

THE WHAM REPORT

Societal Impact of Research Funding for Women's Health

IN RHEUMATOID ARTHRITIS

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Women's
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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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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.

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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.

Research impact analysis is a framework for supporting decision-making about research funding allocation. Economic modeling aids with such impact analysis. 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 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 National Institutes of Health (NIH) extramural RA portfolio devoted to women's health, estimated at 7 percent of the total portfolio. 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 on RA yields benefits beyond investing in general research. The ROI is higher for scenarios in which research funding has three times the impact on women's health out-

comes than on men's health outcomes. Assuming an equal impact of research on women and men results in lower returns.

Large returns result from very small health improvements.

Assuming 0.1 percent or less total health improvement from reduced age incidence of RA and reduced disease severity has the following results:

- For the U.S. population, more than 70,000 years with RA can be saved over 30 years, with substantial gains in health-related quality of life.
- The ROI is 174,000 percent for doubled investment in women's health research with an assumption of only 0.1 percent improvement in health outcomes.

Doubling the investment would have an expected ROI of 15 percent if it succeeded in generating health improvements of 0.1 percent with a 0.07 percent probability, or a 1 percent health improvement with only a 0.01 percent probability.

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

Policy Opportunities

Large societal gains may be possible by increasing investment in women's health research on RA. 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:

- *Increase research funding directed at women's health within RA.* The potential gains from women-focused research are substantial, given the limitations in knowledge about women and RA.
- *Pursue research on the biology of RA in women, including early identification, and identify barriers to diagnosis in women.*
- *Expand research agendas to address relationships between RA and work productivity impacts.* The ways in which RA limits work productivity could be a useful lens through which to evaluate current and potential future treatment effectiveness. Given the evidence of societal gains caused by the work productivity gains possible with research, this is a fruitful area for study.



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

- *Raise awareness of the potential value of investment in women's health research in RA.* The ways in which women's health research is disadvantaged relative to general research require further study, but investing not just in the research agenda but also the careers of those who can pursue that agenda is critical. Identify such obstacles 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 depends 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. Leaders across multiple other business sectors need to understand the consequences of underinvestment for workforce productivity and the health care burden associated with RA. These communities are key to informing future research investment strategies.

The results can inform funding prioritization by funders, legislators, and the business community, demonstrating the potential for improving research on women's health and the impact of doing nothing—making no change from the status quo.



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: brain health, oncology, heart health, 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 autoimmune disease, RA 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 the business community. The advisers' input enabled us to finalize key assumptions and the model structure.

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.

Why Focus on Rheumatoid Arthritis?

RA is an autoimmune disease with higher prevalence in women than men (National Institute of Arthritis and Musculoskeletal and Skin Diseases, 2019). Prevalence estimates in the United States have ranged from approximately 4 percent to 6 percent (Park, Mendy and Vieira, 2018). 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, with more women than men reporting hand pain and disability (Urits et al., 2020). Current estimates project that women will continue to account for the majority of RA cases, accounting for more than 58 percent of all cases in 2040 (Hootman et al., 2016).

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 the impact of the disease and its treatment on health-related quality of life (Grant and Buxton, 2018). These models include disease burden and societal productivity costs and benefits.

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.

Determining the Research Investment

The models assume that increased research funding reduces the incidence of disease, reduces the severity of disease for those who are diagnosed, and improves health-related quality of life.

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. Within the portfolio of extramural funding for RA research from the NIH over the past five fiscal years, funding with a specific focus on women's health research accounted for 7 percent of total funding (NIH, 2020c). The disease burden is high (Hootman et al., 2016), and greater investments are likely to yield a favorable ROI for women—particularly, because of the higher prevalence among women—and for society.

Few studies have employed models stratified by sex or gender to test the sex and gender differences of RA. In a review of the literature on gender differences for Alzheimer's disease, coronary artery disease, and RA, RAND researchers determined that the majority of RA-focused studies used sex and gender as a descriptive or control variable. Using a microsimulation model approach, we examine the impact of funding on health outcomes and economically quantified societal burden from RA.

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 RA. The models followed a cohort representing the U.S. population of adults ages 25 to 65 and simulated the progression of each person’s health in the sample over a 30-year time horizon. The decision to focus on the working-age population was in recognition of the impact that RA has on the ability to work. 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).²

Rheumatoid Arthritis Model

We assumed that impacts of increased funding occur through 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.

By tying different funding scenarios to incurred societal burden, the model quantifies how funding amounts affect the societal burden of RA in terms of health expenditures, productivity loss, and decreased quality of life. The impact on QALYs (and not just on absolute lost life years) is important to quantify for RA, given the ways in which the disease affects individuals and the long duration of disease

² For a detailed technical appendix describing the specifics of the microsimulation model, please visit www.rand.org/t/RRAT08-3.

for many patients. 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 approach to relating funding to health improvements, life status, and costs is summarized in Figure 1 as the conceptual model guiding this work.

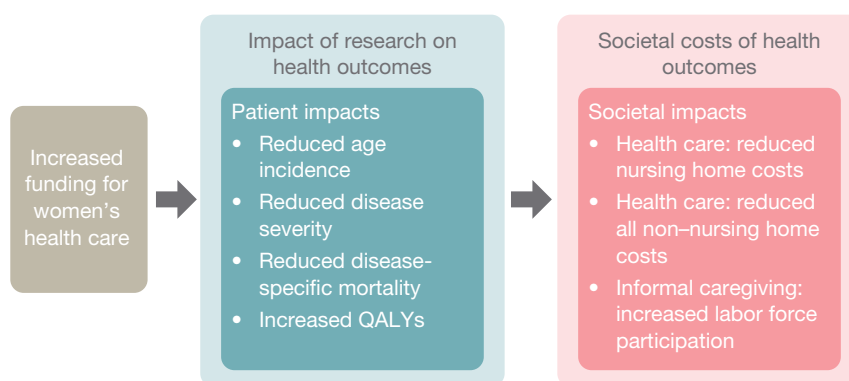
We determined estimates of RA onset following Norton et al., 2014, and separating individuals with RA into four classes, indexed by the severity at onset and progression.

We determined our assumptions on the return on research investment (that is, the impact of funding levels on health outcomes) using prior research on funding investment return (Grant and Buxton, 2018). We calculated the return on research investment using the following specific health outcomes: age incidence of disease, improved detection rates and earlier detection in the disease course, severity (with the assumption of reduced severity and reduced time in more-severe stages of disease), and reduced mortality due to disease.

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 include 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.

FIGURE 1

Conceptual Model of Research Impacts on Patient and Societal Burden of Rheumatoid Arthritis



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 and non-Hispanic white males.

Time Horizon

The cohort was created as a representative sample of the United States, following age and gender distributions for individuals ages 25 to 65 and using existing disease rates by age and gender. 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 impact (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.

Investment Impacts on Health Improvements

The model provides the ROI for each of the following health improvement impacts, first separately and then assuming all three impacts occur together:

1. decreased age incidence of disease (probability of onset at a given age)
2. delay in progression to more-severe levels of disease, with the assumption that innovations will reduce severity and slow progression
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 uncertainty regarding overall health improvements that investment in research can produce, we examined three levels of improvement: 0.1 percent, 0.2 percent, and 1 percent improvement. That is, we estimated the reduced disease incidence, reduced severity, and improved quality of life together to sum to an overall health improvement at these three levels. Results for the lowest level, 0.1 percent, are presented here.

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 RA 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

The benchmark for the baseline percentage of research on women's health was funding levels for RA research within the funded portfolio of the NIH. To estimate this level, we retrieved all titles and abstracts for RA using NIH RePORTER, the publicly available interface of funded extramural NIH projects (NIH, 2020c). The following terms were used to search the retrieved titles and abstracts to determine the total number of women-focused projects: "women," "sex," "gender," and "female." Projects without these terms in the title or abstract were excluded from the women-focused research set examined.

The total RA project funding level was calculated using the NIH Research, Condition, and Disease Categorization (RCDC) codes (NIH, 2020a). 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. 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: a 0.1 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 the simulated improvements in the health and economic outcomes. In the next section, we consider the resulting impact on costs scaled up from the model cohort to the U.S. population ages 25 to 65 of approximately 175 million people.



FIGURE 2

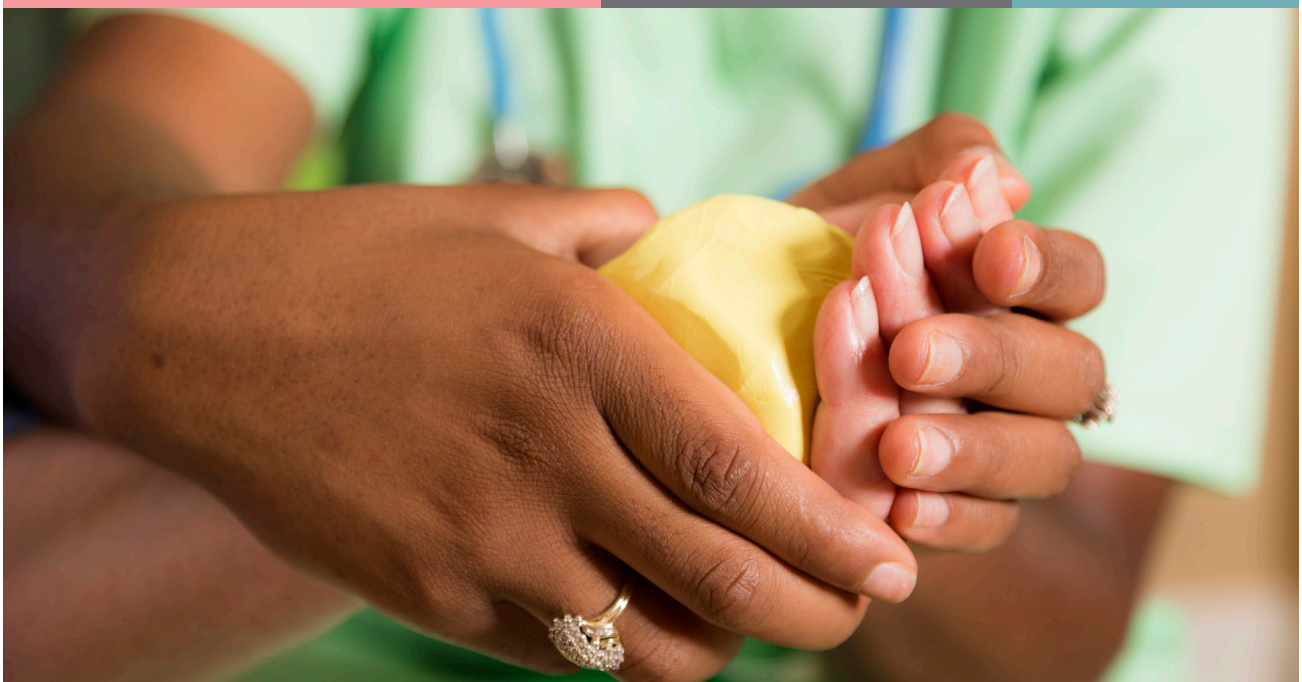
Health and Economic Improvements of Increased Funding for Women's Health Research in Rheumatoid Arthritis



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

Decreased Disease Burden

The modeled health improvements generated a reduction in RA disease burden in terms of life years with RA. Women have more than 61,600 fewer life years with RA, and men have about 9,000 fewer life



years with RA. The impact on women's years with RA is more than six times that of men's.

Increased Quality of Life

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. Finally, we directly decreased the reduction in quality of life for RA 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, this improvement captures a much larger effect, which is represented for women by approximately 223,000 more life-year equivalents of a fully healthy adult, measured in QALYs, and 34,000 more years for men. The impact on QALYs for women is substantial relative to men, but both are positive.

Lost Productivity for Patients

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

The impact of these productivity gains is about six times larger for women than for men.

Caregiver Productivity

With a reduction in RA burden, there is also less informal care given. This allows those caregivers to spend more time in paid labor. We estimate that the health improvement leads to 4,500 fewer lost life years of work provided to women and nearly 1,000 fewer years provided to men.

Impact on Cost Outcomes

For the health and economic outcomes, the largest driver of gains is the reduction in lost QALYs. Patient work productivity is the next largest driver (see Figure 3).

FIGURE 3

Change in Costs Over 30 Years of Increased Funding for Women's Health in Rheumatoid Arthritis



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

The overall reduction in costs was about \$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 the increased productivity for RA patients, representing more than \$680 million. The total across these three categories is about \$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.

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 RA portfolio and assuming a small 0.1 percent health improvement), the ROI would exceed 174,000 percent.



Discussion

Health research investments affect society through many pathways. For RA, the health-related quality of life impacts from modest health improvements are large. Improved work productivity for individuals with RA yields additional societal-level benefits. Even if only labor productivity and reduced health care costs are included in the gains, the ROI is still positive.

For RA, large societal gains would result from investments that yield very small overall increments in health improvement. Overall magnitude of impact is in line with similar research on 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 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 when 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.

Estimates for the time from investment to a discernible impact of investment for health research are about 13 to 25 years. Future research may accelerate that timeline.

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 decisionmaking about research funding allocations:

- *Increase research funding directed at women's health within RA.* The potential gains from women-focused research are substantial, given the limitations in knowledge about women and RA relative to information about men and RA.
- *Pursue research on the biology of RA in women, including early identification, and identify barriers to diagnosis in women.*
- *Expand research agendas to address relationships between RA and work productivity impacts.* The ways in which RA limits work productivity could be a useful lens through which to evaluate current and potential future treatment effectiveness.

Broader actions that could improve decisionmaking about research funding involve increasing awareness of the current state of



funding directed toward women's health in RA 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 in RA.* The ways in which women's health research is disadvantaged relative to general research requires further study, but investing not just in the research agenda but also in the careers of those who can pursue that agenda is critical. Identify such obstacles 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 depends on an understanding of 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 the health care burden associated with RA. These communities are key to informing future research investment strategies.

Although the higher prevalence of RA among women has led to health research with impacts for women as well as men, a focused investment on women's health research could yield large impacts on women's health-related quality of life in particular.

Conclusion

Understanding the full range of societal impacts from health research investment requires the 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. Although the higher prevalence of RA among women has led to health research with impacts for women as well as men, a focused investment on women's health research could yield large impacts on women's health-related quality of life in particular. The limitations that result from RA affect work productivity, and this represents another important avenue to realize the impacts of health research innovation. In conjunction with detailing the research agenda, the financial investment needed to realize the goals of that agenda requires planning. These analyses suggest that investing more in research on women's health in RA 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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References

- 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.
- Baird, Matthew D., Melanie A. Zaber, Andrew W. Dick, Chloe E. Bird, Molly Waymouth, Grace Gahlon, and Lori Frank, *Research Funding for Women's Health: A Modeling Study of Societal Impact. Findings for Rheumatoid Arthritis*, Santa Monica, Calif.: RAND Corporation, WR-A708-3, 2021. As of xxx 2021: https://www.rand.org/pubs/working_papers/WRA708-3.html
- 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
- , "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>
- 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-Elseyed, 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.



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omen'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 rheumatoid arthritis (RA). RA was chosen partly because of its higher prevalence in women than men, with some symptom profiles differing by sex. 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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