthropist

THE WHAM COLLABORATIVE

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

Dr. Wendy Bennett, MD, MPH, Associate Professor of Medicine, Johns Hopkins School of Medicine; Co-Director, Johns Hopkins Center for Women's Health, Sex, and Gender Research

Dr. Roberta Brinton, PhD, Director, UA Center for Innovation in Brain Science, University of Arizona Health Sciences

Dr. Robynne Chutkan, MD, Founder and CEO, Digestive Center for Wellness

Dr. Nicola Finley, MD, Principal and Founder, Dr. Nicola, PLLC

Marsha Henderson, Associate Commissioner for Women's Health, FDA (retired)

Dr. Marjorie Jenkins, MD, Dean, University of South Carolina School of Medicine Greenville Chief Academic Officer, Prisma Health-Upstate

Dr. Hadine Joffe, MD, MSc, Founding Member and Lead Scientific Advisor to the WHAM Collaborative; Executive Director, Mary Horrigan Connors Center for Women's Health Research, Brigham and Women's Hospital; Vice Chair for Psychiatry Research, Department of Psychiatry, Brigham and Women's Hospital; Paula A. Johnson Associate Professor of Psychiatry in the Field of Women's Health, Brigham and Women's Hospital

Dr. Wendy Klein, MD, MACP, Former Medical Director, Health Brigade

Dr. JoAnn Manson, DrPH, MD, Michael and Lee Bell Professor of Women's Health, Medicine, Harvard Medical School Co-Director, Women's Health, Brigham and Women's Hospital Professor, Epidemiology, Harvard T.H. Chan School of Public Health Chief, Preventive Medicine, Brigham and Women's Hospital

Dr. Alyson McGregor, MD, Associate Professor of Emergency Medicine, The Warren Alpert Medical School of Brown University Director, Division of Sex and Gender in Emergency Medicine

Dr. Michelle Mielke, PhD, Associate Professor of Epidemiology and Neurology, Mayo Clinic Co-Director, Specialized Center for Research Excellence on Sex Differences, Mayo Clinic

Dr. Lisa Mosconi, PhD, Director, Women's Brain Initiative, Weill Cornell Medicine; Associate Director, Alzheimer's Prevention Clinic, Weill Cornell Medicine; Associate Professor, Neuroscience in Neurology and Radiology, Weill Cornell Medicine; Adjunct Assistant Professor, Department of Psychiatry

Dr. Erica Ollmann Saphire, PhD, President and CEO, La Jolla Institute for Immunology

Dr. Charlotte Owens, MD, Vice President and Head of the Research and Development, Center for Health Equity and Patient Affairs, Takeda

Dr. Judith Regensteiner, PhD, Director, Center for Women's Health Research, University of Colorado Anschutz Medical Campus, Professor of Medicine, Internal Medicine and Cardiology, University of Colorado Anschutz Medical Campus

Dr. Stacey Rosen, MD, Senior Vice President for Women's Health, Katz Institute for Women's Health, Northwell Health Partners Council Professor of Women's Health, Hofstra North Shore-LJI School of Medicine at Hofstra University

Dr. Kathryn Sandberg, PhD, Professor and Vice Chair for Research, Department of Medicine, Georgetown University Medical Center, Director, Center for the Study of Sex Differences in Health, Aging, and Disease, Georgetown University Director, Predoc and Postdoc Training Program, Georgetown-Howard Universities Center for Clinical and Translational Science

Dr. Antonella Santuccione Chadha, PhD, Co-Founder, Women's Brain Project Head Stakeholder Liaison, Alzheimer's Disease, Biogen International Medical Manager, Alzheimer's Disease, Roche Diagnostics Europe

Dr. Suzanne Steinbaum, DO, Private Practice Cardiologist Co-Founder and President, SRSHeart

Connie Tyne, Executive Director, Laura W. Bush Institute for Women's Health

Dr. Annabelle Volgman, MD, Founder and Medical Director, Rush Heart Center for Women; Professor of Medicine, McMullan-Eybel Chair for Excellence in Clinical Cardiology, Rush University Medical Center

Dr. Nicole Woitowich, PhD, Research Assistant Professor of Medical Social Sciences, Feinberg School of Medicine, Northwestern University, Center Administrator, Institute for Innovations in Developmental Sciences, Chair, The WHAM Collaborative

RESEARCH ADVISORY PANEL

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.

Soo Borson, MD, Professor of Clinical Family Medicine, University of Southern California Professor Emerita, University of Washington School of Medicine

Roberta Brinton, PhD, Director, Center for Innovation in Brain Science, University of Arizona Health Sciences

Susan Dentzer, Senior Policy Fellow, Duke-Margolis Center for Health Policy

Lou Garrison, PhD, Professor Emeritus, Comparative Health Outcomes, Policy, and Economics (CHOICE) Institute, School of Pharmacy, University of Washington

Hadine Joffe, MD, Vice Chair for Research, Department of Psychiatry, Executive Director, Mary Horrigan Connors Center for Women's Health and Gender Biology, Paula A. Johnson Professor of Psychiatry in the Field of Women's Health, Harvard Medical School

Pei-Jung (Paige) Lin, PhD, Associate Professor of Medicine, Center for the Evaluation of Value and Risk in Health, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center

Beth Burnham Mace, MS, Chief Economist and Director of Outreach; National Investment Center for Seniors Housing & Care (NIC)

Suzanne Schrandt, JD, Founder, CEO & Chief Patient Advocate, ExPPect, LLC

Deborah Sundal, MA, Senior Vice President, Scientific and Academic Partnerships, UnitedHealth Group Research & Development

Nicole Woitowich, PhD, Research Assistant Professor, Department for Medical Social Sciences, Feinberg School of Medicine Center Administrator & Director of Strategic Communications, Institute for Innovations in Developmental Sciences, Northwestern University

Julie Wolf-Rodda, Senior Vice President of Development, Foundation for NIH

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.

As part of an initiative of Women's Health Access Matters (WHAM; whamnow.org), a nonprofit entity, RAND Corporation researchers examined the impact of increasing funding for women's health research, beginning with a focus on the following three disease areas: brain health, immune and autoimmune disease, and cardiovascular disease.

Research impact analysis is a framework for supporting decision-making about research funding allocation. Microsimulation models provide a method of quantifying the potential future impact of additions to research investment. Using microsimulation analyses, we examined the societal cost impact of increasing research funding in three diseases that present a large disease burden for women for each of the three disease areas noted above: Alzheimer's disease and Alzheimer's disease–related dementias (AD/ADRD), coronary artery disease (CAD), and rheumatoid arthritis (RA). 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 for patients, and quality-adjusted life years (QALYs). We calculated impacts across 30 years of doubling the current funding provided by the largest federal research investment—the National Institutes of Health (NIH) extramural portfolio—devoted to women's health. This funding is estimated to be 12 percent of the total

NIH portfolio for AD/ADRD, 4.5 percent for CAD, and 7 percent for RA. The impact of a current investment was assumed to occur in ten years, with benefits accruing after that.

Key Takeaways

Investing in women's health research yields benefits beyond investing in general research. The ROI is higher for most scenarios in which research funding impact is assumed to be higher for women than men. Assuming an equal impact of research on women and men generally results in lower returns.

Large returns result from very small health improvements attributable to increased women's health research funding. Savings include increased life years, reduced years with disease, fewer years of functional dependence, and reductions in disruptions to work productivity.

The aggregate cost savings to society are $932 million for AD/ADRD, $1.9 billion for CAD, and $10.5 billion for RA, reflecting the different impact of each disease for the full population.

The results establish the potential for investment in women's health research 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. 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.

Together, these findings suggest the potential for societal-level value from investment in women's health research. Such an investment yields benefits for all people because knowledge is gained, but the specific emphasis on women's health can support downstream socio-economic benefits that improve on research not focused on women.

Further examination of differential impacts of disease and treatment by gender is warranted, particularly in terms of the informal caregiving improvements and challenges that increased research investment can yield.

Finally, this work supports an examination of the impacts of research in terms of ROI to provide a tool for funders and the business community to improve decisions about research prioritization.

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 WHAM nonprofit foundation, RAND Corporation researchers examined the impact of increasing funding for women's health, beginning with a focus on three disease areas: brain health, immune and autoimmune disease, and cardiovascular disease.

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. AD/ADRD (brain health), CAD (heart health), and RA (autoimmune disease) were chosen as important case studies 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 the business community. The advisers' input enabled us to finalize key assumptions and the model structure.

The Impact of These Diseases on Society

The choice of disease areas to examine follows a review of the impact of these diseases in terms of illness burden and costs to society, including costs associated with health care and caregiving. The prevalence of disease by gender differs for the three diseases, with the highest prevalence differences for RA. More than 52 million adults in the United States have been diagnosed with RA, and more than 20 million adults had arthritis-attributable activity limitation in 2010–2012 (Hootman et al., 2016). Some symptom profiles differ by sex (Urits et al., 2020). Current estimates project that women will continue to account for the majority of RA cases, accounting for over 58 percent of all cases in 2040 (Hootman et al., 2016).

AD/ADRD results in substantial illness burden, health care costs, caregiving burden, and mortality (AARP and National Alliance for Caregiving, 2020; Johnson et al., 2014). As with many diseases, women are more likely than men to be informal caregivers for someone with AD/ADRD. One of the greatest economic challenges of AD/ADRD to women is the cost of the informal care they deliver; women bear substantially more of the cost of that informal caregiving than men (Yang and Levey, 2015). Recognizing these societal costs, the federal government established the first Professional Judgment Budget for AD/ADRD in 2017. The only other areas that have received this type of federal investment are cancer and the human immunodeficiency virus (HIV; Consortium of Social Science Associations, 2015; NIH, 2019).

For late onset AD/ADRD, gender differences in informal caregivers are a prominent part of the differential gender impact, with more women than men serving as informal caregivers. The caregiving burden associated with CAD is not quite as high, and the caregiving burden for RA is substantially different from that of AD/ADRD and CAD, given lower disease-related mortality impacts.

The impact on work productivity differentiates RA from AD/ADRD in terms of societal impacts, with CAD providing an intermediate work productivity profile that is helpful for comparisons across the three areas.

Although disease burden evidence is limited in terms of gender effects for all three diseases, heart disease mortality differences by gender make CAD a useful comparator. For heart disease, the 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). Disease progression differs by gender and differences, as do treatment patterns and treatment access (Morrison and Ness, 2011; Zhao et al., 2020).

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 (see, for example, Grant and Buxton, 2018). *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]

We 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. Models allow funding impacts to be quantified in economic terms. Models also provide a way to quantify impact of the disease and its treatment on health-related quality of life (Grant and Buxton,

---

[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, 2020b).

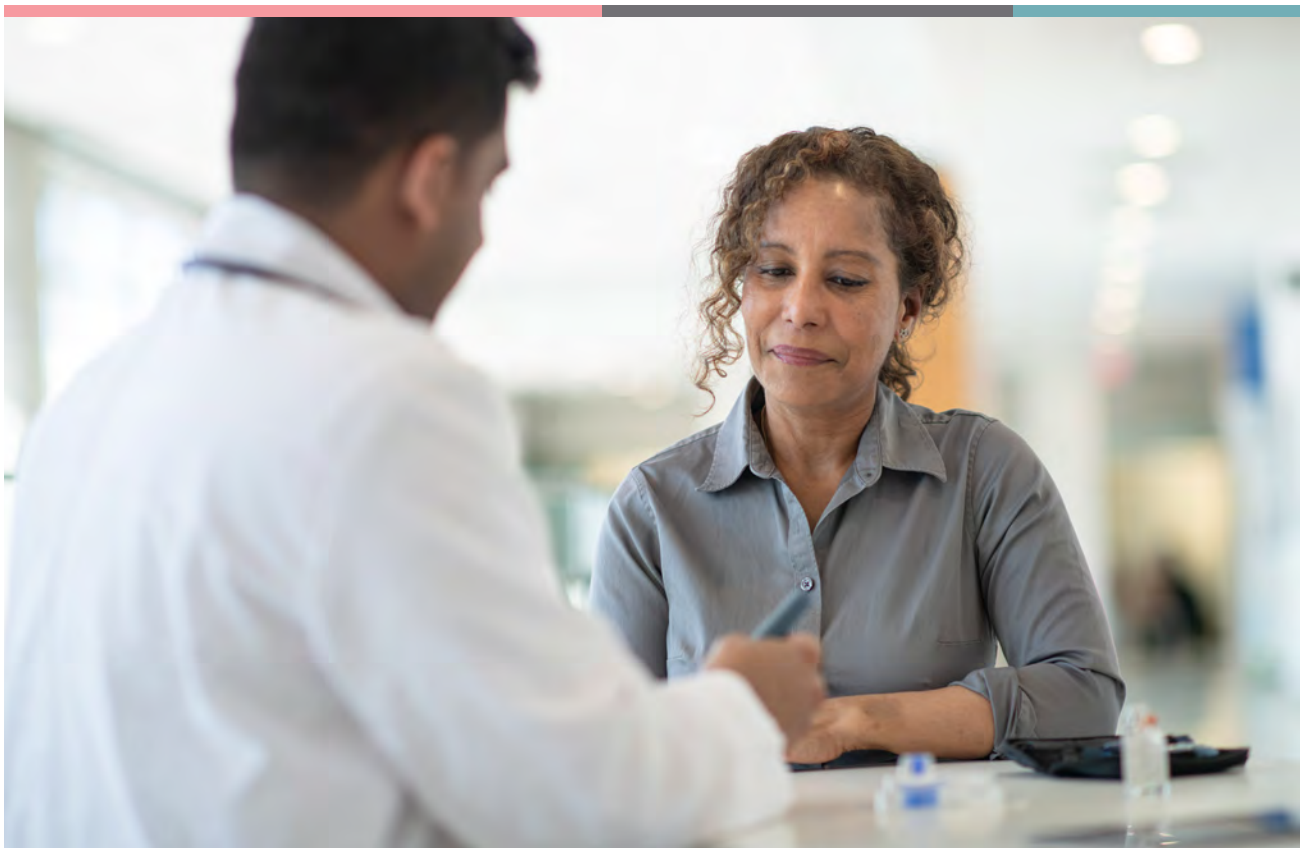
For the purposes of these analyses, we refer to sex and/or gender research generally; assumptions are about sex and/or gender research focused on women.

2018). These models include disease burden and societal productivity costs and benefits.

Determining the Research Investment

To construct models of the impact of research investment, we used current levels of funding from the NIH. Certainly, the universe of funding extends beyond the NIH and includes advocacy organizations, the biopharmaceutical industry, and philanthropic organizations (Cummings, Reiber, and Kumar, 2018). The NIH's share of clinical 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 results using NIH funding levels can be considered a lower bound on the possibilities for research investment.

To estimate the baseline level of research funding for women's health in each disease area, we retrieved all titles and abstracts in this research portfolio using NIH RePORTER, the publicly available interface of funded extramural NIH projects (NIH, 2020c). 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). All costs are presented in 2017 U.S. dollars.

The total AD/ADRD project funding level was calculated using the NIH Research, Condition, and Disease Categorization (RCDC) codes (NIH, 2020a). The total funding level in 2019 for AD/ADRD was $2.398 billion dollars, and 12 percent of that was invested in women-focused projects in 2019, according to the method described in this section (NIH, 2020a; Sekar, 2020). For CAD, 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.

Of the 880 extramural funded projects in RA from 2015 through 2019, 6.6 percent were focused on women's health specifically. We used 7 percent as the baseline proportion of women-focused funding in the RA portfolio. The 7 percent increment was added to the 2019 amount of $85.7 million to double the level of investment in women's health research to $91.7 million, for an increase of $6.0 million.

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. The models followed a hypothetical cohort of approximately one million adults and simulated the progression of each person's health in the sample over a 30-year time horizon. For CAD and RA, the focus was on working-age adults age 25 and older. For AD/ADRD, the cohort represents the U.S. population of individuals who have or could develop late-onset AD/ADRD beginning at age 65, along with working-age informal caregivers age 35 and older. All models assumed 100 percent mortality at age 99. After generating a base case to establish baseline health care costs, we generated a model with the assumption that increased investment improves health outcomes and thus lowers costs (see Figure 1).

Research Impacts

We assumed that impacts of increased funding occur through health care innovations that reduce age incidence of disease, reduce disease severity, and improve health-related quality of life. We quantified the innovation impact through costs of medical care, work productivity, and healthy life years gained or lost. These models examine the impact of increased sex- and gender-based health research on women, their families, and the economy.

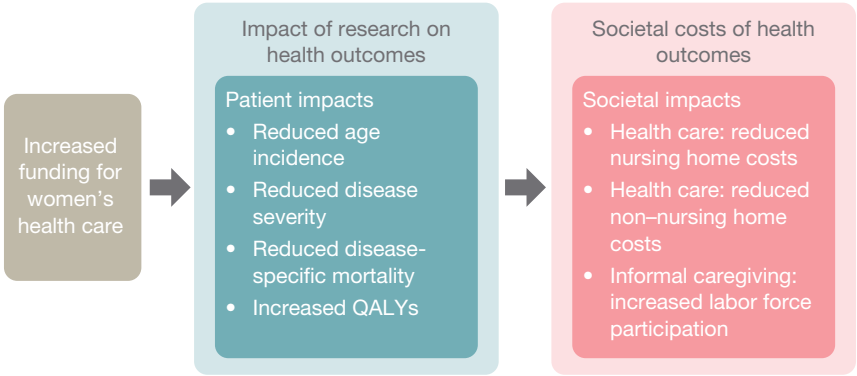
The Models

By tying different funding scenarios to incurred societal burden, the model quantifies how funding amounts affect the societal burden

of the selected diseases, including health expenditures, productivity loss, and decreased quality of life. The impact on QALYs (not just on absolute lost life years) is important to quantify, given the ways in which these diseases affect individuals and the long duration of disease for many patients. The QALY is one way in which monetary value can be assigned to disease impact (Grant and Buxton, 2018). A QALY provides a way to express both length of life and quality of life in a single metric, and it is often used to guide decisions about the value of health care interventions as a metric for disease impact and impact of health innovation (Grant and Buxton, 2018). The approach to relating funding to health improvements, life status, and costs is summarized in Figure 1, the conceptual model guiding this work.

FIGURE 1

Conceptual Model of Research Impacts on Patient and Societal Burden



A Key Contribution: Addressing Future Earnings Equality

In the United States, earnings for white males exceed those of Black and Latino males and exceed 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 versus non-Hispanic white males.

Time Horizon

The cohort was created as a representative sample of the United States according to age and gender distributions. For the models, the representative cohort of around 1 million lives is moved through a 30-year time horizon, with impact of investment expected to be realized ten years from initiation.

We chose a ten-year investment impact time point 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 life span of the majority of the cohort.

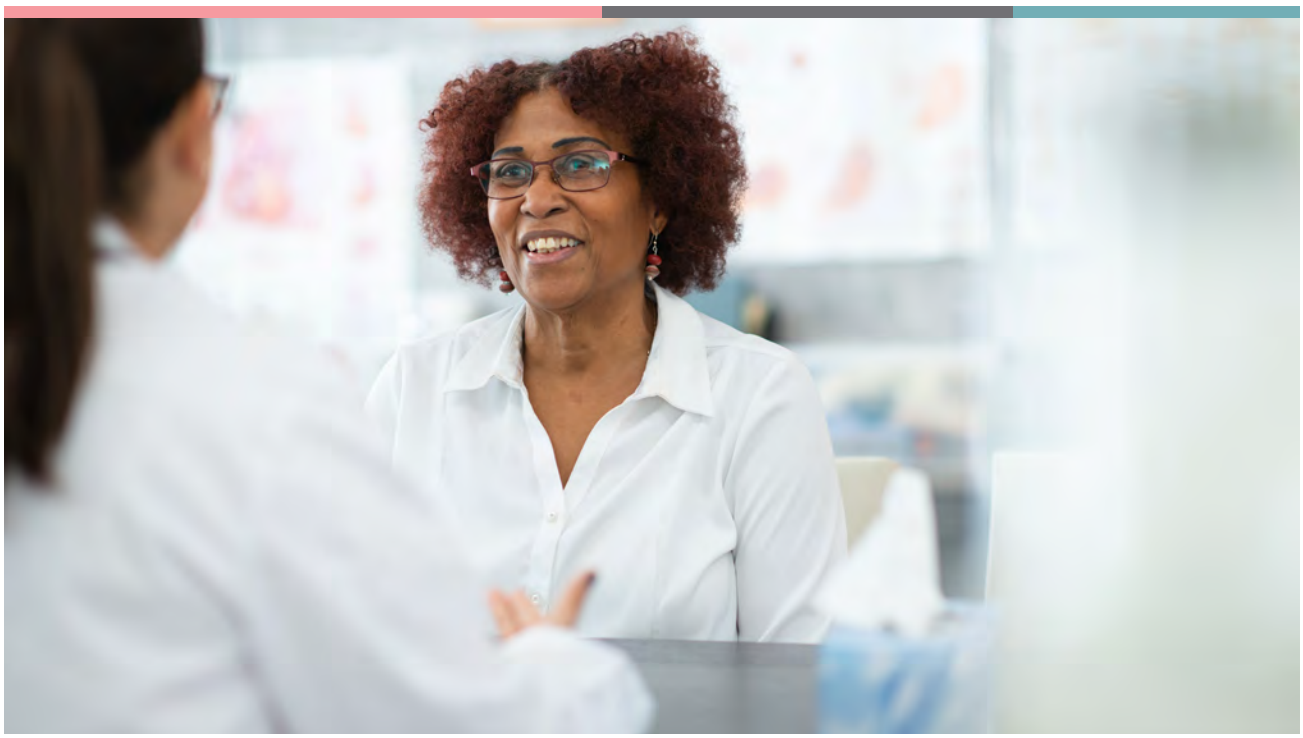
Investment Impacts on Health Improvements

The model provides the ROI for three of the following four health improvement impacts together, depending on the disease area:

1. decreased age incidence of disease, the probability of onset at a given age (AD/ADRD, CAD, RA)
2. delay in progression to more-severe levels of disease, with the assumption that innovations will reduce severity and slow progression (AD/ADRD, RA)
3. decreased disease-specific mortality rates, with the assumption that innovations improve survival probabilities for those with the disease (CAD)
4. improvements in health-related quality of life, with the assumption that reduction in symptoms and more functional independence would account for more QALYs (AD/ADRD, CAD, RA).

How Much Health Improvement?

Given the uncertainty regarding overall health improvements that investment in research can produce, we examined three levels of improvement for each disease. The lowest examined level of health



improvement is reported here. The lower disease prevalence for RA relative to AD/ADRD and CAD necessitated setting the lower bound of health improvement to 0.1 percent to enable the examination of pathways through which cost savings could occur. That is, the reduced disease incidence, reduced severity, and improved quality of life were estimated to sum to an overall health improvement at these three levels.

We used prior research on funding investment return as a basis for assumptions on the 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, severity with assumption of reduced severity and reduced time in more-severe stages of disease, and reduced mortality due to disease.

We simulated the effects of increasing funding for health research on women in terms of economic outcomes, including the monetary value of patients being able to stay in the labor force longer as a result of decreased disease burden and reduced productivity loss for informal caregivers.

Who Benefits?

We set an assumption that investing in women's health research yields more of a benefit for women than men but that all people benefit from the increased research investment. We set the ratio of improvement as 3:1 for women to men. We compared the results to those assuming an equal impact of general research investment.

The model provides information on the ROI associated with multiple innovation impacts.

Value of Investing in Women's Health Research

To further understand investment impact, we calculated the minimum probability of success of the investment generating a target of 15 percent ROI for a given health improvement. Results are presented for the doubling investment scenario.

Results

We present the health and economic improvements and resulting impact on costs for the lowest level of health improvement examined for each disease. We also present the resulting ROIs. In addition, we calculated the probability of success necessary to have an expected ROI of 15 percent.[2]

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

Figures 2 through 7 present the simulated improvements in the health and economic outcomes.

Decreased Disease Burden

The burden of AD/ADRD disease is reduced with the modeled health improvements, a function of both fewer people getting the disease and a shorter disease duration for those with AD/ADRD because of slowed progression. A 0.01 percent health improvement results in more than 5,500 fewer life years with AD/ADRD for women and nearly 900 fewer life years with AD/ADRD for men.

For that same small, modeled health improvement of 0.01 percent, the reduction in CAD disease burden in terms of life years with CAD was of even greater magnitude. Women have nearly 40,000 fewer life years with CAD, and men have more than 13,000 fewer life years with CAD.

The lowest level of health improvements examined for RA was 0.1 percent, chosen because of the lower overall mortality associated with RA and reflecting the differences between disease impacts for RA

A 0.01 percent health improvement results in more than 5,500 fewer life years with AD/ADRD for women and nearly 900 fewer life years with AD/ADRD for men.

[2] For the full results, please visit www.rand.org/t/RRA708-1.

compared with AD/ADRD and CAD. For this level of health improvement, the magnitude of impact is similar to CAD. Women have more 61,600 fewer life years with RA, and men have about 9,000 fewer life years with RA.

Increased Life Expectancy

For AD/ADRD, a 0.01 percent health improvement results in nearly 4,000 additional life years lived, more than 6,000 fewer years with AD/ADRD, and nearly 4,000 fewer nursing home years. Women realize more than 2,800 additional life years from innovations, and men realize more than 1,000 additional life years from innovations.

For CAD, 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.

No increase in life expectancy was assumed for RA, given the disease course and available data.

Reduced Institutionalization in AD/ADRD

Women have more than 2,100 fewer life years in nursing homes, and men have more than 1,400 fewer life years in nursing homes. Assuming a year of nursing home care costs $100,000, these 3,500 fewer years represent a cost savings of $350 million, far exceeding the magnitude of the doubled investment in women's health research funding (see Figure 3).

Lost Productivity for Patients

For RA, delaying the onset or progression of the disease allowed individuals to have more-productive careers, resulting in around 24,500 more equivalent years of full-time employment for women and around 3,900 more for men. The impact of these productivity gains is around six times larger for women than men.

There are two ways in which the health improvements increase employment and earnings for the CAD population. First, fewer years of CAD create less lost earnings, given the earnings penalty for CAD patients. Second, more years of life allow for more years of work. In both cases, the effect is limited to those who are age 65 or younger. We estimate that these effects yield around 8,000 more equivalent years of work for women and 3,000 for men.

Lost Productivity for Caregivers

For AD/ADRD, lost productive years for those providing informal care shows the impact of reduced institutionalization caused by slowed progression to severe stages, along with the impact of reduced disease age incidence. Of note is that there are approximately 300 *fewer*

lost years of productivity given in care for women as a result of the health improvements, resulting in an overall gain in work productivity for informal caregivers because of the impact of health innovation on women. In contrast, informal caregivers lose additional productivity (about 500 years) because of informal care given to men.

For AD/ADRD, the informal caregiving context is key to understanding potential investment impacts. Assuming that formal health care support for the less severe levels of impairment remains limited, the informal caregivers make up the care shortfall. Because some men are kept out of nursing homes, which would have shifted care to formal caregivers, informal caregivers pick up the increased care need instead. Countering this effect is the smaller number of individuals with the disease, which ultimately reduces overall productivity loss for the informal caregivers.

For CAD, caregiver productivity drops by around 2,000 years for women and 500 years for men. Innovations result in more years of life for patients, but more of those years at a less severe level of impairment lead to an added burden in terms of informal caregiving.

RA burden reduction from research innovation results in less informal care. For caregivers who are able to spend more time in the workforce, we estimate that the health improvement leads to 4,500 fewer lost life years of work provided to women and nearly 1,000 fewer provided to men.

Increased Quality of Life

For AD/ADRD, the 0.01 percent health improvement is associated with a large improvement in quality of life, approximately 16,000 additional full life-year equivalents. Unlike the other results, the impact on quality of life results from all three of the health improvements modeled: reduced age incidence, delayed progression, and increased quality of life. That is, delayed disease onset reduces the years of AD/ADRD burden, which increases quality of life, measured in QALYs. Slowed progression of the diseases also improves quality of life because people spend more years in less severe states. We directly decreased the reduction in quality of life for AD/ADRD 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 a given severity.

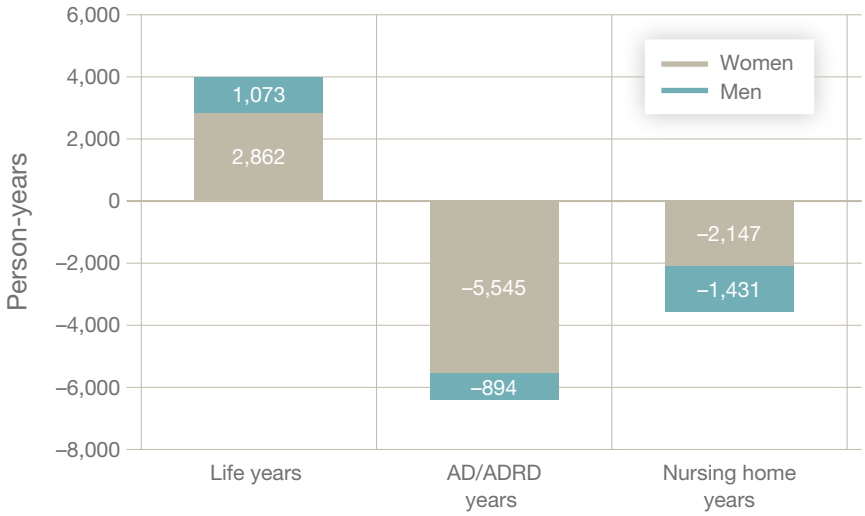
> Delayed disease onset reduces the years of AD/ADRD burden, which increases quality of life, measured in QALYs.

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. As with AD/ADRD, 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 a given severity. 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.

Delayed disease onset reduces the years of RA burden, which increases quality of life. Slowed progression of the diseases also improves quality of life because people spend more years in less severe states. Again, we directly decreased the reduction in quality of life for 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 a given severity. For these reasons, the QALYs capture a much larger effect, which is represented by approximately 223,000 more life-year equivalents of a fully healthy adult for women and 34,000 more for men (measured in QALYs). The impact on QALYs for women is substantial relative to men, but both are positive.

FIGURE 2

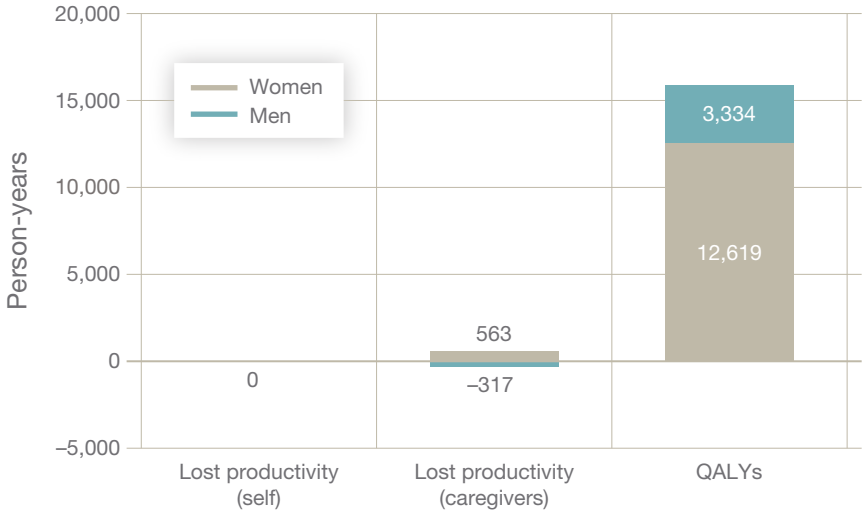
Health and Economic Improvements from Women's Health Research Investment in AD/ADRD: Disease Years and Institutionalization



NOTE: Figure represents the U.S. population age 35 and older of about 179 million, of which about 7 million had AD/ADRD.

FIGURE 3

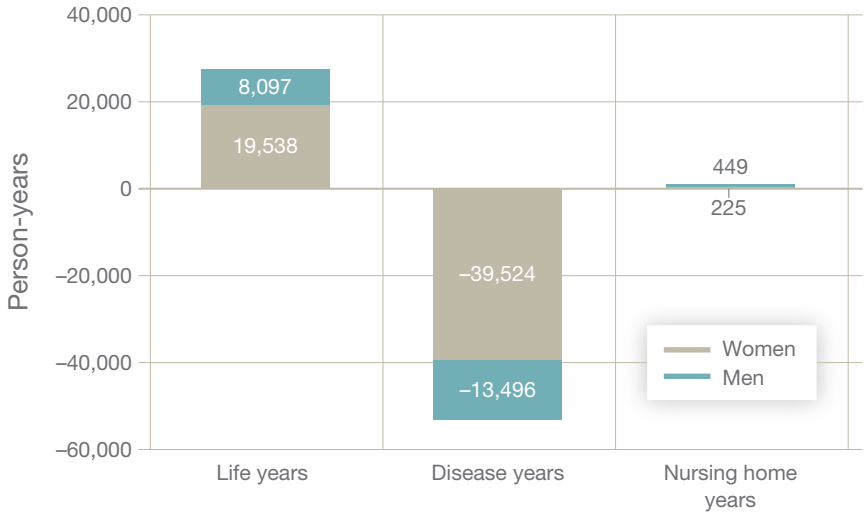
Health and Economic Improvements from Women's Health Research Investment in AD/ADRD: Quality-Adjusted Life Years and Productivity



NOTE: Figure represents the U.S. population age 35 and older of about 179 million, of which about 7 million had AD/ADRD.

FIGURE 4

Health and Economic Improvements from Women's Health Research Investment in CAD: Disease Years and Institutionalization



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

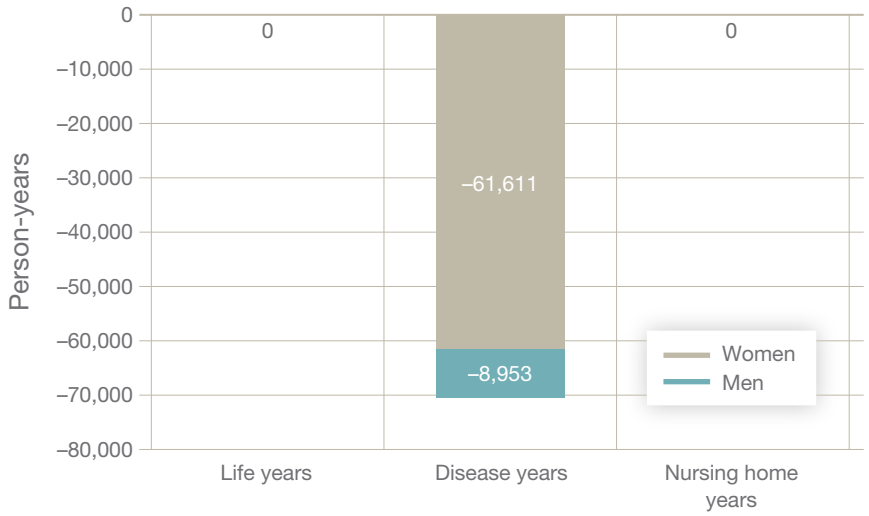
FIGURE 5

Health and Economic Improvements from Women's Health Research Investment in CAD: Quality-Adjusted Life Years and Productivity

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

FIGURE 6

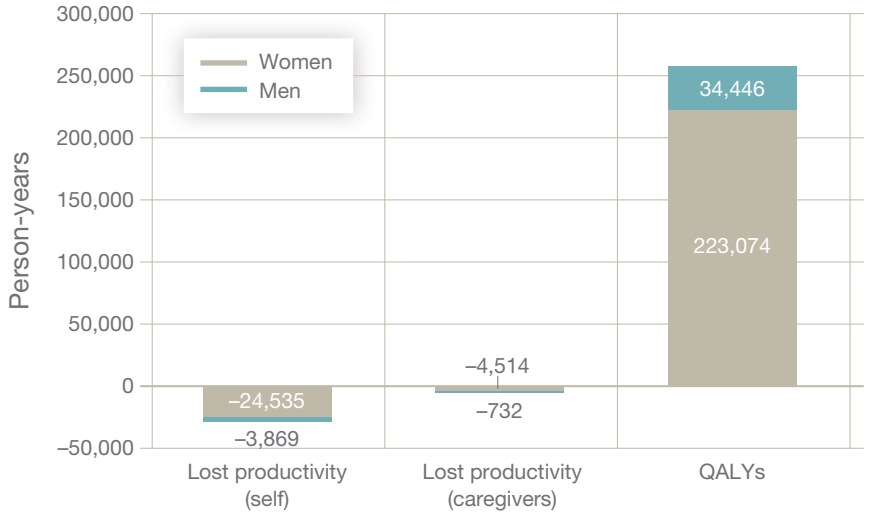
Health and Economic Improvements from Women's Health Research Investment in RA: Disease Years and Institutionalization



NOTE: Figure shows a 0.1 percent health improvement, which is three times larger for women than men.

FIGURE 7

Health and Economic Improvements from Women's Health Research Investment in RA: Quality-Adjusted Life Years and Productivity



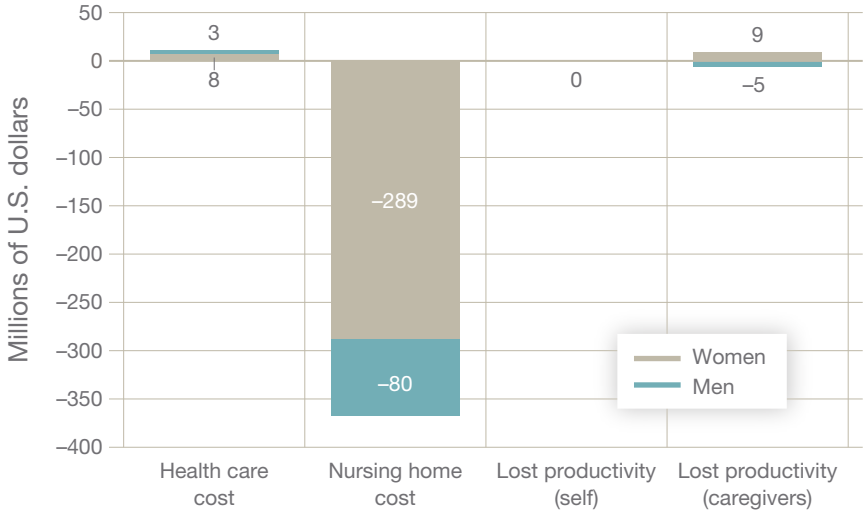
NOTE: Figure shows a 0.1 percent health improvement, which is three times larger for women than men.

Impact on Cost Outcomes

Costs associated with the lowest level of health improvement vary by sector examined (see Figures 8 through 10). The modeled investment in women's health for AD/ADRD would yield an overall reduction in costs of around $930 million over 30 years (in 2017 dollars). Approximately 40 percent of that cost reduction is a result of fewer nursing home stays. Noncare health care costs demonstrate a very small increase as a result of fewer years of formal institutional care. The costs of lost productivity of informal caregivers is also exceedingly small.

FIGURE 8

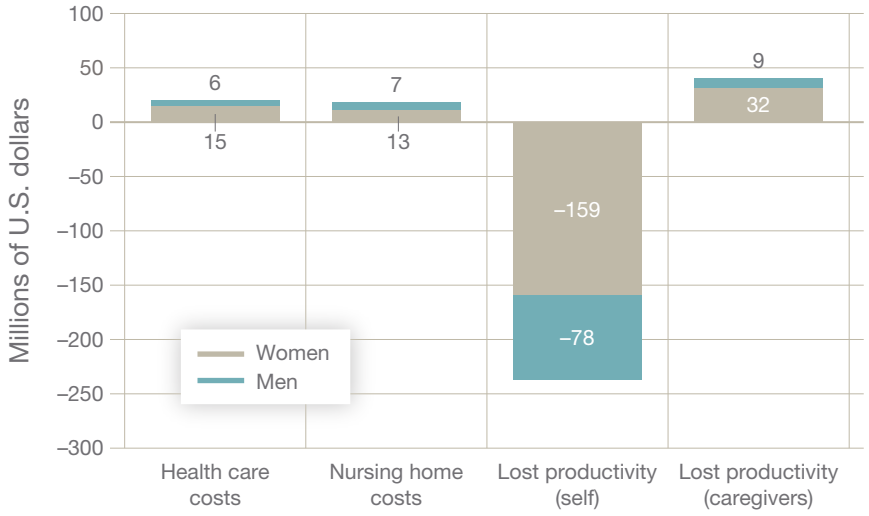
Change in Costs with Increased Funding for Women's Health Research in AD/ADRD



NOTE: Costs associated with the 0.01 percent health improvement vary by sector examined.

FIGURE 9

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

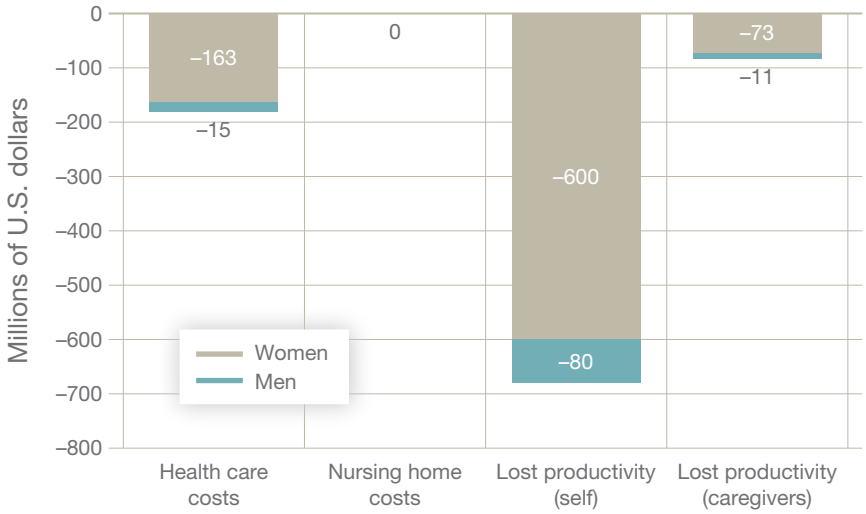


NOTE: Figure shows a 0.01 percent health improvement, which is three times larger for women than men.

For CAD, the overall reduction in costs was around $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.

FIGURE 10

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



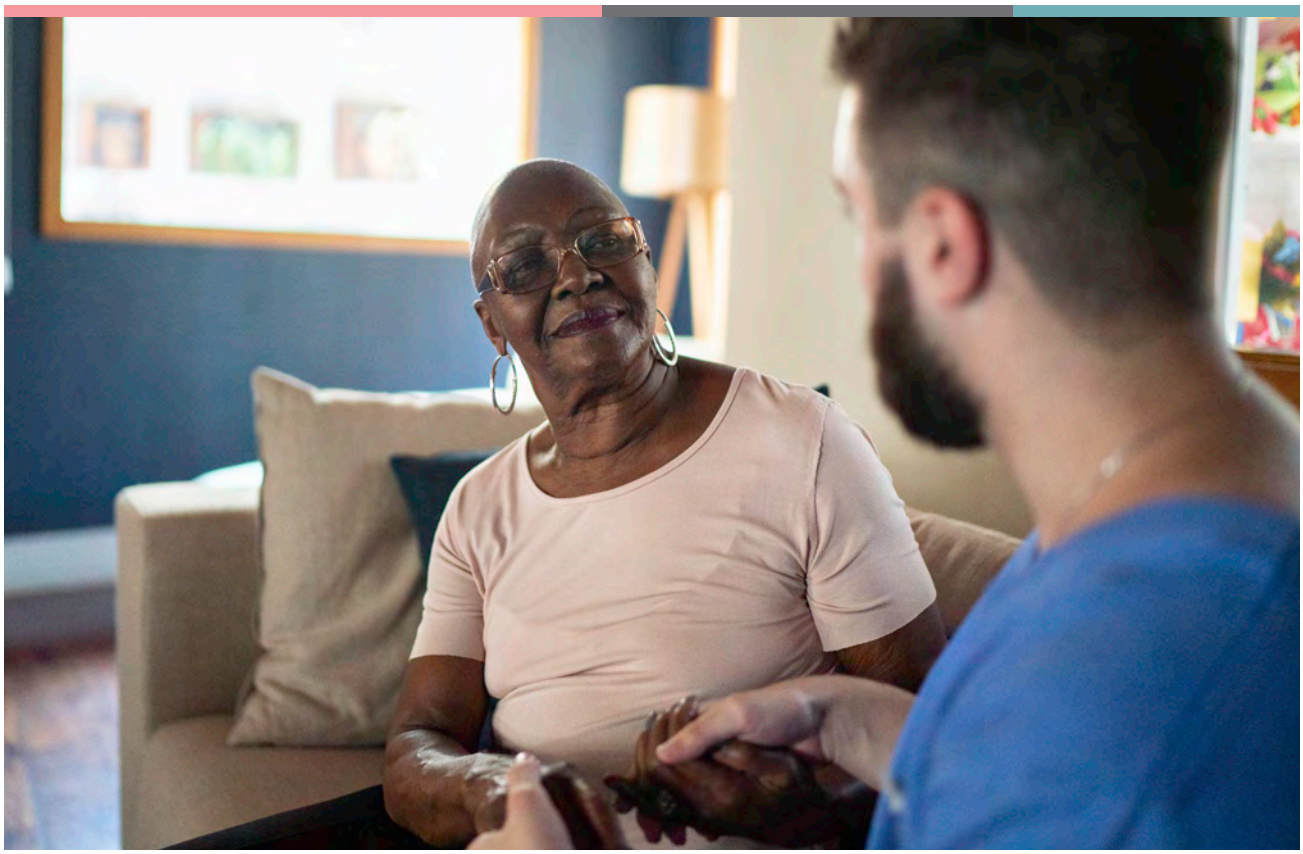
NOTE: Figure shows a 0.1 percent health improvement, which is three times larger for women than men.

For RA, the largest driver of gains is a reduction in lost QALYs. Patient work productivity is the next-largest driver. The overall reduction in costs was around $10.5 billion over 30 years (in 2017 dollars). About 87 percent of the costs are from female patients, and 13 percent are from male patients. Approximately 90 percent of the cost reductions are from fewer lost QALYs (from improved quality of life), with the next most important improvement related to increased productivity for RA patients, which represents more than $680 million. The total across these three categories is around $940 million. If these investments bring about the 0.1 percent improvement in health, the cost savings from decreased health care expenditures and increased labor productivity of $940 million easily cover the investment, not including the much larger improvement in quality of life.

If these investments bring about the 0.1 percent improvement in health, the cost savings from decreased health care expenditures and increased labor productivity of $940 million easily cover the investment, not including the much larger improvement in quality of life.

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 AD/ADRD portfolio and assuming the small 0.01 percent health improvement), the ROI is 224 percent. The result suggests that, in the face of large potential gains, an increase in investment may pay off over several decades.



When doubling the investment and assuming the small 0.01 percent health improvement for CAD, 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.

When doubling the investment in women's health research within the RA portfolio and assuming a 0.1 percent health improvement, the ROI exceeds 174,000 percent.

This result suggests that modest increases in funding for women's health research have the potential to yield very large gains.

Discussion

Health research investments affect society through many pathways. For the three diseases we examined, health-related quality of life impacts from modest health improvements are large. Improved work productivity for individuals with disease or their informal caregivers yields additional societal-level benefit. Even if only labor productivity and reduced health care costs are included in the gains, ROI is still positive. Generally, large societal gains would result from investments that yield very small overall increments in health improvement across all scenarios. The overall magnitude of impact is in line with similar research on the impact of research investment (Luce et al., 2006). Investing in research targeted to women's health has somewhat higher ROIs than general research that affects women and men equally.

The model assumptions were purposefully kept conservative, assuming relatively small health impacts from research investment. More-optimistic scenarios are not unreasonable. The potential to recognize societal gains is amplified for research devoted to women's health relative to general research, according to the specifications used here.

The overall societal cost savings from modest investment in women's health research could be $932 million for AD/ADRD, $1.9 billion for CAD, and $10.5 billion for RA. The magnitude of impacts differs by disease area examined. For AD/ADRD, the impacts are relatively smaller, reflecting the limitation of patient impacts to those age 65 and older. For CAD, disease burden is greater for older ages but begins prior to age 65 for many. For RA, disease burden begins well before age 65, resulting in larger impacts. The impacts on ROI follow this ordering. Although all ROIs are large and positive, the magnitude of ROI impact for CAD and RA is extremely large.

Investing in research targeted to women's health has somewhat higher ROIs than general research that affects women and men equally.

Investment Size

The size of the investment increments examined in these models is relatively small, and the ROI is a function of assumptions, not just of the size of the investment but also of the magnitude of health improvements that investment yields. The very small health improvements examined here make the direction of impacts robust to smaller overall investments.

One key consideration in modeling using labor force participation and earnings is the selection of earnings profiles. We chose to apply 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.

Time Horizon

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. The models examined here assumed ten years from present-day investment to future realization of health impacts. However, the 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.

Limitations

All microsimulation models involve uncertainty associated with model assumptions. We kept our assumptions as realistic as possible, given the current understanding of disease mechanisms and the near-term outlook for treatments. We calculated age-by-gender incidence and prevalence estimates from a national database, but these estimates are larger than some reports in the literature. Smaller estimates still result in large ROIs but change the nature of the health improvements.

Policy Implications

The results of these analyses suggest several policy actions to inform decision making about research funding allocations:

- *Increase research funding directed at women's health.* The potential gains from women-focused research are substantial, given the limitations in knowledge about disease development and impacts for women relative to men.
- *Pursue research on the biology of disease in women, including early identification, and identify barriers to diagnosis in women.*
- *Expand research agendas to address the complicated relationships between disease and work productivity in women.* Impacts include lost productivity for those with the disease and for informal caregivers, the majority of whom are women.

Broader actions that could improve decisionmaking about research funding involve increasing awareness of the current state of funding directed toward women's health and the potential for such funding to yield a variety of societal benefits. Specifically, we recommend the following:

- *Raise awareness of the potential value of investment in women's health research.* The ways in which women's health research is disadvantaged relative to general research are multifaceted, with major implications for disease burdens.
- *Increasing investments in the careers of those who can pursue that agenda is critical.* Identify obstacles (such as career interruption from caregiving burden for women) and develop strategies to overcome these and systemic factors, such as implicit and explicit bias against women in health research.
- *Raise awareness among the business community of the potential ROI for women's health research.* The viability of women's health research agendas and funding depend on understanding the value on the part of the market for such research. Within the pharmaceutical and biotechnology industry, decisions made by leaders about research investments should be informed by the potential for societal ROI. Across multiple other business sectors, leaders need to understand the consequences of underinvestment on workforce productivity and health care burden. These communities are key to informing future research investment strategies.

The potential gains from women-focused research are substantial, given the limitations in knowledge about disease development and impacts for women relative to men.

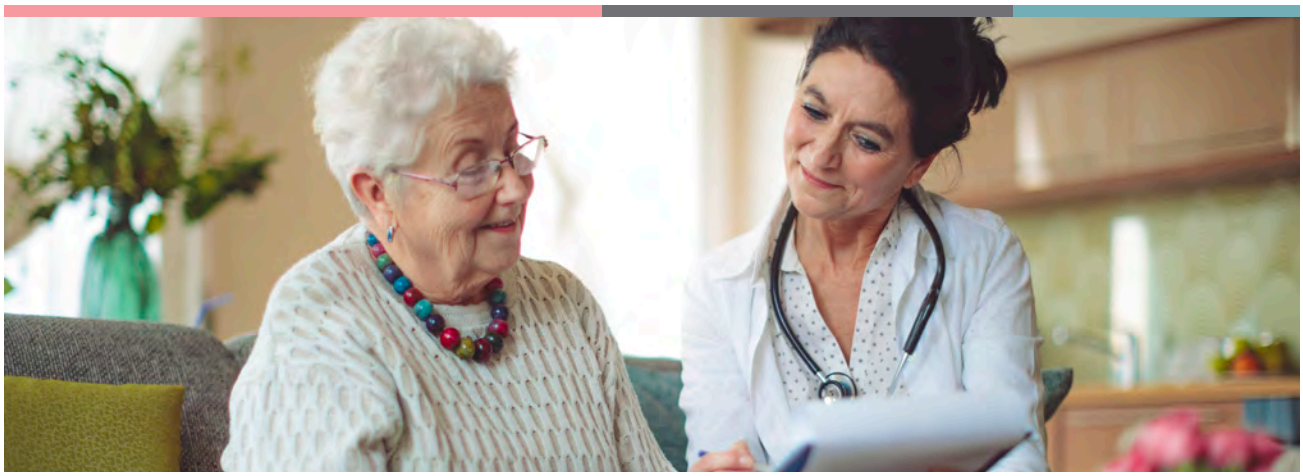
These analyses suggest that doubling the investment in research on women's health is likely to deliver net positive societal impacts in just a few decades.

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. Future investment in women's health may result in large gains in condition status with resulting gains in health-related quality of life. The limitations that result from the impact on work productivity represent another important avenue to realize impacts of health research innovation. The financial investment needed to realize the goals of a research agenda requires planning. These analyses suggest that doubling the investment in research on women's health is likely to deliver net positive societal impacts in just a few decades. Clear understanding of the potential for investment can improve decisions about where and how to invest to recognize positive impacts for women and for society as a whole.

Acknowledgments

We gratefully acknowledge the following researchers who contributed to this work: Jamie Ryan, Alejandro Becerra-Ornelas, Sangita Baxi, and Monica Rico. We also gratefully acknowledge Patricia Stone, Columbia University, for access to the Centers for Medicare & Medicaid Services data via NIH-NINR (R01NR013687), Study of Infection Management and Palliative Care at End of Life Care (SIMP-EL). We also gratefully acknowledge the reviewers of this work, Pei-Jung Lin, Center for the Evaluation of Value and Risk in Health, Institute for Clinical Research and Health Policy Studies, Tufts Medical Center; Sandra Berry, RAND Corporation; and Susan Straus, RAND Corporation.



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.

Bibliography

Alzheimer's Disease and Alzheimer's Disease–Related Dementias

AARP and National Alliance for Caregiving, *Caregiving in the United States. 2020*, May 2020. As of November 17, 2020: https://www.aarp.org/ppi/info-2020/caregiving-in-the-united-states.html

Adam, Paula, Pavel V. Ovseiko, Jonathan Grant, Kathryn E. A. Graham, Omar F. Boukhris, Anne-Maree Dowd, Gert V. Balling, Rikke N. Christensen, Alexandra Pollitt, Mark Taylor, Omar Sued, Saba Hinrichs-Krapels, Maite Solans-Domènech, and Heidi Chorzempa, "ISRIA Statement: Ten-Point Guidelines for an Effective Process of Research Impact Assessment," *Health Research Policy and Systems*, Vol. 16, No. 1, February 8, 2018, p. 8.

Committee on Family Caregiving for Older Adults, Board on Health Care Services, Health and Medicine Division, "Economic Impact of Family Caregiving," in Richard Schulz and Jill Eden, eds., *Families Caring for an Aging America*, Washington, D.C.: National Academies Press, 2016, pp. 123–158.

Consortium of Social Science Associations, "NIH Releases Alzheimer's Disease Bypass Budget Proposal for FY 2017," August 10, 2015. As of November 20, 2020: https://www.cossa.org/2015/08/10/nih-releases-alzheimers-disease-bypass-budget-proposal-for-fy-2017/

Cruz Rivera, Samantha, Derek G. Kyte, Olalekan Lee Aiyegbusi, Thomas J. Keeley, and Melanie J. Calvert, "Assessing the Impact of Healthcare Research: A Systematic Review of Methodological Frameworks," *PLoS Medicine*, Vol. 14, No. 8, 2017.

Cummings, Jeffrey, Carl Reiber, and Parvesh Kumar, "The Price of Progress: Funding and Financing Alzheimer's Disease Drug Development," *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, Vol. 4, June 13, 2018, pp. 330–343.

Grant, Jonathan, and Martin J. Buxton, "Economic Returns to Medical Research Funding," *BMJ Open*, Vol. 8, No. 9, 2018.

Hansen, Johan, Natasha Azzopardi Muscat, Ilmo Keskimäki, Anne Karin Lindahl, Holger Pfaff, Matthias Wismar, Kieran Walshe, and Peter Groenewegen, "Measuring and Improving the Societal Impact of Health Care Research," *Eurohealth*, Vol. 19, No. 3, 2013, pp. 32–35.

Hood, Katherine, "The Science of Value: Economic Expertise and the Valuation of Human Life in US Federal Regulatory Agencies," Social Studies of Science, Vol. 47, No. 4, August 2017, pp. 441–465.

Johnson, Paula A., Therese Fitzgerald, Alina Salganicoff, Susan F. Wood, and Jill M. Goldstein, *Sex-Specific Medical Research: Why Women's Health Can't Wait*, Boston, Mass.: Brigham and Women's Hospital, 2014. As of April 2, 2021: https://www.brighamandwomens.org/assets/bwh/womens-health/pdfs/connorsreportfinal.pdf

Lin, Pei-Jung, Zhou Yang, Howard M. Fillit, Joshua T. Cohen, and Peter J. Neumann, "Unintended Benefits: The Potential Economic Impact of Addressing Risk Factors to Prevent Alzheimer's Disease," *Health Affairs*, Vol. 33, No. 4, April 2014, pp. 547–554.

Luce, Bryan R., Josephine Mauskopf, Frank A. Sloan, Jan Ostermann, and L. Clark Paramore, "The Return on Investment in Health Care: From 1980 to 2000," *Value in Health*, Vol. 9, No. 3, 2006, pp. 146–156.

National Institutes of Health, *Together We Succeed: Accelerating Research on Alzheimer's Disease & Related Dementias*, 2019. As of November 20, 2020: https://www.nia.nih.gov/sites/default/files/2019-07/FY21-bypass-budget-report-508.pdf

——, "Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC)," webpage, February 24, 2020a. As of November 6, 2020: https://report.nih.gov/categorical_spending.aspx

——, "Notice of Special Interest: Sex and Gender Differences in Alzheimer's Disease and Alzheimer's Disease–Related Dementias (AD/ADRD)," August 5, 2020b. As of April 5, 2021: https://grants.nih.gov/grants/guide/notice-files/NOT-AG-20-038.html

—— "Research Portfolio Online Reporting Tools Expenditures and Results (RePORTER)," updated November 7, 2020c. As of November 17, 2020: https://projectreporter.nih.gov/reporter.cfm

Nebel, Rebecca A., Neelum T. Aggarwal, Lisa L. Barnes, Aimee Gallagher, Jill M. Goldstein, Kejal Kantarci, Monica P. Mallampalli, Elizabeth C. Mormino, Laura Scott, Wai Haung Yu, Pauline M. Maki, and Michelle M. Mielke, "Understanding the Impact of Sex and Gender in Alzheimer's Disease: A Call to Action," *Alzheimer's & Dementia*, Vol. 14, No. 9, September 2018, pp. 1171–1183.

NIH—*See* National Institutes of Health.

Scott, Troy J., Alan C. O'Connor, Albert N. Link, and Travis J. Beaulieu, "Economic Analysis of Opportunities to Accelerate Alzheimer's Disease Research and Development," *Annals of the New York Academy of Sciences*, Vol. 1313, No. 1, April 2014, pp. 17–34.

Sekar, Kavya, *National Institutes of Health (NIH) Funding: FY1995–FY2021*, Washington, D.C.: Congressional Research Service, R43341, updated May 12, 2020. As of November 20, 2020: https://fas.org/sgp/crs/misc/R43341.pdf

Yang, Zhou, and Allan Levey, "Gender Differences: A Lifetime Analysis of the Economic Burden of Alzheimer's Disease," *Women's Health Issues*, Vol. 25, No. 5, September–October 2015, pp. 436–440.

Coronary Artery Disease

Adam, Paula, Pavel V. Ovseiko, Jonathan Grant, Kathryn E. A. Graham, Omar F. Boukhris, Anne-Maree Dowd, Gert V. Balling, Rikke N. Christensen, Alexandra Pollitt, Mark Taylor, Omar Sued, Saba Hinrichs-Krapels, Maite Solans-Domènech, and Heidi Chorzempa, "ISRIA Statement: Ten-Point Guidelines for an Effective Process of Research Impact Assessment," *Health Research Policy and Systems*, Vol. 16, No. 1, February 8, 2018, p. 8.

American Heart Association, "Making Progress: Making a Difference," fact sheet, undated. As of December 10, 2020: https://www.heart.org/-/media/files/about-us/policy-research/fact-sheets/ucm_497880.pdf?la=en

Barber, Sharrelle, DeMarc A. Hickson, Xu Wang, Mario Sims, Cheryl Nelson, and Ana V. Diez-Roux, "Neighborhood Disadvantage, Poor Social Conditions, and Cardiovascular Disease Incidence Among African American Adults in the Jackson Heart Study," *American Journal of Public Health*, Vol. 106, No. 12, December 2016, pp. 2219–2226.

Cruz Rivera, Samantha, Derek G. Kyte, Olalekan Lee Aiyegbusi, Thomas J. Keeley, and Melanie J. Calvert, "Assessing the Impact of Healthcare Research: A Systematic Review of Methodological Frameworks," *PLoS Medicine*, Vol. 14, No. 8, 2017.

El-Hayek, Youssef H., Ryan E. Wiley, Charles P. Khoury, Ritesh P. Daya, Clive Ballard, Alison R. Evans, Michael Karran, José Luis Molinuevo, Matthew Norton, and Alireza Atri, "Tip of the Iceberg: Assessing the Global Socioeconomic Costs of Alzheimer's Disease and Related Dementias and Strategic Implications for Stakeholders," *Journal of Alzheimer's Disease*, Vol. 70, No. 2, 2019, pp. 323–341.

Grant, Jonathan, and Martin J. Buxton, "Economic Returns to Medical Research Funding," *BMJ Open*, Vol. 8, No. 9, 2018.

Gulati, Martha, Rhonda M. Cooper-DeHoff, Candace McClure, B. Delia Johnson, Leslee J. Shaw, Eileen M. Handberg, Issam Zineh, Sheryl F. Kelsey, Morton F. Arnsdorf, Henry R. Black, Carl J. Pepine, and C. Noel Bairey Merz, "Adverse Cardiovascular Outcomes in Women with Nonobstructive Coronary Artery Disease: A Report from the Women's Ischemia Syndrome Evaluation Study and the St James Women Take Heart Project," *Archives of Internal Medicine*, Vol. 169, No. 9, 2009, pp. 843–850.

Hammond, Gmerice, Heidi Mochari-Greenberger, Ming Liao, and Lori Mosca, "Effect of Gender, Caregiver, on Cholesterol Control and Statin Use for Secondary Prevention Among Hospitalized Patients with Coronary Heart Disease," *American Journal of Cardiology*, Vol. 110, No. 11, December 2012, pp. 1613–1618.

Hansen, Johan, Natasha Azzopardi Muscat, Ilmo Keskimäki, Anne Karin Lindahl, Holger Pfaff, Matthias Wismar, Kieran Walshe, and Peter Groenewegen, "Measuring and Improving the Societal Impact of Health Care Research," *Eurohealth*, Vol. 19, No. 3, 2013, pp. 32–35.

Luce, Bryan R., Josephine Mauskopf, Frank A. Sloan, Jan Ostermann, and L. Clark Paramore, "The Return on Investment in Health Care: From 1980 to 2000," *Value in Health*, Vol. 9, No. 3, 2006, pp. 146–156.

Merz, C. Noel Bairey, Leslee J. Shaw, Steven E. Reis, Vera Bittner, Sheryl F. Kelsey, Marian Olson, B. Delia Johnson, Carl J. Pepine, Sunil Mankad, Barry L. Sharaf, William J. Rogers, Gerald M. Pohost, Amir Lerman, Arshed A. Quyyumi, and George Sopko, "Insights from the NHLBI-Sponsored Women's Ischemia Syndrome Evaluation (WISE) Study: Part II: Gender Differences in Presentation, Diagnosis, and Outcome with Regard to Gender-Based Pathophysiology of Atherosclerosis and Macrovascular and Microvascular Coronary Disease," *Journal of the American College of Cardiology*, Vol. 47, No. 3, Supplement, February 7, 2006, pp. S21–S29.

Mondesir, Favel L., April P. Carson, Raegan W. Durant, Marquita W. Lewis, Monika M. Safford, and Emily B. Levitan, "Association of Functional and Structural Social Support with Medication Adherence Among Individuals Treated for Coronary Heart Disease Risk Factors: Findings from the REasons for Geographic and Racial Differences in Stroke (REGARDS) Study," *PloS One*, Vol. 13, No. 6, June 27, 2018.

Morrison, Alanna C., and Roberta B. Ness, "Sodium Intake and Cardiovascular Disease," *Annual Review of Public Health*, Vol. 32, 2011, pp. 71–90.

National Institutes of Health, "Research Portfolio Online Reporting Tools Expenditures and Results (RePORTER)," updated November 7, 2020c. As of November 17, 2020: https://projectreporter.nih.gov/reporter.cfm

Nichols, Gregory A., Timothy J. Bell, Kathryn L. Pedula, and Maureen O'Keeffe-Rosetti, "Medical Care Costs Among Patients with Established Cardiovascular Disease," *American Journal of Managed Care*, Vol. 16, No. 3, March 2010, pp. e86–e93.

NIH—*See* National Institutes of Health.

Quyyumi, Arshed A., "Women and Ischemic Heart Disease: Pathophysiologic Implications from the Women's Ischemia Syndrome Evaluation (WISE) Study and Future Research Steps," *Journal of the American College of Cardiology*, Vol. 47, No. 3, Supplement, February 7, 2006, pp. S66–S71.

Scott, Troy J., Alan C. O'Connor, Albert N. Link, and Travis J. Beaulieu, "Economic Analysis of Opportunities to Accelerate Alzheimer's Disease Research and Development," *Annals of the New York Academy of Sciences*, Vol. 1313, No. 1, April 2014, pp. 17–34.

Tibuakuu, Martin, Erin D. Michos, Ana Navas-Acien, and Miranda R. Jones, "Air Pollution and Cardiovascular Disease: A Focus on Vulnerable Populations Worldwide," *Current Epidemiology Reports*, Vol. 5, No. 4, December 2018, pp. 370–378.

Zhao, Min, Mark Woodward, Ilonca Vaartjes, Elizabeth R. C. Millett, Kerstin Klipstein-Grobusch, Karice Hyun, Cheryl Carcel, and Sanne A. E. Peters, "Sex Differences in Cardiovascular Medication Prescription in Primary Care: A Systematic Review and Meta-Analysis," *Journal of the American Heart Association*, Vol. 9, No. 11, June 2, 2020.

Rheumatoid Arthritis

Adam, Paula, Pavel V. Ovseiko, Jonathan Grant, Kathryn E. A. Graham, Omar F. Boukhris, Anne-Maree Dowd, Gert V. Balling, Rikke N. Christensen, Alexandra Pollitt, Mark Taylor, Omar Sued, Saba Hinrichs-Krapels, Maite Solans-Domènech, and Heidi Chorzempa, "ISRIA Statement: Ten-Point Guidelines for an Effective Process of Research Impact Assessment," *Health Research Policy and Systems*, Vol. 16, No. 1, February 8, 2018, p. 8.

Cruz Rivera, Samantha, Derek G. Kyte, Olalekan Lee Aiyegbusi, Thomas J. Keeley, and Melanie J. Calvert, "Assessing the Impact of Healthcare Research: A Systematic Review of Methodological Frameworks," *PLoS Medicine*, Vol. 14, No. 8, 2017.

Grant, Jonathan, and Martin J. Buxton, "Economic Returns to Medical Research Funding," *BMJ Open*, Vol. 8, No. 9, 2018.

Hansen, Johan, Natasha Azzopardi Muscat, Ilmo Keskimäki, Anne Karin Lindahl, Holger Pfaff, Matthias Wismar, Kieran Walshe, and Peter Groenewegen, "Measuring and Improving the Societal Impact of Health Care Research," *Eurohealth*, Vol. 19, No. 3, 2013, pp. 32–35.

Hootman, Jennifer M., Charles G. Helmick, Kamil E. Barbour, Kristina A. Theis, and Michael A. Boring, "Updated Projected Prevalence of Self-Reported Doctor-Diagnosed Arthritis and Arthritis-Attributable Activity Limitation Among US Adults, 2015–2040," *Arthritis & Rheumatology*, Vol. 68, No. 7, July 2016, pp. 1582–1587.

Luce, Bryan R., Josephine Mauskopf, Frank A. Sloan, Jan Ostermann, and L. Clark Paramore, "The Return on Investment in Health Care: From 1980 to 2000," *Value in Health*, Vol. 9, No. 3, 2006, pp. 146–156.

National Institute of Arthritis and Musculoskeletal and Skin Diseases, "Rheumatoid Arthritis: Who Gets Rheumatoid Arthritis?" webpage, last reviewed September 2019. As of November 23, 2020: https://www.niams.nih.gov/health-topics/rheumatoid-arthritis#tab-risk

National Institutes of Health, "Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC)," webpage, February 24, 2020a. As of November 6, 2020: https://report.nih.gov/categorical_spending.aspx

——, "Research Portfolio Online Reporting Tools Expenditures and Results (RePORTER)," updated November 7, 2020c. As of November 17, 2020: https://projectreporter.nih.gov/reporter.cfm

NIH—*See* National Institutes of Health.

Norton, Sam, Bo Fu, David L. Scott, Chris Deighton, Deborah P. M. Symmons, Allan J. Wailoo, Jonathan Tosh, Mark Lunt, Rebecca Davies, Adam Young, and Suzanne M. M. Verstappen, "Health Assessment Questionnaire Disability Progression in Early Rheumatoid Arthritis: Systematic Review and Analysis of Two Inception Cohorts," *Seminars in Arthritis and Rheumatism*, Vol. 44, No. 2, October 2014, pp. 131–144.

Park, Juyoung, Angelico Mendy, and Edgar R. Vieira, "Various Types of Arthritis in the United States: Prevalence and Age-Related Trends from 1999 to 2014," *American Journal of Public Health*, Vol. 108, No. 2, February 2018, pp. 256–258.

Scott, Troy J., Alan C. O'Connor, Albert N. Link, and Travis J. Beaulieu, "Economic Analysis of Opportunities to Accelerate Alzheimer's Disease Research and Development," *Annals of the New York Academy of Sciences*, Vol. 1313, No. 1, April 2014, pp. 17–34.

Urits, Ivan, Daniel Smoots, Henry Franscioni, Anjana Patel, Nathan Fackler, Seth Wiley, Amnon A. Berger, Hisham Kassem, Richard D. Urman, Laxmaiah Manchikanti, Alaa Abd-Elsayed, Alan D. Kaye, and Omar Viswanath, "Injection Techniques for Common Chronic Pain Conditions of the Foot: A Comprehensive Review," *Pain and Therapy*, Vol. 9, No. 1, June 2020, pp. 145–160.

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, with a focus on the following three disease areas: brain health, immune and autoimmune disease, and cardiovascular disease. Using microsimulation analyses, the research team studied the societal cost impact of increasing research funding in three diseases that present a large disease burden for women: Alzheimer's disease and Alzheimer's disease–related dementias (AD/ADRD), coronary artery disease (CAD), and rheumatoid arthritis (RA).

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

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.

For more information on this publication, visit www.rand.org/t/RRA708-4.

IMAGE CREDITS: Page II, Dean Mitchell/Getty Images | pages 2–3, Radovanovic96/Getty Images | page 4, Rawpixel.com/Adobe Stock | page 6, FG Trade/Getty Images | page 8, FatCamera/Getty Images | page 9, amazing studio/Adobe Stock | page 10, vitapix/Getty Images | page 13, FG Trade/Getty Images | page 14, FatCamera/Getty Images | page 16, SolStock/Getty Images | page 19, nazar_ab/Getty Images | page 27, FG Trade/Getty Images | page 28, Orawan/Adobe Stock | page 33, Eva-Katalin/Getty Images | back cover, inews77/Adobe Stock.

www.rand.org

RR-A708-4