



# Women's Health Innovation Opportunity Map 2023

50 High-Return Opportunities  
to Advance Global Women's Health R&D

A report of the **Innovation Equity Forum**, sponsored by the  
Bill & Melinda Gates Foundation and US National Institutes of Health

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**About the Bill & Melinda Gates Foundation**

Guided by the belief that every life has equal value, the Bill & Melinda Gates Foundation works to help all people lead healthy, productive lives. In low- and middle-income countries, it focuses on improving people's health and giving them the chance to lift themselves out of hunger and extreme poverty. In the United States, it seeks to ensure that all people—especially those with the fewest resources—have access to the opportunities they need to succeed in school and life.

**About the National Institutes of Health**

The National Institutes of Health (NIH), a part of the US Department of Health and Human Services, is the United States' biomedical research agency—making important discoveries that improve health and save lives. Its mission is to seek fundamental knowledge about the nature and behavior of living systems and to apply that knowledge to optimize health and prevent or reduce illness for all people.



## Letter from NIH Office of Research on Women's Health

There was a time when clinical decisions being made about health care for women were based solely on findings from studies of men—without any evidence illustrating that they were applicable to women. The NIH Office of Research on Women's Health (ORWH) was established in September 1990 in response to congressional, scientific, and advocacy concerns of a lack of systemic and consistent inclusion of women in NIH-supported clinical research. Today, ORWH serves as the focal point for women's health research at NIH.

ORWH works with 27 NIH Institutes, Centers, and Offices to strengthen NIH support for research on diseases, disorders, and conditions that affect women. Seminal policy changes, like the NIH policy requiring scientists to consider sex as a biological variable (SABV) across the research spectrum, enhance the reproducibility, rigor, and transparency of science. Further, working groups like the NIH Working Group on Women in Biomedical Careers help support and advance women in scientific careers.

On behalf of NIH, I want to thank the Bill & Melinda Gates Foundation for the opportunity to partner on the Innovation Equity Forum (IEF). IEF serves as a critical forum to unleash global efforts to implement innovative solutions to improve the health of all women across various sectors and geographic regions.

The IEF provides a platform for a network of diverse stakeholders to form partnerships and formulate innovative ideas to advance the health of women. This cross-sector collaboration brings together brilliant minds from across the world to work together to improve and advance the health of women. Promoting research on women's health remains a global priority that enables us to support women and girls in all aspects of their lives.

Sex and gender differences can have a significant impact on how medical conditions affect a person. For example, these differences are apparent through ways in which diseases are prevented, diagnosed, and treated in women as evidenced by how pain is experienced by women. While we at NIH are committed to the SABV policy, we cannot do it alone. Events like IEF highlight how global connections and partnerships can help disseminate the principles of the SABV policy as best practice to enhance reproducibility, rigor, and transparency in research and improve the health of women.

We must work together and look at opportunities from a scientific, societal, and economic lens to integrate sex and gender into biomedical research. This integration is critical for rigorous science, maximizing returns on research investment, and advancing women's health. From laboratory and preclinical investigations, through translational studies and clinical care, this approach can lead to better science and innovation enabling biomedical research to achieve its greatest potential. Despite progress made, consideration of sex and gender influences is inconsistently applied across the biomedical ecosystem, highlighting an unmet need.

Since establishment in 1990, the work, reach, and impact of ORWH has significantly expanded. Science and the health of women greatly benefit from the ongoing dedication of ORWH and its partners. Moving forward, we must work together on a global scale and across sectors to form partnerships to advance the health of women. The intersectionality of women must be the focus in all future research endeavors to ensure the implementation of effective policies that benefit all women. We can learn from one another to help women and girls live their healthiest lives from head to toe.

Sincerely,

**Janine Austin Clayton, MD**

Director, NIH Office of Research on Women's Health



## Letter from the Bill & Melinda Gates Foundation

In July 2023, I had the opportunity and privilege to be part of an unprecedented gathering of individuals who put aside their individual organizational priorities to focus on the needs of women. We were all there because we see and feel the need to bring women's health to the forefront. Because we all recognize the importance and impact of elevating women through health. When women thrive, we all thrive. That gathering was the Innovation Equity Forum (IEF), a two-day workshop of a committed group of over 250 diverse stakeholders and was a pivotal point in a months' long effort to discuss, prioritize, and articulate specific opportunities to advance women's health research & development (R&D) and first solution strategies.

The collaboration behind the creation of this report, the *Women's Health Innovation Opportunity Map*, is groundbreaking, historic, and utterly necessary. The IEF and the Opportunity Map process were co-created by a diverse group of researchers and experts across sectors and countries. We intentionally designed this process to break down traditionally siloed areas of research and advocacy and to elevate voices that are too often underrepresented in R&D agenda-setting, including those of experts in low- and middle-income countries, to ensure the Opportunity Map meets their needs.

Women's health R&D has been relegated to the sidelines and seldom attains the attention that it deserves. Women, who make up half of the world's population, are historically underrepresented in biomedical research and clinical trials. Women, even as the experts of their own lived experiences, are rarely at the decision-making tables that impact their health. And, despite being one of the best investments in global progress, women's health and women's health R&D are consistently underfunded.

At the Bill & Melinda Gates Foundation, we believe that women are at the core of healthy families, vibrant communities, and prosperous societies. That's why progress on women's health—including innovations designed to meet women's unique health needs—is catalytic. Innovations can help us save millions of lives and spark *billions* of dollars of economic returns. We are thrilled to support and stand alongside this vibrant community of researchers, funders, experts, and advocates who are advancing research on women's health and giving the women's health R&D space a unique voice and identity.

My sincere thanks to all who contributed to this Opportunity Map, and particularly our colleagues at the US National Institutes for Health for co-leading this effort with us.

It is my hope that the *Women's Health Innovation Opportunity Map* will light the way for new research and funding opportunities, support consolidated advocacy efforts, and serve as a tool that will drive global action and investments in women's health. I am incredibly honored and excited to be a part of this stakeholder group uniquely focused on issues related to women's health R&D.

Sincerely,

**Ru-fong Joanne Cheng, MD, FACOG**

Director, Women's Health Innovations, Bill & Melinda Gates Foundation



## Letter from the IEF Co-Chairs

The Bill & Melinda Gates Foundation and the National Institutes of Health are long-standing partners and champions for research in women's health. As recently as 2020, our organizations represented nearly 60 percent of funding for sexual and reproductive health.<sup>1</sup> Yet, the growth potential for the women's health R&D sector is far greater than our combined efforts. It was only natural for us to explore opportunities to work together and broaden our organizations' individual efforts; this is how the idea of the Innovation Equity Forum emerged with the objectives to 1) convene a global community of key stakeholders and gatekeepers of health innovation around women's health R&D, 2) mobilize and accelerate innovations to improve women's health through a shared understanding of select critical women's health R&D priorities and 3) foster cross-sector multinational partnerships to advance R&D efforts in women's health innovation through enhanced coordination and collaboration. This report presents the outcome of this effort: a contemporary map of women's health innovation opportunities designed to inform global women's health R&D strategies.



We are excited and grateful that within less than a year, we were able to coalesce a Forum of over 250 stakeholders—from philanthropists, venture capitalists, biopharmaceutical companies, and startups in women's health to government regulators, patient advocates, and researchers. The group was formed to provide an inclusive and collaborative space for diverse perspectives to grapple with structural biases<sup>2</sup> and ideate on how best to enhance the pipeline for introducing innovations that improve women's health globally—from disentangling policy and market failures to fostering promising cross-sector partnership models. We culminated this effort by hosting the Innovation Equity Forum on NIH's campus in July 2023 to foster collaboration across sectors and geographic regions – the energy in the room was palpable and many highlighted the unique and groundbreaking nature of the event in its effort to build a broad coalition around women's health innovations.



This Opportunity Map is among our teams' ongoing efforts to advance women's health equity. When we integrate sex, gender, and intersectionality into R&D solutions, and when we center women's voices as patients, leaders, and decision-makers, we see improvements in data and insights and spur researchers and entrepreneurs to fill the innovation gap to address unmet needs in women's health across the lifespan.

### Your involvement is critical to the success of the Innovation Equity Forum

While we've tried to be inclusive and intentional in bringing in voices from a variety of geographical and organizational backgrounds, we know that we were not able to include everyone and this Opportunity Map is only the first step in engaging stakeholders to advocate for and accelerate resources toward women's health innovation. We welcome your ideas and partnership to unlock new funding, strengthen advocacy, and speed up innovations that advance the global women's health R&D ecosystem. We are building momentum to prioritize women's health, and we hope you will join us.

Sincerely,

#### IEF Co-Chairs

Jamie White, MS, ORWH, NIH  
Dr. med. Maike Scharp, MScPH, Bill & Melinda Gates Foundation

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<sup>1</sup> At the time of this report, no comprehensive figure exists that estimates total funding across all of women's health.

<sup>2</sup> R&D for women's health is neglected relative to burden due to biases in burden calculations (disability-adjusted life years) for female predominant conditions, biases in research that begin in discovery/preclinical and persist through all product development phases, low R&D funding for conditions that create greater burden for women, and reduced product pipeline relative to conditions with similar incidence.

# Executive Summary

This Women's Health Innovation Opportunity Map identifies 50 opportunities that are critical for catalyzing innovation to improve the health of women. We, the Innovation Equity Forum, urge stakeholders across the research and development (R&D) ecosystem to draw inspiration from and act on these highlighted opportunities to advance equitable, high-return innovations for women's health.

## Background

Women's health is an underserved area for innovation, facing disproportionately low R&D funding relative to its burden. A misconception predominates that women's health is restricted to women's reproductive years—disregarding the full life course; this must change. While stakeholders are beginning to address innovation gaps in women's health, including advancing sex- and gender-based training and gendered medicine, no coordinated agenda across sectors with a global focus exists to align their efforts.

To address this need, the Bill & Melinda Gates Foundation and the National Institutes of Health initiated an inclusive, consultative, cross-sector effort to generate a Women's Health Innovation Opportunity Map as a collaborative framework to advance women's health innovation.

This Opportunity Map has three key components. First, it lays out nine broad *topics* of women's health innovation with unique challenges, needs, and objectives. For each topic, leading *opportunities* were identified based on their potential for impact, readiness to scale, innovation feasibility, focus on women's unmet health needs, and ability to improve health equity. Finally, specific *solution strategies* articulate actionable ways to realize each opportunity and create impact within the next 15 years. As such, this Opportunity Map provides a guide that stakeholders across the women's health R&D ecosystem—from researchers to entrepreneurs, investors, government bodies, biopharmaceutical companies, civil society, and more—can use to advance high-impact investments and initiatives to improve women's health.

## Methodology

A Forum of over 250 experts and stakeholders—representing over 50 countries and diverse perspectives across various geographic regions and sectors that work in women's health—gathered to develop the Opportunity Map. Members convened monthly from January to July 2023 and were organized into 11 sub-committees that identified and developed opportunities within each topic. They evaluated these opportunities against five criteria (PRIME), generating scores that the members compared by scorer demographics. This consultative process culminated in July with the Innovation Equity Forum (IEF) convening, where Forum members and special guests convened in-person and virtually for a hybrid meeting. During this event, participants engaged in information exchanges and participatory decision-making discussions. In topic-focused breakout groups, they selected leading opportunities for inclusion in this report and formulated actionable solution strategies to realize each opportunity.

## Call to action

This Opportunity Map outlines a bold and actionable plan to address critical priorities for advancing women's health innovation. Publishing the Opportunity Map marks the first step to gather stakeholders in the women's health R&D ecosystem and coalesce around impactful investments or important steps and opportunities needed to improve women's health.

**We call all innovators, influencers, and advocates from across the women's health R&D ecosystem to work together to realize the opportunities presented in this report, including:**

1. **Commit to equitable inclusion, participation, and funding of women** across the R&D continuum, including embedding sex and gender considerations at all stages.
2. **Invest in the areas of women's health innovation** highlighted in this report that address critical needs for diverse groups of women and have high return on investment potential, including financial returns and health and social benefits.
3. **Create a partnership** with the objective to strengthen the R&D ecosystem across the full scope of women's health.

## Scope for the Women's Health Innovation Opportunity Map

<b>Health issue</b>	Unmet needs in women's health, including for <ol style="list-style-type: none"><li>1. Female-specific health conditions</li><li>2. Conditions that affect women disproportionately</li><li>3. Conditions that affect women differently</li><li>4. Conditions that are under-studied or under-resourced for women</li></ol>
<b>Affected population</b>	Women (including female assigned at birth, transgender, and non-binary people), across their lifespan, worldwide, across different demographics including race, ethnicity, age, generation, socio-economic status, caste, and more
<b>Timeframe for impact</b>	Medium- to long-term (within 15 years)
<b>Types of R&amp;D opportunities</b>	<ol style="list-style-type: none"><li>1. Description: to assess the burden or risk factors for the health issue</li><li>2. Discovery: to discover or develop effective interventions to reduce or control the health issue</li><li>3. Development: to improve upon or scale pre-existing and effective interventions</li></ol>
<b>Partners whose values are represented</b>	Funders, researchers, clinicians, patients, program implementers, policymakers, product and service providers, and women
<b>Expected returns from investment</b>	Accelerated innovation for women's health and, ultimately, reduction in morbidity and mortality with increased well-being

# Improving women's health unleashes a powerful engine for change



By prioritizing resources and efforts along five criteria...

Potential for impact

Readiness

Innovation

Matters to women

Equity

...With four lenses in mind...

Serving the underserved

Sex and gender influences

Life course perspective

Quality of life and well-being

...We can advance opportunities to lay stronger foundations for equitable innovation...

## 1 | Data and modeling

1. Collect, harmonize, utilize, and **report granular data (qualitative and quantitative) for health elements and determinants** to inform prioritization, develop models, and innovate products for women's health across the life course.
2. Support **capacity to collect, harmonize, utilize, and report granular data** (qualitative and quantitative) for health elements and determinants to inform prioritization, develop models, and innovate products for women's health across the life course.
3. **Update and expand burden of disease metrics** to better account for sex and gender-related conditions, long-term sequelae, and socio-cultural gender biases (including input data gaps, disability weighting, and duration assumptions).
4. Identify and **fill data gaps related to calculating return on investment (ROI)** in women's health R&D, including economic models and ROI for disease-specific areas.
5. Develop approaches for **incorporating qualitative information and proxy indicators into models**, including unstructured narrative data.

## 2 | Research design and methodologies

1. Advance **sex- and gender-intentional research design and analysis** during all stages of research (including preclinical and clinical) to generate endpoints, outcome measures, and evidence relevant for women across the life course, and to evaluate heterogeneity of treatment effects by sex and gender.
2. Promote knowledge- and resource-sharing on the **preclinical and clinical research landscape in LMICs and other under-resourced settings** to strengthen research activities and promote collaborations that advance women's health.
3. Strengthen the use of **computational and bioinformatics modeling** (reducing the use of animal models) and machine and deep learning approaches to better understand the biological basis of diseases affecting women and inform product development, risk identification, and treatment approaches—including by leveraging existing datasets and unbiased common data elements.
4. Support **in vitro translational model development**—such as organoids and organ-on-a-chip systems—to ensure more extensive clinical and translational characterization of diseases, conditions, and differences by sex and gender.

## 3 | Regulatory and science policy

1. Ensure the implementation of **sex- and gender-intentional science policy frameworks** that cover all aspects of the R&D lifecycle for medical products and healthcare innovations—including ethical, legal, and societal implications—with harmonization and collaboration mechanisms to accelerate their development.
2. Require **legal and/or regulatory frameworks** covering all aspects of the R&D lifecycle for medical products and healthcare innovations to systematically apply **sex- and gender-intentional approaches and evidence at all stages of development** to drive sex- and gender-specific interventions (e.g., ensuring clinical studies capture relevant differences in disease trajectory and outcomes across sex and gender, including novel endpoints).
3. Require reporting and timely updates of **sex- and gender-specific outcomes in healthcare product labeling and package inserts**.
4. Advance data harmonization and standardization efforts to drive **sex-, gender-, and age-disaggregated post-market surveillance** with common indicators specific to women's health.
5. Assess and implement **regulatory and policy incentives** that will promote investment and address barriers and disincentives, to accelerate the pace and volume of development, de-risk R&D in women's health, ease market authorization, and improve access to innovations that improve women's health.

## 4 | Innovation introduction

1. Create robust and ongoing **data repositories to catalyze women's health product development** and accelerate the successful introduction of these products into new markets.
2. Establish **centralized innovation hubs** specifically focused on the design and commercialization of solutions for women's health and well-being.
3. **Improve pathways to market** for women's health solutions by accelerating commercialization, regulatory review, reimbursement, and access.
4. Create **new pathways to fund innovation**.
5. Support **market shaping approaches** that enable suppliers to develop innovations accessible in LMIC settings by incentivizing payors and market entry and addressing demand and scale issues.

## 5 | Social and structural determinants

1. Ensure that **women's needs and voices guide national and global research agendas** through broad representation and reflection of different communities.
2. Conduct a **global review of social determinants of health interventions** with an emphasis on those that focus on vulnerable populations of women; based on review, develop equitable standards for inclusion of social determinants of health considerations for women's health research.
3. Research the **intersectional impacts of gender roles, power dynamics, and economic agency** (e.g., decision-making, unpaid work) on women's health.
4. Increase **representation of women, sexual and gender minorities, and other marginalized populations in the review of research grants** in women's health R&D.
5. Research **traditional and cultural practices** that promote women's health outcomes and well-being.

## 6 | Training and careers

1. Create and implement resources for **educating the current and future research and healthcare workforce on women's health and sex and gender influences** on health.
2. Advocate among educational policymakers and institutional decision-makers for the **integration of women's health and sex and gender considerations into education and training**.
3. Investigate **barriers and enablers for the participation, progression, and leadership of women in R&D, entrepreneurship, and healthcare careers**, and use successful practices to create reference tools.
4. Establish **safeguards for women's rights** within countries globally to receive STEMM education and pursue STEMM, R&D, and entrepreneurship careers and leadership positions.
5. Enhance **men's allyship** to activate opportunities for women to pursue STEMM, R&D, and entrepreneurship careers and leadership positions.

## ...To benefit women across the spectrum of conditions that affect them uniquely, differently, or disproportionately...

### 7 | Communicable diseases



1. **Assess the burden of disease** and costs resulting from infections that affect women disproportionately or differently, including reproductive tract infections, infections in pregnancy, and pathogens with outbreak potential.
2. Stimulate R&D to explore **associations between microbes (pathogens, commensals) and conditions that primarily or disproportionately affect women**.
3. Develop and evaluate **vaccines and other prevention interventions** for infections that disproportionately impact women and evaluate maternal immunization to protect the mother-infant dyad.
4. Develop **improved diagnostic tests for STIs and other reproductive tract infections**, including affordable point-of-care and self-testing products.
5. **Expand therapeutic options for infections in women**, including during pregnancy and breastfeeding.

### 8 | Non-communicable and chronic conditions



1. Evaluate **sex- and gender-related differences in the evolution and presentation of cardiometabolic diseases** and responses to available therapies to inform the development of optimal prediction, prevention, screening, diagnosis, monitoring, and treatments for women, with a specific focus on ischemic heart disease, diabetes, and obesity.
2. Evaluate **sex- and gender-related differences in outcomes and responses to medications** (including chemoprevention, chemotherapy, immunotherapy, and targeted therapy) to inform the development of prevention strategies, screening and diagnostic tools, and treatments for lung, colorectal, and gynecological cancers.
3. Evaluate **sex- and gender-related differences in the evolution and presentation of neurological disorders** and responses to available therapies to inform the development of prevention strategies, screening, diagnostics, monitoring, and treatments for women, with a specific focus on dementia, migraine, and pain.
4. Develop prevention interventions, screening and diagnostic tools, and treatments that account for **sex- and gender-specific elements in mental health disorders** across diverse settings and across the life course, with a specific focus on post-traumatic stress disorder (PTSD), depression, and anxiety.
5. Evaluate **sex- and gender-related differences in the evolution and presentation of autoimmune disorders** and responses to available therapies to inform the development of prevention, screening, diagnosis, and treatment options for women, with a specific focus on systemic lupus erythematosus (lupus), rheumatoid arthritis, osteoporosis, and autoimmune thyroid diseases.

### 9 | Female-specific conditions



1. Investigate the **biological and external mechanisms of female gynecological health conditions** and develop tools and therapies for prevention, diagnosis, treatment, and non-invasive monitoring of conditions, including normal menstruation and disorders such as polycystic ovarian syndrome, endometriosis, adenomyosis, and fibroids.
2. Stimulate R&D on the **role of the vaginal microbiome** in health and illness and develop interventions to address vaginal dysbiosis and foster a low-risk vaginal microbiome.
3. Increase research on **prenatal, intrapartum, and postpartum conditions and risk factors associated with adverse maternal health outcomes** to enable the development of diagnostics, treatments, and prevention, including artificial intelligence/machine learning tools.
4. Investigate evidence gaps in understanding the **role of micronutrients**, including iron and folic acid, and their formulation for improving maternal outcomes.
5. Create and support **biobanks with diverse, linked milk and blood samples** that can be accessed for research, including assessing the safety of prescription and over-the-counter medication use during pregnancy and breastfeeding.
6. Develop **improved, accessible contraceptive technology** with fewer side effects and more prolonged efficacy.
7. Understand **how policies that influence reproductive care impact women's health** to support the development of new modalities for the full range of reproductive care.
8. **Optimize fertility potential**, including in males, by developing new, affordable diagnostic tools and treatments.
9. Develop **self-administered solutions and new biomaterials** such as mesh products and stem cells to support safe and effective treatment options for conditions such as urinary incontinence and prolapse in women.
10. Develop novel, evidence-based, and specific **diagnostics and treatments for symptoms of menopause**, such as hot flashes, insomnia, joint pain, mental health disorders, and genitourinary syndrome.



...Powered by global collaboration, knowledge sharing, and mutual commitment.



### 10 | Partnership for Women's Health R&D



1. Create a **partnership with the objective to strengthen the R&D ecosystem** across the full scope of women's health.

# Contents

Executive Summary .....	6
Acronyms & Key Terms .....	11
Introduction: The Case for Women’s Health Innovation .....	14
Methodology .....	21
Cross-Cutting Topics: Opportunities and Solution Strategies .....	24
1   Data and Modeling.....	25
2   Research Design and Methodology.....	31
3   Regulatory and Science Policy .....	36
4   Innovation Introduction.....	43
5   Social and Structural Determinants.....	49
6   Training and Careers.....	54
Issue-Specific Topics: Opportunities and Solution Strategies.....	59
7   Communicable Diseases .....	60
8   Non-Communicable & Chronic Conditions.....	66
9   Female-Specific Conditions.....	72
Cross-Sector Partnership for Women’s Health Innovation .....	83
Conclusion .....	87
References.....	89
Appendices .....	99
Appendix 1: Methodological Detail .....	100
Appendix 2: Innovation Equity Forum demographics.....	104
Appendix 3: Summary of Criterion Scores by Topic and Criterion .....	106
Appendix 4: Criterion Scores by Topic.....	108
Online Supplemental Appendices .....	118

# Acronyms & Key Terms

## Acronyms

<b>AI</b> – Artificial intelligence	<b>PD-L1</b> – Programmed death-ligand 1
<b>AIDS</b> – Acquired immunodeficiency syndrome	<b>PPH</b> – Postpartum hemorrhage
<b>AMC</b> – Advance market commitment	<b>PoCT</b> – Point-of-care test
<b>AMR</b> – Antimicrobial resistance	<b>POP</b> – Pelvic organ prolapse
<b>CHNRI</b> – Child Health and Nutrition Research Initiative	<b>PTSD</b> – Post-traumatic stress disorder
<b>CVD</b> – Cardiovascular disease	<b>R&amp;D</b> – Research and development
<b>DALY</b> – Disability-adjusted life year	<b>ROI</b> – Return on investment
<b>FDA</b> – US Food and Drug Administration	<b>RTI</b> – Reproductive tract infection
<b>GDP</b> – Gross domestic product	<b>SABV</b> – Sex as a biological variable
<b>HICs</b> – High-income countries	<b>SDOH</b> – Social and structural determinants of health
<b>HIV</b> – Human immunodeficiency virus	<b>SGM</b> – Sexual and gender minority
<b>HPV</b> – Human papillomavirus	<b>SOGI</b> – Sexual orientation and gender identity
<b>HSV</b> – Herpes simplex virus	<b>STEMM</b> – Science, technology, engineering, mathematics, and medicine
<b>IBD</b> – Inflammatory bowel disease	<b>STI</b> – Sexually transmitted infection
<b>IEF</b> – Innovation Equity Forum (“Forum”)	<b>SUI</b> – Stress urinary incontinence
<b>IUD</b> – Intrauterine device	<b>TB</b> – Tuberculosis
<b>IVF</b> – In-vitro fertilization	<b>US</b> – United States
<b>LMICs</b> – Low- and middle-income countries	<b>UTI</b> – Urinary tract infection
<b>ML</b> – Machine learning	<b>VC</b> – Venture capital
<b>NGO</b> – Non-governmental organization	<b>WHO</b> – World Health Organization
<b>NIH ORWH</b> – US National Institutes of Health Office of Research on Women’s Health	<b>YLDs</b> – Years of healthy life lost due to disability
<b>PCOS</b> – Polycystic ovary syndrome	<b>YLLs</b> – Years of life lost due to premature mortality
<b>PD-1</b> – Programmed cell death protein 1	

## Key Terms

**Communicable diseases:** Diseases caused by bacteria or viruses, transmitted between people either directly through contact with bodily fluids, contaminated surfaces, or through the air, or indirectly through contact with animals or vectors.

**Disability-Adjusted Life Year (DALY):** A measure of disease burden that combines years of life lost due to mortality and years of life lived in a state of less than optimal health.

**Equity:** Fairness and justice in responsibilities and access to benefits for all, including across different geographic regions and intersectional factors such as gender identity, age, nationality, race/ethnicity, caste, ableism, and more. Equity is achieved by eliminating structural barriers resulting from historical and present-day power imbalances, discrimination, mistreatment, and abuse and meeting individuals', groups', and organizations' unique needs.

**FemTech:** Technology, including products, services, software, and diagnostics, designed to address health and wellness issues that present only in women, mostly in women, and differently in women.

**Gender:** A social and structural variable that includes identity, expression, roles and norms, relations, and power. Gender is considered separately from sex. Gender can influence health through a variety of pathways, such as care-seeking behavior and access, biased care provision, and differential exposures and protective factors as a result of gender norms (e.g., gender differences in sexual behavior; gender norms increasing the risk of depression) (Petersen & Hyde, 2010; Piccinelli & Wilkinson, 2000).

**Harmonization:** Reducing variation and improving alignment between standards, practices, and regulations. *Data harmonization* refers to reconciling disparate data fields, formats, and elements into standardized datasets.

**Intersectionality:** The understanding that different social categorizations—such as race, ethnicity, socioeconomic status, sexual and gender identity, and more—can uniquely combine to create interdependent systems of discrimination and privilege.

**Life course:** Different stages of a person's life from birth through adolescence and adulthood until death. This report often uses life course when considering stages specific to women's lives, including menarche, reproductive years, pregnancy, peri-menopause, and post-menopause.

**Non-communicable and chronic conditions:** Diseases that are not transmitted between people, persist or recur over time, and are often not curable.

**PRIME Criteria:** Standards by which the Innovation Equity Forum evaluated the opportunities presented in the Women's Health Innovation Opportunity Map. The criteria include Potential for impact, Readiness, Innovation, Matters to women, and Equity. To learn more about the PRIME criteria, see Figure 2 in Methodology.

**Research and development (R&D):** Novel and systematic work that increases the stock of knowledge—including knowledge of disease burdens, protective and risk factors, and effective interventions—and devises new or improves existing applications using the

available knowledge (OECD, 2015).<sup>3</sup> The R&D continuum includes 1) Description, which includes identifying and defining the subject matter— i.e., as in basic research; 2) Discovery, which includes utilizing knowledge to solve a problem—i.e., as in applied research; and 3) Development, which includes improving upon and scaling innovations.

**Return on investment:** A performance measure to evaluate the value generated by an investment compared to the cost. When using the term “ROI,” both financial and societal returns on investment are considered.

**Sex:** A biological variable—including anatomy, physiology, genetics, and hormones—that can influence health through a variety of pathways; for example, endocrine and immune system differences impact disease acquisition, presentation, and progression, and structural differences in the brain increase women’s risk of concussion (Massey et al., 2021; Gupte et al., 2019). In this report sex is often referred to as sex as a biological variable (SABV).

**Sex and gender considerations:** Recognizing and accounting for the influences of sex as a biological variable, gender as a socio-cultural variable, and their interactions on health.

**Sex- and gender-sensitive/intentional approaches:** Approaches to R&D and its subfields that examine and address sex and gender considerations throughout education, design, implementation, analysis, reporting, policymaking, and other activities, to reduce gender gaps and inequities.

**Social determinants of health:** The factors that shape the conditions in which people live, including social, economic, and legal forces, systems, and policies that determine opportunities and access to high-quality jobs, education, housing, transportation, built environment, information and communication infrastructure, food, and healthcare; the social environment; and other conditions of daily life. Individual factors such as race, ethnicity, gender identity and expression, disability status, veteran status, and age also significantly influence health outcomes (National Institute of Nursing Research, 2013).<sup>4</sup>

**Structural determinants of health:** The social, economic, and political mechanisms that influence access to and availability of resources (Solar & Irwin, 2010).<sup>5</sup> These systems generate and perpetuate socioeconomic and health inequities between groups of people.

**Women:** When using the term women in the context of “women’s health,” “women” is inclusive of both sex as a biological variable and gender as a social variable across the life course, including girls and adolescents. This includes people assigned female at birth, transgender women, transgender men, and non-binary people affected by the topics covered by this report. The authors recognize that not all people who identify as women have the same reproductive anatomy, and not all people who were assigned female at birth identify as women.

**Women’s Health:** The phrase “women’s health” is used to highlight the interest in all areas of health related to women, including conditions associated with both sex as a biological variable and gender as an intersecting social determinant of health. This includes diseases and conditions that present only in women, disproportionately in women, and differently in women.

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<sup>3</sup> Adapted definition.

<sup>4</sup> Adapted definition.

<sup>5</sup> Adapted definition.



# Introduction:

The Case for Women's Health Innovation

# Introduction:

## The Case for Women’s Health Innovation

Women’s health innovation represents a significant untapped opportunity for improved well-being, more resilient households, stronger economies, and increased financial returns

### **Women’s health includes conditions that present only in women, mostly in women, and differently in women**

The conventional understanding of women’s health—which mainly centers on reproductive and maternal health—must be redefined: the health of women includes the overall health and well-being of women’s bodies and minds across their life course, as well as the consideration of sex and gender in all aspects of disease and treatment (NIH ORWH, 2019). The influence of sex and gender on risk factors, symptoms, disease outcomes, and treatment responses is well-established in research. For example, biological factors such as pregnancy can impact disease severity, while gender norms—such as women serving in caregiving roles—can impact disease acquisition (Lawry et al., 2023). Understanding and addressing these factors is fundamental to meeting women’s health needs. Tremendous potential lies in innovative approaches to conditions for which effects on women are historically understudied. These include conditions that impact women differently—such as cardiovascular disease and malaria—and conditions that present disproportionately in women—such as dementia and autoimmune disorders. Research in women’s health also includes investigation of socio-cultural factors, including the effects of gender-based violence, bias in care delivery, social norms, and relational power dynamics on health and well-being (WHO, n.d.).

### **Women’s health innovation investments generate transformative benefits across the R&D ecosystem**

While it is essential to transform disease-specific research to incorporate a sex and gender lens, this alone is insufficient to generate and sustain benefits for the health of women. Strategic investments across the R&D ecosystem can foster the inclusion and elevation of women at every research phase, including data collection, clinical trial design and participation, training and career advancement, development of regulatory and science policy, and consideration of social and structural factors.

### **Investing in women’s health improves individual well-being and yields broad economic and societal benefits**

Although women have a longer life expectancy than men, they experience distinct variations in mortality and morbidity across the life course that are often unaddressed by healthcare. Maternal morbidity and mortality and menopause, for example, are events unique to women in a particular life stage. Around the world, women spend more years with poorer quality of life, both in terms of health and well-being, than men (Carmel, 2019). Women also experience increased risk of acquisition and more severe outcomes due to differences in sex and gender related to specific conditions—such as dementia—leading to lower quality of life (Awordine et al., 2018). Tailoring prevention, screening, diagnostics, and treatments for diseases and conditions to account for sex and gender differences, as well as for women’s context and environment, is crucial to support their health and well-being. Women in low- and middle-income countries (LMICs), women of color, sexual and gender minority (SGM) populations, women with disabilities, and other populations face compounded social and economic



**A US\$300 million investment in women’s health research could generate US\$13 billion in economic returns.**

challenges. By addressing intersectional and underlying social and structural factors, we can empower women to make informed decisions, pursue their ambitions, and live healthier lives. Healthy women transform societies.

When women globally have access to appropriate, high-quality care, they are better able to live the lives to which they aspire, improve their households' resilience to shocks, advance their education and careers, and increase household earnings. As women frequently serve as family caregivers, healthy women contribute to healthier households with better nutrition and improved healthcare decision-making capacity. Additionally, women power their local economies through greater workforce participation and improved productivity. A study estimated that a US\$300 million investment in women's health research could generate US\$13 billion in economic returns (Baird et al., 2022). Another modeling study estimates that reducing maternal deaths significantly boosts countries' gross domestic product (Kirigia et al., 2006). Centering women's health produces positive ripple effects for the health of everyone, leading to more equitable and prosperous communities worldwide.

### **Market opportunities to develop new products and technologies targeted to women's health make financial sense for funders**

The FemTech sector is witnessing rapid growth, with over 60 percent of FemTech companies founded after 2017 (Levoitz et al., 2023). By 2030, the women's health market could range from US\$97 billion to upwards of US\$1.2 trillion, with a pipeline of new diagnostic devices, digital platforms specifically catered to meet women's health needs, and more (FemTech Analytics, 2022; Barreto et al., 2021). Despite this market potential, as of 2022, just seven active women's health-specific investment funds managed approximately US\$125 million combined, representing just 0.02 percent of healthcare startup investments in 2022 (Levoitz et al., 2023). Non-cancer women-specific conditions account for just two percent of the healthcare product pipeline, despite the burden of these diseases often far outweighing funding allocations (Kemble et al., 2022).

Improving women's health outcomes not only reduces health expenditures but also reduces dependence on caretakers and improves work productivity. For Alzheimer's disease and rheumatoid arthritis—two conditions that disproportionately affect women—models suggest that doubling the current National Institutes of Health (NIH) investment and achieving even a modest .01 percent improvement in health outcomes could result in significant cost savings of US\$932 million and US\$10.5 billion, respectively. Models also suggest that coronary artery disease research for both men and women results in a greater benefit in terms of life expectancy and disease-free years for women (Baird et al., 2022).

Opportunities exist to advance our understanding and management of conditions such as menopause and cardiovascular disease, which significantly impact women's quality of life and are understudied in women. Menopause, which affects one billion women worldwide at any given time, represents an estimated US\$600 billion market opportunity (Hinchcliffe, 2020). Opportunities exist for funders to invest in multiple markets for potential products; with four billion women worldwide, interventions designed for different geographic settings can multiply the returns not just for the funder but also for women, health systems, and societies.

### **Women's health innovation is under-represented in R&D relative to the burden**

Advancements in science and medicine spanning multiple disciplines, from genomics to infectious disease, have the potential to reshape the trajectory of our understanding of conditions affecting women. Recent research has identified links between seemingly



**By 2030, the women's health market could range from US\$97 billion to upwards of US\$1.2 trillion.**

unrelated diseases affecting women, including the potential correlation between bacterial infections and endometriosis or ovarian cancer (Harris, 2023). Further investigation of these links and the development of vaccines, diagnostics, and treatments for this cascade of diseases and conditions necessitates coordination and collaboration across medical specialties and partnerships across academia, government, the private sector, and more.

Within the R&D ecosystem, women's health receives limited attention due to the following:

- 1) Limited data to support the business case for new products;
- 2) Hesitation from investors and manufacturers due to perceived risk and liability;
- 3) Under-prioritization of career development for women amid a historically biased and male-dominated R&D industry.

The status quo is inequitable; new approaches are needed to develop innovative women-specific products and technologies for conditions that affect women exclusively or disproportionately and those that affect women differently than men.



### **Funding favors conditions that affect men more than women**

A recent analysis of NIH funding in *Nature* reveals that female-dominant conditions are underfunded relative to the death and disability they cause, compared to nearly all other conditions—not just those that are male-dominant (Smith, 2023). Migraines—which predominantly impact women—receive just 10 percent of the funding in proportion to the burden, while prostate cancer receives funding in proportion to its burden. Despite advancements in R&D in cardiovascular disease (CVD)—which affects men and women—little funding is directed toward women-specific solutions, such as drugs specifically tested for safety and efficacy in women. Between 2008 and 2019, just 4.5 percent of NIH-funded CVD projects specifically investigated gender-based differences in symptoms, presentation, and treatment efficacy for women, despite women’s lower likelihood of receiving treatment and significantly higher risk of death following a heart emergency (Antipolis, 2022).

### **Sex and gender data limitations appear across the R&D ecosystem, with harmful impacts on women**

Sex and gender biases in data abound. Structural challenges—such as the lack of suitable animal models for postpartum hemorrhage and restrictions that exclude pregnant women from clinical research—limit the available data to inform women’s experience of care. A recent study of bias in clinical trials found significant underrepresentation of female participants in 7 out of 11 disease areas, including CVD, the primary global cause of death for women (Feldman et al., 2019). Women represent just one-third of participants in clinical trials aiming to treat CVD, and the impacts of this underrepresentation are significant. In one study of digoxin, a heart failure treatment, the failure to consider sex differences resulted in a five-year delay in recognizing a higher risk of death among women taking the drug (Baird et al., 2022; Rathore et al., 2002).

Although more researchers are disaggregating data by sex, a bias toward a binary view of sex limits the diversity of sex and gender identities represented in data and reporting. Researchers often prioritize identifying the statistical significance of findings, with a tendency to exclude non-binary and transgender human participants due to their relatively smaller representation in the overall population or pool samples which does not allow for analysis based on sex and other factors. However, SGM populations face significant and disproportionate health disparities that warrant intentional focus and inclusive practices in innovation and research design (Bauer et al., 2017).

### **Perceived barriers to the introduction of products for women limit the product pipeline**

Product introduction to address diverse women’s health needs would benefit from de-risking efforts. Maternal and reproductive health innovations in particular face challenges in upstream and downstream stages of development. Upstream, concerns of potential congenital birth defects linked to trials of new maternal health products deter investor interest due to liability concerns. Subsequent limited development of maternal and obstetric products reinforces perceptions of limited market size, despite extensive health needs during pregnancy. In reproductive health, the opposite problem arises; the presence of highly effective and safe contraceptives gives a false impression that the market is saturated, which creates a high bar for introducing new contraceptives that outperform current methods, have fewer side effects or are better tailored to women’s needs.

### **Structural and systemic factors have historically perpetuated inequities in women’s health innovation, but solutions are actively reshaping the landscape**

In the past, science policy and legislation excluded women of childbearing age from enrolling in clinical trials due to fears of potential congenital anomalies. Perceptions of the



When results from males are improperly generalized to females, the missing results for females and inattention to sex and gender lead to errors and false conclusions...Studies with irreproducible results, biases, or unforeseen toxicities put people at risk of being harmed, contributing to the erosion of public trust in medicine and science. (White et al., 2021)

difficulty of studying animal and human female participants due to fluctuating hormone levels led to the male body serving as the standard for decades. Today, the inclusion of women and SGM populations in research studies and across the full ecosystem of R&D is reaping benefits for women’s health innovation (Liu & Mager, 2016). Incorporating standards for sex as a biological variable and training on sex and gender at medical schools can build a pipeline of future clinicians and researchers—of all genders—who prioritize sex and gender considerations and approach diseases and conditions with a sex- and gender-informed lens (White et al., 2021). We envision a world where researchers, scientific editors and reviewers, product developers, and other stakeholders fully engage women in the development of innovations that serve them and their diverse lived experiences.

## The opportunities highlighted in this report require the entire ecosystem—and new models for partnership and power-sharing among stakeholders—to advance women’s health innovation

This report presents high-impact, high-need opportunities primed to accelerate women’s health innovation and deliver a high return on investment (ROI) —both financial and impact-related. Experts from patient advocates and academics to venture capitalists and philanthropists have aligned on this set of solution strategies to create more and better products and technologies that meet the health needs of women globally and advance their positional power throughout the R&D ecosystem. Realizing the potential of this report will only be possible through coordination across the spectrum of R&D stakeholders and the creation of new partnerships to promote gender equity and the health of women worldwide.

We acknowledge the uneven power distribution among various stakeholders in women’s health R&D. Funders—both public and private—exert outsized power and influence in shaping the women’s health innovation agenda. Within pharmaceutical companies, for example, concerns prevail about risk and liability in research for pregnant women. Institutional funders exert significant financial sway over which conditions, diseases, geographic regions, and institutions receive funding, resulting in conditions that affect women remaining underfunded, despite willing and capable researchers and clinicians to pursue R&D. Governments play diverse roles—from partnering with academia and industry to advance R&D, to providing payor benefits and regulating products—with higher-income countries often wielding more influence than lower-income countries. While these roles provide positional and funding power, government agencies often contend with limited resources to advance all priorities. Wielding even less power are the patients themselves, often represented by civil society and advocacy organizations. Patient advocacy groups have strong agendas to raise with legislators and at high-level fora but lack the resources to advance their priorities without support from major funders. Within these groups are voices further made vulnerable by discrimination or social contexts, such as women from LMICs, SGM populations, older people, people with disabilities, non-native English speakers, and people with other intersecting identities.

### The solution strategies put forth by this report must be complemented by broader ecosystem-strengthening efforts to improve women’s health

We acknowledge that service delivery and access to care are critical components of health.

This report spotlights upstream R&D and conditions needed to spur innovation and not all potential efforts to strengthen women’s health innovation. Instead, this report highlights actionable R&D opportunities for women’s health that are most primed for near-term investment.

## Stakeholders in the women’s health R&D ecosystem

The women’s health innovation landscape includes stakeholders with diverse motivations and skillsets, representing different geographic regions, and possessing different forms of power and influence. Engaging them collectively as partners, and leveraging their individual strengths, will be key to building a robust and equitable R&D ecosystem for women’s health.

Each opportunity in the report calls one or more of the following groups to action, as indicated by the icons below

Role in advancing women’s health R&D



**Communities and Community Organizations** represent patients, advocates, and healthcare professionals who are passionate about women’s health. Health-focused civil society, non-governmental and advocacy organizations, implementing agencies, and media platforms often rally around specific diseases or conditions. These organizations tend to approach women’s health holistically, with increasing attention on social determinants of health.

Elevate the needs of diverse and underrepresented groups of women



**Researchers and Academia** include a wide range of stakeholders, including academic researchers and institutes, public and private research centers, organizations that monitor the R&D pipeline, journals and publishers, and entities responsible for establishing standards for R&D professional education. These organizations identify promising R&D opportunities and seek funding to move products from concept to development.

Advance sex- and gender-informed research and practices throughout the R&D life cycle



**Health Care Workers and Systems** include the stakeholders within health systems who contribute to the delivery of care such as frontline professionals, pharmacies, and support staff, as well as health system managers and professional associations. It also includes organizations dedicated to strengthening health systems, including program implementers, financiers of delivery and commodities, and others.

Elevate R&D needs and opportunities tailored to specific service delivery settings, and work with partners to co-create solutions



**Public and Philanthropic R&D Funders** are the government, multilateral, and philanthropic institutions and financing mechanisms that fund women’s health R&D. Given their financial power, the strategies of these institutions have tremendous influence on the market for innovations. Women’s health R&D funding is concentrated in these institutions due to relative under-investment by the pharmaceutical industry and venture capital.

Invest in under-resourced areas, and work with partners to harmonize funding efforts



**Private Sector** includes pharmaceutical and medical device companies, venture capital firms, startups, trade associations, and other businesses innovating for women’s health R&D. The fast-growing FemTech sector funds consumer products, digital health applications, and medical products and technologies designed for women’s needs. Private sector incentives are distinct from other stakeholders. Financial returns are often the primary driver, while social responsibility, customer, employee, or shareholder perception, and regulatory environment also influence decisions.

Invest in untapped but high-return areas of women’s health R&D, and elevate needs for de-risking innovation



**Payors and Insurers** are third party entities that pay for women’s healthcare, such as single payor public programs, socialized care, or private insurance providers. They may be organized at the national or subnational level. Payors’ purchasing behavior is influenced by regulations and/or market dynamics such as competition, demand from corporate or institutional customers, investor pressure, and other financial considerations.

Prioritize the availability of solutions that address women’s health needs



**Regulatory and Standard-Setting Agencies** include institutional, national governmental, and multinational bodies responsible for regulating pharmaceuticals and medical products, establishing policies that influence healthcare purchasing and access for women, and providing R&D oversight. These decisions are informed by current health, economic, and social considerations, research, legislation, and cooperative agreements.

Ensure sex- and gender-explicit frameworks are in place to guide other stakeholders toward a stronger pipeline of solutions that improve women’s health



# Methodology

# Methodology

The Women’s Health Innovation Opportunity Map was developed between January and August 2023 using an adapted Child Health and Nutrition Research Initiative (CHNRI) methodology followed by stakeholder-driven discussions. **Figure 1** illustrates key steps,<sup>6</sup> and more details are available in **Appendix 1**.

## The Opportunity Map focuses on unmet short-to medium-term needs in women’s health innovation

The scope of this exercise includes opportunities that address specific diseases and conditions, including female-specific health conditions and conditions that affect women disproportionately or differently, many of which are understudied in women. The opportunities also address structural and systemic factors influencing innovation and the R&D continuum, including description, discovery, and development.

Service delivery research was excluded from the scope due to the focus on R&D and because opportunities to strengthen service delivery are often context-specific. Additionally, areas with well-established R&D agendas—such as breast cancer—were excluded to call attention to unmet and underserved women’s health needs.

For opportunities to be considered, their timeframe for realizing impact should be within 15 years, though many opportunities may yield positive effects sooner. Anticipated returns from future investment in women’s health innovation opportunities include accelerated innovation, substantial market potential, and better health and socio-economic outcomes for all.

## The Gates Foundation and NIH engaged over 250 stakeholders in a highly consultative process

The Innovation Equity Forum (IEF, “Forum”)—composed of over 250 diverse stakeholders from academia, healthcare, pharmaceutical companies, venture capital, startups, multilateral institutions, advocacy, and other sectors—served as the primary consultative body in shaping the content of this report. The sponsors intentionally selected members and continued to add stakeholders through recommendations from existing members, considering their subject matter expertise and experience across a broad range of women’s health-related disciplines, sectors, and geographic regions. This approach aimed to generate an inclusive, globally applicable, and widely accepted Opportunity Map. The sponsors encouraged members to contribute not only as experts in their field but also as individuals and advocates and to uplift the values and perspectives of the constituencies their organizations serve.

Members—83 percent of whom identify as women—represent 52 countries, with 38 percent from LMICs. See **Online Supplemental Appendix 1** for the full Forum membership and **Appendix 2** for their demographic details.

<sup>6</sup> Forum membership expanded over time as members suggested additional invitees who could provide desired geographic and professional expertise.

**Figure 1. Opportunity Map Development**



Forum members provided substantial input on the topics and criteria used to score opportunities (see **Figure 2**, with additional information on methodology in **Appendix 1**). Within 11 topic-specific sub-committees, members landscaped resources and drew on their technical expertise to define the topic scope and develop critical opportunities for action and investment.

Members scored up to 15 opportunities per topic by the PRIME criteria and reviewed scores to select which opportunities would advance to discussions at the IEF convening. At this convening, held in July 2023, Forum members and select guests joined a series of plenaries, panels, and breakout discussions to identify up to five leading opportunities per topic and develop specific solution strategies for each opportunity, which are detailed in the following sections.

**Figure 2: PRIME criteria used to score opportunities**

<b>Potential for impact</b>	Would have a high return on investment—meaning a measurable reduction in morbidity and/or mortality, economic benefits to society, and/or improvement in the quality of life for women
<b>Readiness</b>	Can scale sustainably to reach the desired impact—considering technical, social, political, and economic factors
<b>Innovation</b>	Is scientifically feasible—meaning the science and technology can advance within 1-5 years to enable impact within 15 years
<b>Matters to women</b>	Would address women’s unmet health needs—as defined by women and uniquely tailored based on lived experiences
<b>Equity</b>	Would improve health equity, address the needs of diverse populations, and avoid exacerbating, sustaining, or creating additional health inequities among women with different lived experiences





# Cross-Cutting Topics: Opportunities and Solution Strategies

# 1 | Data and Modeling

To ensure that women receive evidence-based, tailored healthcare, the evidence base itself must be complete, rigorous, and representative. Accurate and accessible data are essential to understanding health conditions, informing diagnoses and treatment plans, and driving investment decisions and innovations. Women’s health, however, is not accurately measured nor consistently understood.

Women’s health research and data collection are underfunded and exclude the experiences of diverse populations based on race, ethnicity, age, gender, sexual orientation, geography, and socio-economic status, among other factors. Insufficient recognition and recording of gender as a socio-cultural variable distinct from biological sex inhibits researchers’ understanding of gendered differences in disease burden, prevention, and treatment. Crucial data gaps also exist across the lifespan. The key metric used for global health funding and prioritization—the disability-adjusted life year (DALY)—suffers from gaps in data on morbidity, particularly regarding sex- and gender-related differences in care-seeking behavior, access to quality care, and social restrictions and stigma that affect participation in surveys. Society has normalized intrusive symptoms—like those associated with premenstrual syndrome and menopause—as inevitable aspects of female biology, which discourages measurement of their frequency and impact. These and other data disparities across the R&D spectrum lead to surveillance, modeling, market sizing, product design, policy and investment decisions, and outcome measurements that are not appropriately tailored to women’s true health needs.

Innovation is greatly needed in the types of data that are captured (quantitative and qualitative), methods for data collection (technological and human approaches), and applications (in analysis and modeling and for decision-making). Advancing a clearer understanding of, and metrics for, sex- and gender-based women’s health will catalyze more significant funding, collection, reporting, and usage of data disaggregated by sex and gender. Strengthening a sex- and gender-informed data value chain across the lifespan will enhance understanding of women’s health needs, policy and programmatic decision-making, and, ultimately, healthcare and outcomes for all.



## Key Stakeholders

-  Communities and Community Organizations
-  Researchers and Academia
-  Health Care Workers and Systems
-  Public and Philanthropic R&D Funders
-  Private Sector
-  Payors and Insurers
-  Regulatory and Standard-Setting Agencies



**Opportunity 1.1** | Collect, harmonize, utilize, and report granular data (qualitative and quantitative) for health elements and determinants to inform prioritization, develop models, and innovate products for women’s health across the life course.

Researchers face limitations in understanding the diseases and disease determinants that have the greatest impact on the health of women across the life course. The limitations stem from inadequate measurement of indicators in an age-sex-specific fashion or aggregation of data that obscures age, life stage, and sex. Additionally, disparities in women’s health outcomes that are associated with various facets of identity—such as race and ethnicity, socio-economic status, or gender identity—are also obscured when data are measured and reported in aggregate. Furthermore, existing data sets’ applicability to health equity is limited by a historical lack of standard operational definitions for measuring these dimensions. For example, most data sets only reflect sex assigned at birth, leading to potential misclassification and an inability to characterize all groups regarding sexual orientation and gender identity (SOGI). Achieving an international, harmonized standard for sex and SOGI data collection will require collaboration among diverse stakeholders to ensure cultural acceptability and widespread support.

### Solution Strategies

- A) Establish an international body of stakeholders to develop policies that articulate minimal data elements that should be collected across different data sources, as well as requirements and incentives for their inclusion. These stakeholders should include multilaterals (including the WHO, which sets reporting standards), regulators, foundations, funders, governments, and health coordinating bodies.
  - a. Minimum core data elements that should be collected and reported across different types of data collection include sex, gender, age, life stage (e.g. pre-menarche, reproductive, peri-menopause, post-menopause) race, ethnicity, income, country, time use, history of trauma and gender-based violence, and disability.
  - b. These minimum elements should be complemented with qualitative data on ageism, gender discrimination, influences of racism/colonialism, and lived experiences, including economic, political, social, and geographical.
  - c. Guidance tools should be developed in collaboration with relevant stakeholders for core minimum data collection—and complementary qualitative data collection—highlighting the purpose, definition, and reporting channels of these data across various types of data sources.
- B) Create study networks for research and data harmonization to ensure adequate and appropriate data collection for women across the life course—from pre-puberty through post-menopause—and across social and structural determinants of health.
- C) Create an international data and modeling community of practice across sex, gender, and social determinants of health stakeholders to establish recommendations for standardized methods of collecting, reporting, analyzing, and disseminating health data in a sex- and gender-specific way; to ensure implementation; and to engage in continuous learning.
  - a. The community of practice’s recommendations should target critical data collection gaps, e.g., standardizing electronic platforms of clinical data from low-resource settings and rural areas, improving the representation of populations historically lacking access to health services and facilities, etc.
  - b. The community of practice’s recommendations may include developing a checklist to assess for gender intentionality of data collection activities, including and beyond the minimal data elements described above.

### Cross-Reference:

To see more on **data standardization and harmonization**, see: Regulatory and Science Policy 3.4 and Social and Structural Determinants of Health 5.3.B.

### Key Stakeholders:





**Opportunity 1.2** | Support capacity to collect, harmonize, utilize, and report granular data (qualitative and quantitative) for health elements and determinants to inform prioritization, develop models, and innovate products for women’s health across the life course.

To reap the potential benefits of more granular data to improve decision-making on women’s health innovation, technical capacity is needed for appropriate data collection, extraction, analysis, and reporting. As comprehensive sex- and gender-intentional data collection is not consistently practiced across different regions and institutions, this shift necessitates training for researchers, local health workers, community leaders, and women.

### Solution Strategies

- A) Emphasize and request plans for training researchers, health workers, community leaders, women, and others involved in data collection on how to collect minimum data elements—including but not limited to sex and gender—that will advance sex- and gender-sensitive analysis. Stakeholders, including funders and regulators, should support these plans.
- B) Monitor implementation and incentivize such training by establishing requirements from research accreditation bodies, honor rolls, rewards, etc.

### Cross-Reference:

To see more on **training on sex- and gender-informed data collection and utilization**, see: Data and Modeling 1.5, Research Design and Methodologies 2.1.C, Regulatory and Science Policy 3.1.B, Innovation Introduction 4.2.C, and Training and Careers 6.1

### Key Stakeholders:





**Opportunity 1.3** | Update and expand burden of disease metrics to better account for sex and gender-related conditions, long-term sequelae, and socio-cultural gender biases (including input data gaps, disability weighting, and duration assumptions).

The disability-adjusted life year (DALY) is one of the key metrics used to prioritize products and assess impact in global health. DALYs are a summary measure of population health that accounts for mortality and non-fatal health consequences by summing years of life lost due to premature mortality (YLLs) and years lived with disability (YLDs). The quantity and quality of data available to estimate mortality are generally better than for measuring morbidity. Morbidity data are also subject to differences in care-seeking behavior, access to quality care, and social restrictions and stigma that affect participation in surveys—all of which may be exacerbated by disparities across gender, age, race, ethnicity, and socio-economic status. The data inputs and modeling framework for the widely-used DALY measure should be strengthened to more comprehensively reflect the full impact of health conditions affecting women.

Furthermore, the DALY estimation framework exclusively measures health loss and does not account for downstream effects that matter to women, such as impacts on educational attainment or career advancement, social standing, agency, well-being, and relationships. This gap highlights the need to identify—or develop—and disseminate complementary metrics that move beyond health loss and account for a broader concept of well-being.

These updated and expanded metrics—which should reflect the input of diverse stakeholders—will illuminate the actual burden of conditions affecting women. The metrics will also help to demonstrate the true market size for new products to prevent and treat conditions affecting women and would allow for funders to appropriately direct R&D resources and funding toward conditions with the greatest burden.

### Solution Strategies

- A) Improve data inputs for estimating YLDs beyond only incidence and prevalence: measure the nature, severity, timing, and duration of non-fatal sequelae of diseases and injuries, and ensure that disability weight surveys quantify all health states relevant to women's health (for example, disability weights for pelvic pain exist but not for vaginal bleeding).
  - a. Philanthropy and other financial avenues can support the work of academics surveying women (quantitatively and qualitatively), leveraging methods co-created and co-identified by women, and engaging policymakers as consumers of information.
- B) Identify measures that complement DALYs with other biopsychosocial factors and their interactions (such as relationship status, emotional status, social stigma, integration, educational attainment, earning power, agency) and disseminate their use when discussing the full impact of a disease or condition. Develop novel measures to fill this role if satisfactory measures are not identified.
- C) Capture and establish relationship of early life events to later life sequelae to guide the development of upstream interventions.

### Cross-Reference:

To see more on **burden of disease assessment**, see: Communicable Diseases 7.1 and Female-Specific Conditions 9.10.A.

### Key Stakeholders:





**Opportunity 1.4** | Identify and fill data gaps related to calculating return on investment (ROI) in women's health innovation, including economic models and ROI for disease-specific areas.

Business cases are typically necessary to define a potential return on investment. Calculation, measurement, and maximization of ROI in women's health—including economic models and ROI for specific disease areas—face limitations due to insufficient data and operational definitions. Historically, women's health has been narrowly focused on reproductive and maternal health. As the definition expands to include conditions that impact women uniquely, differently, or disproportionately compared to men, gaps remain in understanding of ROI. ROI is more often measured for curative interventions; while preventive interventions (such as prevention of physical, sexual, or psychological abuse) can yield substantial returns, they require better estimation. Robust economic models are needed to link women's treatment preferences in different settings, the costs and quality of public health and healthcare interventions, and impacts on robust, sex-and-gender-informed measures of disability and well-being (as addressed in Opportunity 1.3). Identifying and filling these data gaps will strengthen the case for investment in women's health innovations.

### Solution Strategies

- A) Identify data gaps related to women's and girls' preferences, agency, spending, and decision-making across conditions affecting them; social and structural determinants of health; access and barriers to interventions (both public health and healthcare) over the life course; and the efficacy of those interventions. Academics, non-governmental organizations (NGOs), and health agencies can lead this work through a literature review of existing studies.
- B) Conduct longitudinal mixed-methods studies and modeling to generate and synthesize evidence on financial and opportunity costs of health events and experiences, including evidence on the links between health and economic outcomes. Data and models—collection and creation of which should be led by academics, NGOs, and regional partners—should take a life course perspective and quantify differences in preferences for services by gender in estimating the impact and efficiency of programs and products.
- C) Invest in research on effective implementation of interventions (e.g., screening) that generate better returns for women and girls—including their cost-effectiveness, coverage, and quality.

### Cross-Reference:

To see more on **making the investment case for women's health innovation**, see Innovation Introduction 4.1.D and 4.4.C.

### Key Stakeholders:





**Opportunity 1.5** | Develop approaches for incorporating qualitative information and proxy indicators into models, including unstructured narrative data.

Although most research is based in the derivation and synthesis of quantitative information, more data may be needed to capture the complexity or diversity of the phenomena under study. Qualitative data can provide context and meaning to quantitative data by explaining the reasons, motivations, or mechanisms behind the quantitative findings, while also potentially reducing bias by capturing different perspectives, experiences, or values. Increasing the use of qualitative data across women's health R&D could improve study reliability and serve as a time- and resource-saving strategy by identifying highly valued variables, enabling flexibility to respond to emerging themes, and validating, complementing, or triangulating the quantitative results.

### Solution Strategies

- A) Bring together an international committee of institutions, governments, funding companies, academic organizations, high-tech and statistical modelers, and social scientists to develop an action plan for developing methods and approaches to leverage qualitative data. This action plan may include the development of use cases; best practice guidelines; templates with clear recommendations, trainings, and short courses to educate and equip stakeholders; and other materials that communities can use to advance and implement qualitative methods, including in models. This process should be inclusive, allowing for different scenarios across communities.
- B) Develop artificial intelligence (AI) tools to incorporate qualitative information into models of diseases, including techniques able to capture linguistics and non-linguistics cues and sources from representative groups of women that can inform and refine unmet needs for designing and developing innovative products and interventions. The development of bioethics standards must accompany the use of these AI tools.

### Cross-Reference:

To see more on **leveraging artificial intelligence and machine learning (AI/ML) to improve women's health**, see: Research Design and Methodologies 2.3, Communicable Diseases 7.1.B, Non-Communicable and Chronic Conditions 8.1.B, 8.2.B, 8.3.B, and 8.5.C, and Female-Specific Conditions 9.3.D and 9.6.B.

### Key Stakeholders:



## 2 | Research Design and Methodology



Despite evidence that sex and gender influence health outcomes, researchers have not consistently considered these influences in the design, data collection, outcome measurement, analysis, and reporting of research, leading to an incomplete understanding of how sex and gender influence health. Preclinical research informs clinical trial design, which in turn informs individuals' treatment. Therefore, female representation in all research stages is crucial to ensure an understanding of potential sex influences on health processes and outcomes. However, both basic research (e.g., animal models) and clinical research use males as the default. For example, a review of dermatological studies found that 60 percent of papers did not disclose the sex of studied cells or animals, and of papers that disclosed sex, 70 percent of the studied cells were male (Kong et al., 2016). In a review of phase I clinical trials for frequently prescribed drugs, only 22 percent of participants were female (Labots et al., 2018). While female participation in phase III trials has improved in recent years due to policy and regulatory changes (Avery & Clark, 2016), a review of over 56,000 articles and clinical trial records found that females were substantially underrepresented relative to the prevalence of key health conditions, particularly in studies of HIV/AIDS, chronic kidney diseases, and cardiovascular diseases (Feldman et al., 2019). Female inclusion alone is insufficient: researchers should also meaningfully analyze outcomes by sex and gender, but such analyses remain limited (Avery & Clark, 2016). Moreover, sub-groups such as pregnant and lactating women are often excluded from trials, and gender minorities are often made invisible by research that adopts a gender binary or uses biological sex as a proxy for gender (Glick et al., 2018). As a result, the scientific community's understanding of the benefits and risks of therapeutic options for these populations is limited.

In addition to increasing female inclusion in study design, researchers should leverage existing and novel methodologies to understand the underpinnings of conditions and diseases in women more comprehensively. For example, novel technologies—from translational models like “organs on a chip” to machine learning and advanced data analytics—offer tremendous potential to deliver personalized care for women across the life course. Further developing these methodologies—and ensuring their ethical and unbiased application—can enhance risk identification, prevention measures, and treatment options fit for diverse populations of women.

Integrating a sex and gender lens across all stages of research design (the structure of studies) and methodologies (the processes and tools used to collect, analyze, and apply data) will enhance the rigor and generalizability of research findings for women while filling critical knowledge gaps and enabling innovation tailored to women's unique health needs. Sex- and gender-intentional design and methods are feasible and precedented. Their adoption will reduce disparities in diagnoses, treatment plans, and outcomes for women.

### Key Stakeholders

-  Communities and Community Organizations
-  Researchers and Academia
-  Health Care Workers and Systems
-  Public and Philanthropic R&D Funders
-  Private Sector
-  Payors and Insurers
-  Regulatory and Standard-Setting Agencies



**Opportunity 2.1** | Advance sex- and gender-intentional research design and analysis during all stages of research (including preclinical and clinical) to generate endpoints, outcome measures, and evidence relevant for women across the life course, and to evaluate heterogeneity of treatment effects by sex and gender.

Despite evidence that sex and gender matter to health outcomes, researchers insufficiently incorporate sex and gender variables across research stages. Inconsistent use of sex and gender variables in data and analysis plans leads to statistically weak or non-existent methodologies to assess inter-group differences. Furthermore, methods to ensure representative and intersectional inclusion of different genders and sexes are often absent. These trends persist across cellular research, animal models, and medical and health research, including clinical trials (Kong et al., 2016; Feldman et al., 2019).

### Solution Strategies

- A) Support academic and industry bodies to develop sex as a biological variable (SABV) and gender analysis policies at the national level, leveraging regional regulatory bodies and ethics review committees to establish policies consistent across regions and countries.
- B) Advocate for research funders to establish SABV and gender analysis requirements for the research they fund—drawing on best practice examples that already exist—and to develop incentives for researchers to incorporate a sex- and gender-lens in their research (e.g., grants to offset the additional costs required to design studies that adequately capture sex differences, which may involve more time and resources). In tandem, advocate for journals and publishers to ensure stronger uptake of standardized SABV reviewing and reporting policies for manuscripts and published research, such as the Sex and Gender Equity in Research (SAGER) guidelines (Heidari et al., 2016) for scholarly literature and the Animal Research: Reporting of In Vivo Experiments (ARRIVE) guidelines for animal research (Percie du Sert et al., 2020).
- C) Develop cross-functional teams (among academic research groups, pharmaceutical companies, etc.) that implement a community-engaged, adaptive design approach. This involves engaging women and relevant research stakeholders from high-income countries (HICs) and low- and middle-income countries (LMICs) in consultations, collaboration, and, ideally, shared leadership roles to understand key needs within specific disease areas and co-design solutions to meet those needs. An adaptive design approach would allow both soliciting women's voices and needs while also following emerging insights from data, including big data.
- D) Identify incentives for and pathways to cultivate champions of sex- and gender-intentional research design and analysis across sectors, especially in the pharmaceutical industry.

### Cross-Reference:

To see more on **training on sex- and gender-informed data collection and utilization**, see: Data and Modeling 1.2 and 1.5, Regulatory and Science Policy 3.1.B, Innovation Introduction 4.2.C, and Training and Careers 6.1.

To see more on **research funding and publishing requirements**, see: Regulatory and Science Policy 3.1.

### Key Stakeholders:





**Opportunity 2.2** | Promote knowledge- and resource-sharing on the preclinical and clinical research landscape in LMICs and other under-resourced settings to strengthen research activities and promote collaborations that advance women's health innovations.

Infrastructure and capacity to conduct preclinical and clinical studies vary among LMICs, and several challenges impede their development. Technical support for using and maintaining advanced equipment may be insufficient, or facilities may lack the necessary equipment to conduct studies. Procuring reagents or kits can be unaffordable, especially with fluctuating exchange rates. As a result, LMICs often rely on shipping samples to HICs where further research and analysis is conducted. Basic research can be disconnected from clinical research; as a result, clinical trials remain disproportionately concentrated in HICs (Drain et al., 2018). Standardizing and certifying laboratories that can participate in preclinical and clinical studies will help democratize opportunities and globalize medical knowledge of different populations.

### Solution Strategies

- A) Develop clinical trial methods that increase the representation of traditionally underrepresented demographics of women—including remote trial participation options, satellite sites, and wearables—and support the development of infrastructure and capacities to enable these methods and improve the clinical trial landscape (e.g., around challenges like limited insurance coverage in LMICs for clinical trials).
- B) Establish regional hubs or centers of excellence to supply LMICs with the biomedical research supplies needed to conduct research and coordinate resource-sharing, technical support, validation, and intellectual property. Amplify these hubs by engaging local non-research community resources where available to proactively support women's participation in research.
- C) Establish a platform to negotiate affordable prices in LMICs for research supplies, similar to the African Medical Supplies Platform that was launched to leverage Africa's bulk purchasing power to secure medical supplies during COVID-19.
- D) Attract large biotech companies to establish presence in LMICs and nurture local biotech companies in LMICs to improve their capacities.

### Key Stakeholders:





**Opportunity 2.3** | Strengthen the use of computational and bioinformatics modeling (reducing the use of animal models) and machine and deep learning approaches to better understand the biological basis of diseases affecting women and inform product development, risk identification, and treatment approaches—including by leveraging existing datasets and unbiased common data elements.

Machine learning, deep learning, and advanced data analytics are emerging tools that offer opportunities for novel and exciting applications of data. Advances in computing power enable researchers to improve data mining capacity and more efficiently combine and integrate information to generate new hypotheses. These approaches can enable a more complete understanding of complex biological pathways and diseases; this knowledge has the potential to accelerate innovation of better treatments and prevention strategies. However, researchers should take steps to mitigate potential biases in existing data sets—including biases due to race, gender, and socio-economic status. An assessment of the adequacy of existing data can determine if more comprehensive prospective data with reduced biases is needed. Investing in emerging data analytics methods can enable shared learning and more efficient research on key drivers of women’s health conditions.

### Solution Strategies

- A) Strengthen existing multi-country databases (including genomic and other omics<sup>7</sup> data, and physical parameters) that can be leveraged via AI/ML methods to understand genetic linkages with women's health conditions—including collaborating with or expanding the US National Human Genome Research Institute, UK Biobank, Human Heredity and Health Africa (H3Africa), and others, and establishing new efforts as needed.
- B) Invest in a few illustrative use cases of developing computational models for women's health conditions—including with collaborators and data from underserved settings—to generate actionable learnings and replicable practices for the field.
- C) Strengthen the infrastructure and capacities required to undertake machine and deep learning applications in LMICs, including through mechanisms like grant opportunities, open-source software and resources, online training resources accessible to LMIC scientists, and more.
- D) Strengthen and promote consistent implementation of data coding and quality standards—including the WHO’s Family of International Classifications, such as the International Classification of Diseases—to facilitate machine learning applications. Uniform standards across clinical records, surveillance data, research studies, and other data sources will enable vast amounts of data to be aggregated across multiple databases and platforms. Potential biases and inaccuracies in data sets can be identified by implementing quality standards, including checks for accuracy, completeness, validity, consistency, uniqueness, timeliness, fitness for purpose, and identification of miscoded data, missing data, and outliers. Such standards should be accessible across geographic regions and translated to multiple languages.

### Cross-Reference:

To see more on **leveraging artificial intelligence and machine learning (AI/ML) to improve women’s health**, see Data and Modeling 1.5.B, Communicable Diseases 7.1.B, Non-Communicable and Chronic Conditions 8.1.B, 8.2.B, 8.3.B, and 8.5.C, and Female-Specific Conditions 9.3.D and 9.6.B.

### Key Stakeholders:



<sup>7</sup> Omics is an emerging multi-disciplinary field encompassing genomics, epigenomics, transcriptomics, proteomics, metabolomics, etc. Large omics datasets and high-throughput methodologies are allowing for accelerated health and disease discovery.



**Opportunity 2.4** | Support in-vitro translational model development—such as organoids and organ-on-a-chip systems—to ensure more extensive clinical and translational characterization of diseases, conditions, and differences by sex and gender.

Within the past decade, micro-physiological systems such as organ-on-a-chip and organoid technologies have emerged as promising alternatives to animal models for biopharmaceutical applications for women’s health. These technologies allow researchers to engineer living tissues and organ units within a controlled environment to mimic the complex biological activity of human organs better than conventional cell culture models while avoiding some of the limitations of animal models. For example, work is underway for organ chips and organoids models for the vagina, cervix, fallopian tube, placenta, and endometrium (Young & Huh, 2021). Researchers are also investigating the use of organ-on-a-chip systems for human pregnancy, which is difficult to study in vivo. The potential benefits are enormous, as reasonable ethical restrictions limit research that would affect mother and fetus and few animal models can capture unique aspects of human pregnancy. These systems can allow for multiple cell types in three-dimensional culture using artificial extracellular matrix materials based on hydrogels to investigate cellular crosstalk including modeling maternal-fetal interactions. While these models are still in their infancy, they hold great potential to advance discovery and development for key women’s health applications. Given recent regulatory pathway openings such as the Food and Drug Administration (FDA) Modernization Act 2.0 (2022)—which newly allows for micro-physiological systems and computational models as alternatives to animal testing before clinical trials for drug development in the US—advancements in these areas are likely to accelerate in the coming years.

### Solution Strategies

- A) Establish a bank of primary cells from diverse populations worldwide to inform more representative in-vitro translational models.
- B) Support public-private sector partnerships to overcome commercial hurdles for advancing and scaling in-vitro translational and computational modeling. Especially with the passing of the FDA Modernization Act 2.0 in the US, many small companies and startups will be active in this space working on commercial solutions. A critical first step will be ensuring quality control early in device development prior to scaling.
- C) Prioritize the development of affordable micro-physiological systems for use in under-resourced settings, including in LMICs. While paper-based point-of-care devices are available in under-resourced settings, extending the use of micro-physiological tools for research studies using simpler, more affordable approaches (including open, non-proprietary technologies) will extend their benefits to even broader populations.
- D) Support technology transfer and training for these technologies to be made more widely available and adapted across geographic regions, including through educational and technology transfer research grants, development of open-source technologies, etc.
- E) Focus on solutions effectively simulating the placental barrier. A significant challenge earlier in the COVID-19 vaccine rollout was that the vaccines were not tested on pregnant women, but in-vitro systems hold promise to enable drug testing across the maternal-fetal interface.

### Cross-Reference:

To see more on **data sharing and biobanks**, see Innovation Introduction 4.1.B, Communicable Diseases 7.2.A, Non-Communicable and Chronic Conditions 8.1.A, and Female-Specific Conditions 9.1.A and 9.5.

### Key Stakeholders:



# 3 | Regulatory and Science Policy



Regulatory and science policies profoundly shape (1) the types of health research pursued and methods used, (2) scientific understanding of the biological mechanisms driving how people experience health conditions across their lives, and (3) the types of health interventions that enter the R&D pipeline, proceed to market authorization, and ultimately reach populations. Policy levers can be utilized across the health research and product R&D ecosystem to promote sex and gender equity in health, address significant gaps in scientific understanding of health conditions affecting women, and introduce interventions that address women’s health needs. These levers include the policies that shape research agendas, funding, product development, research conduct, reporting of findings, and mechanisms for market authorization.

Efforts to include sex and gender considerations in regulatory frameworks are variable and fragmented. For example, the WHO’s global benchmarking tool for national regulatory system standards does not include considerations of sex and gender (Ravindran et al., 2020; WHO, 2021b). Across countries, regulatory decision-making on products used by women varies and may be underenforced, which limits innovators’ ability to design solutions that adequately serve diverse populations. Although sex- and gender-informed guidance exists—such as requirements for industry to submit sex-disaggregated data—implementation and accountability are often lacking. These challenges add to the complexity of bringing a product from concept to market, with regulatory processes that vary considerably across geographic regions and may be unfamiliar to academic researchers and entrepreneurs. In some settings, regulatory requirements lack clarity, consistency, and a benefit-risk approach, which may inhibit innovation—especially from under-resourced entrepreneurs—that addresses differences by sex and gender. In other settings, regulatory and surveillance capabilities need significant strengthening to ensure outcomes by sex and gender are captured and reported.

Science policy is also vital to ensure that women’s health needs are reflected in the products they will use. For example, since the NIH’s SABV Policy was introduced in 2015, approximately half of NIH-funded clinical study participants are women (Carmody et al., 2022). While this progress is noteworthy, women may still be underrepresented in specific disease areas relative to prevalence, and similar policy tools are lacking or underutilized in other geographic regions and sectors. Science policy should prioritize solutions that promote the health of women across the lifespan—including products that are designed for women as well as those used by all sexes and genders—and consider factors including improved health outcomes, causes of women’s morbidity and mortality, public health impact, feasibility, local needs, and novelty. Policy can also introduce incentives and disincentives that spur research relevant to women, such as intellectual property and patent law and other mechanisms to address unique or complex liability concerns or reputational risks associated with products under development.

By adopting the science policy and regulatory tools detailed below, women’s health stakeholders can ensure that sex- and gender-specific insights are identified throughout all stages of the R&D continuum, enabling more tailored innovation and more equitable access.

## Key Stakeholders

-  Communities and Community Organizations
-  Researchers and Academia
-  Health Care Workers and Systems
-  Public and Philanthropic R&D Funders
-  Private Sector
-  Payors and Insurers
-  Regulatory and Standard-Setting Agencies



**Opportunity 3.1** | Ensure the implementation of sex- and gender-intentional science policy frameworks that cover all aspects of the R&D continuum for medical products and healthcare innovations—including ethical, legal, and societal implications—with harmonization and collaboration mechanisms to accelerate their development.

Historically, biomedical researchers and innovators developing new technologies for human health have failed to consider sex- and gender-specific differences in physiology; for decades, many medical specialties defined the standard patient as a 70-kilogram adult male (Clayton, 2016). Studies that do enroll both sexes may not be designed to account for biological differences when collecting, analyzing, and publishing data (Rich-Edwards et al., 2018). This oversight may lead to missed findings, such as variations in responses to therapeutics between sexes and genders (Mauvais-Jarvis et al., 2021), and may overlook adverse effects in female patients, such as reproductive system toxicity or differences in response due to menopausal status. Challenges also surround the inclusion of trans women and non-binary individuals in clinical studies. Since historically the terms sex and gender have been used interchangeably in the medical field, researchers have limited understanding of how cisgender and transgender women respond to clinical interventions. Structural and societal barriers have also limited transgender women's participation in clinical trials (Alpert et al., 2022).

Regulators can play a critical role in overcoming these barriers to promote innovation in women's health by ensuring appropriate recognition of the burden of women's health (Ravindran et al., 2020). Greater recognition could lead to the alleviation of symptoms associated with conditions that are non-life threatening but impact women's quality of life and relationships, and result in improvements in therapeutic offerings and unmet medical needs. Further, harmonization and collaboration mechanisms must be developed between funders, researchers, publishers, regulatory agencies, and civil society to accelerate the development of innovations that improve women's health.

### Solution Strategies

- A) Require plans for appropriate sex- and gender-disaggregated data collection, analysis, and reporting as a condition for research funding from grant-making and funding agencies.
  - a. Any proposed research that does not include adequate sampling and analytical approaches to assess sex or gender differences must justify why this approach has not been adopted (e.g., in the case of conditions that only affect biological males).
  - b. Expectations should be clearly articulated to prospective grantees and researchers, and funding application review and decision processes should embed sufficient assessment of these approaches (with appropriate expertise in peer-review and review committee membership).
  - c. Progress reports and dissemination requirements should ensure that milestones are met (with any needed adjustments in protocols, sampling, and procedures introduced) and agreed-upon methods are implemented in the conduct of the research.
  - d. Funding requirements may appropriately vary for different kinds of research across basic biology, pre- and non-clinical studies, clinical trials, and other types of interventional or observational research.
- B) Ensure adequate representation and prospective consideration of sex differences within industry/pharma-led research by training principal investigators, clinical trialists and designers, and study leaders. Regulators should also ensure accountability; for example, if sex differences are not adequately and prospectively considered and analyzed, an application may not move forward unless otherwise scientifically justified.
- C) Require compliance with SAGER guidelines in publications and centralized databases, such as PubMed Central.
- D) Solicit patient input, particularly women's input regarding specific disease areas or conditions, through engaged research approaches that guide the design and protocols of trials to ensure appropriate and representative inclusion of relevant populations of women across ages and life stages. This includes attention to sampling strategies, indicators, and endpoints, as well as any accommodations that can facilitate the participation of study populations with gendered care responsibilities or other barriers to participation. In turn, patient groups should conduct education and awareness-building activities on the need to understand patient representation, sex differences and outcomes, the importance of inclusion in research, and how to participate.

E) Require evidence whenever possible and as appropriate that addresses sex- and gender-disaggregated considerations around the assessment of efficacy and cost-effectiveness (including WHO evidence considerations) when determining provision, coverage, and reimbursement by bodies and agencies that decide what interventions will be directly provided via public health services or covered or reimbursed under public insurance schemes. This may necessitate the development of new methodologies and approaches, as well as greater investment in evidence generation.

**Cross-Reference:**

To see more on **training on sex- and gender-informed data collection and utilization**, see: Data and Modeling 1.2 and 1.5, Research Design and Methodologies 2.1.C, Innovation Introduction 4.2.C, and Training and Careers 6.1.

**Key Stakeholders:**





**Opportunity 3.2** | Require legal and/or regulatory frameworks covering all aspects of the R&D continuum for medical products and healthcare innovations to systematically apply sex- and gender-intentional approaches and evidence at all stages of development to drive sex- and gender-specific interventions (e.g., ensuring clinical studies capture relevant differences in disease trajectory and outcomes across sex and gender, including novel endpoints).

Regulatory paradigms should be flexible to balancing pre- and post-market requirements as well as evidence for innovations that improve the health of women—including the use of real-world evidence. Women are diverse—with different hormonal statuses, sizes and weights, ages, and racial and ethnic backgrounds. Physical and identity differences across populations may produce variations in outcomes between men and women and within different sub-sets of women across their life course. Finding the right benefit-risk balance is critical in obtaining the correct data at the right time and to ensure understanding of the benefits and risks of products across various populations. The existing benefit-risk paradigm can be used to balance data collection for the groups most likely to benefit with reasonable risk and allow post-market data collection for other sub-groups at later time points. An unstudied or understudied sub-group should not require a higher regulatory burden.

Additionally, guidance for the appropriate inclusion in R&D of all women throughout the lifespan—including women of childbearing potential, pregnant women, lactating women, and menopausal and post-menopausal women—should be synthesized and adoption of such guidance should increase.

### Solution Strategies

- A) Set clear definitions for terminology used (e.g., SABV, women’s health).
- B) Establish a global independent working group of key stakeholders with relevant expertise in science, regulation, and related areas to create a template and decision tree that sponsors can submit to regulatory authorities at various time points throughout their R&D programs, and that outlines a step-by-step plan of action for how and when they will generate sex-specific information. The working group should develop appropriate guidance for each stage of development, and the template should be easily tailored to meet national regulatory needs while facilitating harmonization.
- C) Create an Independent Global Advisory Committee to advise on sex- and gender-based differences; this group could be the sponsor for the template mentioned above and would also be the go-to group to weigh in on decisions that affect sex and gender in R&D. This committee may be encouraged to interact with regulatory agencies to build shared expertise and could be used as a mechanism to share success cases across regions.
- D) Develop a global repository of robust examples of instruments, guidance documents, legal frameworks, case studies, etc., and conduct a landscaping of current regulatory pathways to see where it would be possible to layer on sex-based considerations. This landscaping can inform updates to guidance—or the creation of new guidance—that facilitate innovation relevant to women’s needs today rather than of decades ago, e.g., by informing advocacy efforts for legislative action to drive critical updates.

### Key Stakeholders:





**Opportunity 3.3** | Require reporting and timely updates of sex- and gender-specific outcomes in healthcare product labeling and package inserts.

It is important to highlight the sex and gender disparities in healthcare where women may face unique health challenges, experiences, and outcomes that differ from men. Historically, medical research and product development have predominantly focused on male diseases and outcomes, leading to a lack of understanding and appropriate interventions if female outcomes differ or in conditions that predominantly impact women (Clayton, 2016; Rich-Edwards et al., 2018).

Requiring the reporting of sex- and gender-specific outcomes in healthcare product labeling and package inserts can enhance transparency and provide essential information to healthcare professionals and patients. This data can enable clinicians to make informed treatment decisions, consider potential risks and benefits specific to women (including pregnant women), and improve overall health outcomes.

Post-market surveillance—the monitoring of drugs, medical devices, and other healthcare products after regulatory approval and introduction to the market—is an important activity that generates information required for label revisions. By implementing sex- and gender-disaggregated surveillance, regulators can identify potential safety concerns, adverse events, or disparities in treatment outcomes specific to women.

#### Solution Strategies

- A) Include a section on sex- and gender-specific evidence and outcomes in all product package inserts/labels at the time of product authorization, with relevant information about the nature of the evidence (human vs. animal), relevant details regarding potential differences in benefit-risk assessment, and dosing. Allow for appropriate exclusion of this section in cases where it would be inapplicable or misleading.
- B) Set regulation on an appropriate minimum standard and schedule for required updating of the label, depending on the state of sex- and gender-disaggregated evidence at the time of market authorization and the agreed-upon post-market data collection activities.
- C) Develop guidance and requirements for converting labels of previously authorized health interventions to comply with new labeling norms to assist with updates to product labels and package inserts for products already on the market.

#### Key Stakeholders:





**Opportunity 3.4** | Advance data harmonization and standardization efforts to drive sex-, gender-, and age-disaggregated post-market surveillance with common indicators specific to women’s health.

Although women may be included in substantial numbers in many development programs, outcomes by sex and age are often only analyzed as exploratory sub-groups that are not powered to detect sex differences and are rarely discussed or questioned (Rich-Edwards et al., 2018). Labeling and post-market updates sometimes provide the demographics of the population studied (e.g., percent females versus males). Still, outcomes are usually presented in aggregate rather than by sex. This practice hampers the ability to uncover potential differences by sex once the product is on the market. (e.g., by applying meta-analysis techniques).

### Solution Strategies

- A) Ensure regulations and guidance are routinely amended to incorporate updated best practices for sex-gender data harmonization and standardization. New evidence may include novel endpoints, new/updated technologies, and data uncovering differences between males and females or at different female life stages. For example, regulations can be updated for contraception to provide both hormonal and non-hormonal guidance—as non-hormonal contraception options are needed for women who cannot or will not use hormonal products due to contraindications, medical history, side effects, or other considerations.

### Cross-Reference:

To see more on **data standardization and harmonization**, see: Data and Modeling 1.1 and Social and Structural Determinants of Health 5.3.B.

### Key Stakeholders:





**Opportunity 3.5** | Assess and implement regulatory and policy incentives that will promote investment and address barriers and disincentives, to accelerate the pace and volume of development, de-risk R&D in women's health, ease market authorization, and improve access to innovations that improve women's health.

Challenges arise from the higher costs and longer timelines that may be associated with larger sample sizes required to conduct sex- and gender-specific analyses. These challenges may also slow the approval process for therapeutically novel drugs, impeding progress to improve women's inclusion and sex- and gender-specific analyses. Incentives can address this by motivating and rewarding researchers and developers for adopting a new R&D paradigm that prospectively incorporates sex- and gender-specific considerations in their innovation programs.

### Solution Strategies

- A) Develop policies to prioritize and incentivize innovations that improve the health of women, such as faster approval, tax incentives, funding from the government matched by private investment, zero application fees for programs that appropriately address sex- and gender-based differences, early access to medicines for patients, competitions with prizes, women's health innovation hubs that require women and underserved patients' involvement in determining fund allocation, and more. Developing a decision tree (see 3.2.B) on what specific actions are suitable for incentives will provide clarity to all involved stakeholders.
- B) Establish a pooled insurance scheme to de-risk innovation, e.g., modeling after the vaccine injury compensation fund.

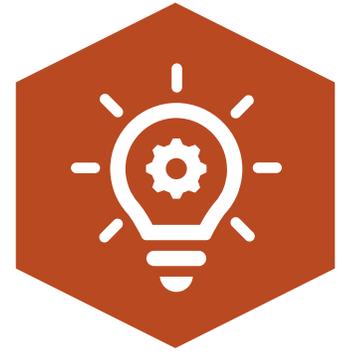
### Cross-Reference:

To see more on **market incentives for women's health solutions**, see: Innovation Introduction 4.3, 4.4.B, and 4.5.

### Key Stakeholders:



# 4 | Innovation Introduction



Introducing new health solutions to new markets successfully requires designing both for users’ needs—including their access to care and willingness and ability to pay—and for delivery systems, including regulatory pathways and payment models. However, several challenges hinder innovators’ ability to design for successful introduction of women’s health solutions, including insufficient funding during critical product development stages, limited support for entrepreneurs pursuing women’s health innovation, and lack of awareness—among both entrepreneurs and investors—of the potential returns from investing in women’s health solutions.

For example, conditions that disproportionately affect women have historically received significantly less research funding, which limits the availability of early-stage science as a foundation for tailored health innovations. Even after product development, entrepreneurs often face funding constraints when trying to scale their manufacturing capacities, resulting in a “valley of death” for promising innovations, especially those intended for under-resourced populations across the globe. Moreover, women-founded companies attract less funding than companies founded by men. In 2022, women received only 2 percent of the capital invested in venture-backed companies in the US, and in Europe, this figure was a mere 0.9 percent (PitchBook, 2023b; PitchBook, 2023a).

Underlying these challenges are insufficient awareness and education among entrepreneurs and investors regarding the available scientific evidence creating opportunities for high-return investments in sex- and gender-tailored innovations. Conducting research and developing solutions tailored to women’s needs across the life course can help mitigate risks associated with launching a new product. For example, better market insight and early identification of potential adverse reactions among key populations can inform strategies for market introduction of a new intervention.

The women’s health R&D space presents a massive opportunity to transform scientific evidence into commercial or public offerings and for strategic investments to strengthen innovation ecosystems to yield substantial returns—both financially and for society. Targeted support for entrepreneurs to introduce products and services that improve women’s health—particularly in under-resourced settings—will help realize this potential. Similarly, innovative funding mechanisms and collaborations between academia, industry, and the public sector can improve the quality and sustainability of the women’s health market. New approaches to shaping health markets will correct current health access inequities, ease supplier challenges, draw attention to new markets, and facilitate scalable, demand-driven innovations.

While historically underserved, the women’s health market has robust consumer demand and increasing funder interest. Women’s health is emerging as one of the fastest-growing fields of innovation; the women’s health industry is projected to be worth over US\$1 trillion by 2027 (Barreto et al., 2021). Through the opportunities laid out below, the next wave of innovation can be accelerated to address this overlooked market and improve the health of diverse populations of women worldwide.

## Key Stakeholders

-  Communities and Community Organizations
-  Researchers and Academia
-  Health Care Workers and Systems
-  Public and Philanthropic R&D Funders
-  Private Sector
-  Payors and Insurers
-  Regulatory and Standard-Setting Agencies



**Opportunity 4.1** | Create robust and ongoing data repositories to catalyze women’s health product development and accelerate the successful introduction of these products into new markets.

Accurate and representative baseline data on women’s health conditions, including data disaggregated by sex and gender, are needed to develop products that best meet women’s health needs. For example, innovators must be able to diagnose current market shortcomings—including affordability, availability, quality, suitable design, and demand—when designing scalable innovations that provide clinical, economic, and end-user value. This requires sufficient data on disease burden, sex and gender influences on health, and the social determinants of health for different populations of women. Collaborative platforms are needed to fill these data blind spots and improve the availability and collection of data on user needs, product requirements, and effective delivery approaches, which will catalyze more targeted product development and successful introduction. This data will also help demonstrate to governments, investors, and other stakeholders that women’s healthcare is not a niche market and that the business case for women’s health innovation is strong.

### Solution Strategies

- A) Create a women’s health medical reporting platform for healthcare professionals worldwide to know about the newest best practices, symptoms, or side effects they notice in women populations.
- B) Create a global data repository for women’s medical data, including molecular (biobanks), clinical (hospital real-world data), and electronic medical records.
- C) Develop systems and tools for collection, quantification, and publishing real-world data on the negative impact of diseases and conditions relevant to women’s health and the positive effects of existing and potential solutions to facilitate rapid women’s health innovation introduction based on real-world evidence.
- D) Share ongoing deep market research with focused dissemination efforts to promote widespread awareness of female health conditions, solutions, and the potential impact of new solutions. Variables should include market value, the health and economic burden of conditions affecting women, access gaps, and potential returns from scaling innovations, stratified by population. Demonstrating, for example, the return on investment for research and innovation for particular women’s health conditions and issues can generate policy support for funding earmarked for these conditions.

### Cross-Reference:

To see more on **making the investment case for women’s health innovation**, see: Data and Modeling 1.4 and Innovation Introduction 4.4.C.

To see more on **data sharing and biobanks**, see: Research Design and Methodologies 2.4.A, Communicable Diseases 7.2.A, Non-Communicable and Chronic Conditions 8.1.A, and Female-Specific Conditions 9.1.A and 9.5.

### Key Stakeholders:





**Opportunity 4.2** | Establish centralized innovation hubs specifically focused on the design and commercialization of solutions for women’s health and well-being.

To strengthen the innovation ecosystem for women’s health and introduce affordable, accessible solutions to women and their healthcare providers, resources must be made available to innovators earlier in the product development process. Innovation and commercialization hubs are not a new concept, but few focus specifically on accelerating solutions for women’s health—particularly for affordable solutions that meet women’s needs in LMICs. Drawing on successful practices developed for such hubs across other disciplines, a network of women’s health innovation hubs should be designed to:

- **Connect innovators with key stakeholders** to improve understanding of unmet women’s health needs—including patients and their advocacy groups, healthcare professionals, academic researchers, angel and institutional investors, donors, commercial partners, and policymakers.
- **Provide incubation, acceleration, mentorship, knowledge-sharing, and dedicated funding** to support product development, from product design to distribution, marketing, and scaling.
  - Startups in the program should receive early-stage funding, resources, and guidance along the product development continuum.
  - Immersive, entrepreneurial training programs should be developed that focus on aiding academic researchers and small companies developing affordable women’s health technologies in navigating the business world, including how to seek capital, plan for market introduction, and understand market forces and challenges in LMICs.
  - Industry-partnered research labs should be established to provide incubator space with mentoring and product development support for startups that develop women’s health products aligned with industry needs.
  - Similar paths should be created for government partnerships, with pathways for government grant funding.
- **Provide education** on sex- and gender-informed product design, including the use of participatory approaches.

This level of targeted support will better equip innovators to iterate toward scalable solutions that improve women’s health. Recognizing that expertise for women’s health innovation comes from all over the world, these supports—and learnings from their implementation—should be shared across regions to ensure that solutions developed anywhere have adequate support to reach the populations that stand to benefit.

### Solution Strategies

- A) Create a physical innovation hub that serves as a center of excellence for women’s health innovation. This center should include research labs, incubation and acceleration programming, events, and continued education for healthcare innovators. This first physical hub can be established within a 2–4-year timeline and serve as a pilot to inform the establishment of virtual programming and regional innovation hubs across both HICs and LMICs. It will inform the curation of best practices for other hubs to replicate success while tailoring for individual and local needs.
  - a. The innovation hub network should have an open-source curriculum that allows wide distribution and adaptation to different geographical and cultural settings and resource availability.
  - b. LMIC hubs will develop the community of entrepreneurs who want to create accessible solutions in LMIC markets, including strengthening networks of venture capitalists and angel investors, educating entrepreneurs on LMIC market entry and commercialization strategies, and building shared availability of information and data.
  - c. Hubs could adopt incubator, accelerator, and/or venture studio models to reduce the risk of startup failure by helping entrepreneurs find product-market fit and raise funds.
  - d. Existing initiatives that may offer lessons in the development of these hubs include the NIH Research Evaluation and Commercialization Hubs (REACH) program, Texas Medical Center Biodesign, Repro Grants, J-labs, CUBE3, Indie Bio, and the Innovation Corps (I-Corps).
- B) Within the innovation hub network, produce hackathons, venture studios, and challenges with specific problem statements to recruit innovators from around the world with promising solutions.

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- C) Develop sex- and gender-based product design educational content and curricula (drawing on progress from initiatives like UCSF Biodesign) for training within the hub network as well as for dissemination and adaptation throughout biodesign, engineering, and medical training programs.
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**Cross-Reference:**

To see more on **training on sex- and gender-informed data collection and utilization**, see: Data and Modeling 1.2 and 1.5, Research Design and Methodologies 2.1.C, Regulatory and Science Policy 3.1.B, and Training and Careers 6.1.

**Key Stakeholders:**



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**Opportunity 4.3 |** Improve pathways to market for women’s health solutions by accelerating commercialization, regulatory review, reimbursement, and access.

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The payment and reimbursement ecosystem for women’s health including private, commercial, and government payors is complex and varies across geographic regions. At the same time, innovative therapies and diagnostics often are introduced with high costs, sometimes limited information on long-term outcomes, and slow provider adoption, all of which reduce the incentive for payors to reimburse for or cover the payment of such innovations. This can lead to less engagement and overall success for critical emerging technologies. Changing the incentive structure for payors and other supply chain stakeholders will strengthen the development of and access to key innovations.

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**Solution Strategies**

- A) Incentivize payors and other stakeholders in the supply chain to improve the availability and visibility of women’s health innovations, e.g., by providing support for the adoption of pilot programs with data capture and analysis, facilitating faster adoption of Current Procedural Terminology Codes, and encouraging partnerships between companies to share risk and costs savings.
  - B) Review and eliminate structural barriers to product development and scaling, such as lack of billing codes and the need for a prescription.
  - C) Perform a global review of solutions for women’s health and create a transnational global access plan, including therapeutics and medical devices that are approved in one country and could seek approval in another nation that the solution owner is not prioritizing.
  - D) Strengthen regulatory incentives and policies that accelerate solutions that improve women's health through increased funding, faster regulatory approval, faster commercialization, and anticipated coverage.
- 

**Key Stakeholders:**





#### Opportunity 4.4 | Create new pathways to fund innovation.

Resource availability is often a limiting factor in developing and scaling innovation. Despite limited funding, innovators across multiple sectors are trying new approaches to overcome market challenges and deliver resources at high-leverage points in a product's development. For example, "fast grant" programs in the women's health space, such as Repro Grants, provide rapid funding decisions for short-term funding to incentivize scientists to focus on the basic research that drives innovation. Other sectors have pooled resources and capacities to foster collaboration between academia, industry, government, and the public with the objective of promoting economic development (e.g. the European Market for Climate Services). Such innovative pathways, including from less traditional bodies, hold promise to accelerate the development of women's health innovation.

To enhance innovation in basic, translational, and clinical research and to increase access and equity in healthcare globally, a new funding approach should center underserved women and girls throughout the R&D continuum, from discovery and development to validation and healthcare integration. By coordinating disparate efforts and addressing key bottlenecks in both HIC and LMIC settings, funders for women's health can establish an innovation pipeline that spans every stage in the cycle of innovation, yielding products tailored for use among specific underserved populations from the outset.

#### Solution Strategies

- A) Create a new multi-billion-dollar fund to invest in early-stage R&D innovations. This fund may address the "valley of death" (transforming it to the "valley of birth") by providing US\$20-50M grants to advance solutions through clinical validation. This fund would fill the gap following government funding for basic research and before venture capital is willing to invest due to high-risk research and validation. This fund should be financed and led through a partnership between philanthropists, mission-related investors, and governments, and it should encourage design thinking around usability at the point of need and cultural and social considerations.
- B) Create tax incentive programs (similar to those found in Maryland and the UK) for angels and venture capitalists to invest in women's health startups.
- C) Fund market and health economics and outcomes research that demonstrates the quantitative business case for investment in women's health innovation, e.g., through case studies.
- D) Create a "fund of funds" to diversify and increase the proportion of VC funding going to FemTech startups, particularly those led by women and underrepresented investors. The fund might invest in other funds with certain priorities, such as founder attendance of FemTech pitch events, diversity of partners of the funds, diversity of fund portfolio, priority for emerging funds, and more.

#### Cross-Reference:

To see more on **making the investment case for women's health innovation**, see Data and Modeling 1.4 and Innovation Introduction 4.1.D.

#### Key Stakeholders:





**Opportunity 4.5** | Support market-shaping approaches that enable suppliers to develop innovations accessible in LMIC settings by incentivizing payors and market entry and addressing demand and scale issues.

Market shaping represents a significant opportunity to advance women's health innovation by addressing market shortcomings and optimizing market dynamics. Common issues including fragmented services, lack of access, and funding constraints in many LMICs have continually hampered the introduction and scaling of women's health products that are routinely available in high-income settings. These products often fall into a "market trap," characterized by a cycle of low demand, limited competition, and supply shortages. This cycle often leads to higher prices for end buyers, well above the production and shipping costs.

Successful market-shaping initiatives in global health have focused on aligning stakeholders on the most critical objectives, allowing them to navigate competing priorities and make collective tradeoffs to build a stronger market with a sustainable set of market characteristics, in terms of affordability, availability, assured quality, appropriate design, and awareness by end users (USAID, 2014). Market-shaping initiatives can encourage suppliers to develop innovations that are accessible and scalable in LMIC settings by reducing transaction costs, increasing market information, and balancing the risks for suppliers and buyers. Successful strategies in other health product markets may hold lessons for further application to women's health, including:

- **Advance market commitments (AMC):** Funders agree to buy a product at established pricing identified through market analysis. This mechanism motivates suppliers without undue risk to donors or other buyers.
- **Volume guarantees:** Buyers explicitly agree to purchase a minimum quantity of an existing product, usually paired with a long-term supply contract that sets pricing for several years. A volume guarantee purchase agreement offsets some supplier risk and allows buyers to negotiate lower prices and better terms, as well as invest more confidently in demand generation with communities.
- **Coordinated ordering:** Negotiations are streamlined to lower transaction costs, enabling manufacturers to respond efficiently and reduce lead times.
- **Variant Optimization:** Guidelines or arrangements are designed to steer demand toward a specific, optimized set of products. This approach aggregates fragmented demand into larger orders, which encourages new suppliers to enter markets and allows existing suppliers to achieve economies of scale.

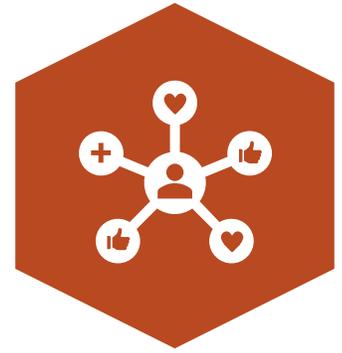
### Solution Strategies

- A) Develop a market-shaping strategy for scaling women's health solutions, particularly in LMICs. This involves identifying key market failures and barriers, defining market-shaping objectives, and developing a theory of change. It also includes identifying potential market-shaping interventions and developing a monitoring, evaluation, and learning plan. Lastly, it involves comprehensive analysis of current market shortcomings on aspects such as affordability, availability, guaranteed quality, suitable design, and awareness.
- B) Implementing market-shaping interventions. Based on this strategy, engage with relevant stakeholders, implement interventions, monitor progress, and adapt interventions as needed based on monitoring and evaluation findings and changing market conditions. Interventions might include:
  - a. Configuring LMIC access price arrangements within R&D investment planning from the outset for each new medicine, considering and exploring external R&D subsidies, AMCs, cross-subsidization approaches (with HIC pricing and revenues supporting LMIC pricing), early licensing to local pharmaceutical companies to reduce manufacturing and overhead costs, etc.
  - b. Aggregating planned orders and providing market transparency to stimulate supply and encourage cost-efficient production that supports reduced prices.
  - c. Incentivizing payors for innovations introduced to LMICs to scale and reach affordable volumes.
- C) Share learnings and best practices from different market-shaping interventions, and advocate for the adoption of successful strategies by other stakeholders.

### Key Stakeholders:



# 5 | Social and Structural Determinants



Social and structural determinants of health are the factors that shape the conditions in which people live. These include social, economic, and legal forces, systems, and policies that determine opportunities and access to high-quality jobs, education, housing, transportation, built environment, information and communication infrastructure, food, and healthcare; the social environment; and other conditions of daily life (National Institute of Nursing Research, 2013). Individual factors such as race, ethnicity, gender identity/expression, disability status, veteran status, and age also significantly influence health outcomes. These contextual factors significantly affect the health of all women. Global and national research agendas should address both the root causes of disparities and inequities and the impact of social and structural determinants on women’s health,<sup>8</sup> including community-level factors, such as cultural norms and practices. They should also consider the intersectional nature and compounding effects of these factors on women, such as the effect of gender roles and race together on health status. Upstream R&D practices can better integrate these factors in women’s health innovations and measure their broader impact on communities and societies.

Women’s health innovations focused solely on individual behavior change or treatments may not address the underlying social and structural factors contributing to poor health outcomes. Furthermore, ignoring the historical context and root causes of inequity may limit the impact potential of innovations and research. By addressing these factors, researchers can develop interventions that are more likely to improve women’s health outcomes in the long term and advance health equity among all women, including adolescent and post-menopausal women, women from low- and middle-income countries (LMICs), sexual and gender minority (SGM) populations, and women of color. New frameworks such as syndemic care models—which study diseases alongside socio-economic status, health system infrastructure, traditional and cultural contexts, and more—can help (Mendenhall et al., 2017). By prioritizing social and structural determinants in women’s health innovation, researchers and funders can more comprehensively understand the root causes of health disparities and inequities and develop effective interventions to address them. Researchers must also demonstrate to funders the wide-ranging benefits of new interventions—financial return on investment *and* impact—for women and for societies. This starts with measuring the social and structural factors that affect women.

The featured opportunities call for women’s health innovation to account for and address the social contexts that promote or worsen women’s health and rights. Innovators must actively consider social and structural factors to develop contextually relevant interventions for all women, including SGM populations and people assigned female at birth. The leading opportunities do not address all factors that impact women’s health; they are designed to be actionable, not just aspirational. Partners should support the introduction of more equitable, sustainable, and culturally appropriate women’s health solutions by addressing root causes of inequities and elevating diverse populations of women at all stages of the R&D continuum.

## Key Stakeholders

-  Communities and Community Organizations
-  Researchers and Academia
-  Health Care Workers and Systems
-  Public and Philanthropic R&D Funders
-  Private Sector
-  Payors and Insurers
-  Regulatory and Standard-Setting Agencies

<sup>8</sup> Women in the context of “women’s health” is defined in the Key Terms on page 14.



**Opportunity 5.1** | Ensure that women's needs and voices guide national and global research agendas through broad representation and reflection of different communities.

It is essential to recognize that women are not a monolithic group. Research agenda-setting exercises must ensure that all women's voices are heard and that the voices of women who have historically been disempowered (e.g., people of color, SGM populations, women with disabilities, and women who represent intersections of identities) are elevated. This may take many forms, from ensuring representation as decision-makers in crafting policies that impact women's health to sourcing and recognizing women's needs from sources beyond peer-reviewed medical journals.

#### Solution Strategies

- A) Advocate for public and private funders to identify and engage diverse populations in every stage of every project, from planning to dissemination, such as through requests for proposals requirements. Ensure that engaged populations have power to shape the projects in which they are involved.

#### Key Stakeholders:



**Opportunity 5.2** | Conduct a global review of social determinants of health interventions with an emphasis on those that focus on vulnerable populations of women; based on review, develop equitable standards for inclusion of social determinants of health considerations for women's health research.

Populations of women that are unhoused, from rural areas, immigrants/refugees, low-income, and face language/cultural differences, among other life circumstances and identities, face compounding factors that impact their health outcomes. Comprehensive interventions often incorporate social and structural components that improve health outcomes beyond medical treatment courses. Social determinants must be included as part of research studies on women's health. For example, when conducting research in cardiovascular disease, in addition to including the typical risks and co-morbidities such as obesity and hypertension, measurements of social determinants should also be included, such as socio-economic status, education and health literacy, stress and mental health, workload and time constraints, and access to healthcare.

#### Solution Strategies

- A) Curate and collect current reviews on SDOH interventions from various journals, associations, and researchers. Since relevant evidence may exist outside peer-reviewed journals, seek completed interventions and evaluations that were published without peer-review.
- B) Convene partners globally to discuss the curated data review, focusing on interventions that work or do not work to inform women's health outcomes, and develop equitable standards for inclusion of social determinants of health in women's health research.
- C) Develop a widely accessible data repository or library of resources on SDOH interventions and best practices. Identify and disseminate key findings beyond traditional methods (i.e., medical journals), such as through conferences, storytelling, art, and social media.

#### Key Stakeholders:





**Opportunity 5.3** | Research the intersectional impacts of gender roles, power dynamics, and economic agency (e.g., decision-making, unpaid work) on women's health.

Structural and systemic factors affect women's economic agency, such as discrimination and bias, education barriers, unpaid caretaking for children and older people, and social and cultural norms—all of which impact women's economic choices, access, opportunities, and health outcomes. For example, traditional gender roles may assign women primary responsibility for caregiving and household duties, leading to increased stress, mental health issues, and reduced access to healthcare services. Studies have shown that gender norms influence health-related behaviors, such as care-seeking and weight control, as well as exposure risk, such as to sexual or physical intimate partner violence (Weber et al., 2019). These gendered expectations can also limit women's autonomy and decision-making power regarding their own health. Understanding the prevailing gender roles in a specific context and having global perspectives and contextual variations on gender roles and women's health is crucial for examining their impact on women's health. Furthermore, research and interventions that address intersections of different systems of oppression are more likely to have the desired health impacts.

### Solution Strategies

- A) Develop standards and guidelines to identify, engage, and address gender norms through a consultative process.
  - a. Convene women from different countries and regions to inform the standards.
  - b. Conduct a comparative study across countries to compare and contrast the impact of gender roles, power dynamics, and economic agency on women's health across different countries and cultural contexts.
  - c. Conduct longitudinal studies that follow women across time and comparative studies across different regions to understand the long-term impacts of gender roles and economic agency and their intersections on women's health.
- B) Develop validated measures of economic agency, unpaid labor, and caregiving burden on women's health through a consultative process that includes diverse groups of women and men to ensure it is a transformative approach with broad buy-in.
- C) Examine the impacts of digitalization, technological advancements, and access to digital platforms on women's economic agency, empowerment, and health outcomes through research on digital platforms/technologies and their potential to enhance economic opportunities, empower women economically, and promote better health outcomes.

### Cross-Reference:

To see more on **data standardization and harmonization**, see: Data and Modeling 1.1 and Regulatory and Science Policy 3.4.

### Key Stakeholders:





**Opportunity 5.4** | Increase representation of women, sexual and gender minorities (SGM), and other marginalized populations in the review of research grants in women's health R&D.

Women who have been historically disempowered, stigmatized, disinvested, and understudied should be better represented in the review process, particularly when grant-making agencies and funders are considering research grants that impact these populations. Adequate understanding or appreciation of the health and social contexts of these groups will allow for appropriate consideration of their needs and an informed evaluation of relevant projects. This could have important implications for the volume and quality of supported R&D research on the health of women made vulnerable by their identity or social contexts. For example, reviewers of SGM health research projects should be able to acknowledge and include SGM perspectives and considerations and to speak adequately on these topics in review panels.

### Solution Strategies

- A) Increase representation on grant review panels by forming external auxiliary bodies (e.g., advisory boards) composed of individuals with specific lived experience and/or expertise (e.g., SGM populations). The auxiliary bodies, tailored to the relevant research needs, should be empowered to veto studies that are not culturally appropriate or congruent and rescue proposals that were not recommended for funding due to a lack of relevant expertise and experience among prior reviewers.
- B) Provide intentional and focused training for members of marginalized communities to be reviewers. Disseminate tailored or adapted training so private or community groups can use it.
- C) Develop standards for recruitment based on lived experience and/or research experience with marginalized communities (e.g., SGM populations or racial and ethnic minorities) and expertise in the field via expert panel sessions or change advisory boards.

### Key Stakeholders:





**Opportunity 5.5** | Research traditional and cultural practices that promote women's health outcomes and well-being.

In some cases, traditional cultural practices (e.g., female genital mutilation) compromise women's health and well-being (OHCHR, n.d.). However, other cultural practices (traditional food, social structures and support, doulas and birth attendants, massage) may promote women's health outcomes and well-being (Dennis et al., 2007). Women's health stakeholders should recognize negative connotations and biases around traditional, cultural, and spiritual practices. They should seek to understand, test, and elevate efficacious and safe practices rather than stigmatize them. By intentionally studying and incorporating traditional and cultural practices into medical standards of care, women can have an improved, contextually appropriate experience of care.

### Solution Strategies

- A) Identify current safe and efficacious traditional, cultural, and spiritual practices in LMIC populations by surveying women on their cultural, traditional, and spiritual practices that they believe help them in various aspects, including mental health, pregnancy outcomes, etc.
  - a. Consider geography-specific and context-specific (e.g., humanitarian crisis in conflict situations) studies. Develop inclusive research protocols with appropriate outcome measures to assess efficacy and safety.
- B) Identify historically safe and efficacious traditional, cultural, and spiritual practices in LMIC populations by surveying older women on no longer practiced/historical cultural, traditional, and spiritual practices that they believe helped them in various aspects, including mental health, pregnancy outcomes, etc.
  - a. Consider geography-specific and context-specific (e.g., humanitarian crisis in conflict situations) studies. Develop robust trial protocols with outcome measures to assess efficacy and safety.
- C) Achieve region/country-specific WHO endorsement of identified traditional, cultural, and spiritual practices and document endorsements in a central data repository of practices globally.

### Key Stakeholders:



# 6 | Training and Careers



Improving women’s health requires an understanding of sex and gender influences on health among those developing, implementing, and monitoring innovation—including researchers, programmers, regulators, and more. Although the scientific community increasingly recognizes that sex, gender, and their interactions affect health outcomes across most conditions, education programs across health and R&D professions have not systematically incorporated considerations of sex and gender. This deficit constrains researchers’ understanding of and ability to apply sex and gender considerations in patient care, research design, and product development (Kling et al., 2022; Thande et al., 2019). Integrating sex- and gender considerations into training and curricula at all stages of the learner continuum—and eventually into patient care—requires engaging sex and gender researchers, curriculum developers, leadership, faculty, and learners in developing materials through an inclusive approach.

Beyond strengthening education, support is needed to better enable women’s contributions to R&D. Women’s participation and leadership in R&D-related fields and across the broad biomedical workforce can enhance scientific discovery, and women have historically driven the design and development of innovations that address their health needs, yielding better interventions and improved outcomes (Plank-Bazinet et al., 2017). In fact, an analysis of over 1.5 million research papers found a strong positive correlation between women authors and the likelihood of a study including sex and gender analysis—highlighting that support for women’s career development and advancement within R&D fields enables more women-inclusive research and innovation (Nielsen et al., 2017). Another study found that all-female inventor teams are 35 percent more likely than all-male teams to patent women’s health products in the US, suggesting that the gender gap among inventors has resulted in thousands of missing female-focused interventions over the past few decades (Koning et al., 2021).

Societal and structural inequities have historically hindered women’s full participation and advancement in their careers. Women in science, technology, engineering, mathematics, and medicine (STEMM) face persistent challenges, including entrenched bias against women in leadership, sexism, sexual harassment, microaggressions, and unequal promotion rates. Despite a growing proportion of women researchers, women publish fewer papers, are less likely to collaborate internationally (Elsevier, 2017), are less likely to be credited with authorship or receive a patent (Ross et al., 2022), and hold fewer endowed faculty positions than men (Thorndyke et al., 2022). Gender pay inequities are unexplained by factors like seniority, career breaks, and part-time work (Connolly & Holdcroft, 2009). Such inequities stem from factors like organizational constraints and culture, the differential impacts of career and family demands, and bias in hiring, promotion, publishing, salary, and funding (Shannon et al., 2019; Moss-Racusin et al., 2012). For example, women scientists in East Africa face higher burdens of unpaid work and gender-based violence compared to their men colleagues, which affects their individual mental and physical health (Hafkin, 2016). Together, these inequities impact women’s well-being and lead to attrition, further reducing workforce diversity.

By supporting harmonized interventions across education, training, and policy, as set out in the opportunities below, stakeholders can strengthen the workforce required to advance innovation that improves women’s health.

## Key Stakeholders

-  Communities and Community Organizations
-  Researchers and Academia
-  Health Care Workers and Systems
-  Public and Philanthropic R&D Funders
-  Private Sector
-  Payors and Insurers
-  Regulatory and Standard-Setting Agencies



**Opportunity 6.1** | Create and implement resources for educating the current and future research and healthcare workforce on women’s health and sex and gender influences on health.

Awareness of the impacts of sex and gender on health and disease is limited, partially stemming from limited consideration of these factors in published research. The limited data to support a broader discussion of sex and gender influences on health has led to a lack of emphasis on these topics in health education. In addition, some clinicians and researchers mistakenly believe that sex and gender impacts only matter in reproductive health and assume that education in obstetrics and gynecology covers the topic sufficiently. Even when educators recognize the need to teach the broader impacts of sex and gender, they face challenges like limited faculty resources and development opportunities. Educators also raise concerns on insufficient time in curricula to add additional material on sex and gender, missing the opportunity to weave in sex and gender into existing curricula. Embedding this information into existing curricula can help learners across R&D and healthcare professions to understand that sex and gender are determinants of health across all areas, not separate considerations for certain conditions. Driving change in this area will require engaging faculty, learners, and leaders using both “bottom-up” and a “top-down” approaches (Templeton et al., 2019).

### Solution Strategies

- A) Create new—or amplify existing—educational content that addresses women’s health from a sex and gender perspective that can be adapted and tailored to all healthcare and R&D-related fields and evolve over time.
  - a. Create dynamic materials and instructor guides with links to online resources (videos, exercises, etc.) so that instructors can readily adapt and use the materials for their teaching purposes (including identifying where new faculty or courses are needed). Resources should be updated regularly and readily available to both faculty and learners.
  - b. Equip learners to interrogate the impacts of sex and gender on health topics, especially if these are not included in lectures or other learning materials. With the right resources, learners can help to effect needed change in curricula.
- B) Integrate sex- and gender-informed educational content into curricula and training across all healthcare and R&D-related fields and across the continuum of learners and develop metrics to track integration.
  - a. Develop a dissemination and uptake strategy for sex- and gender-informed educational content. Sensitize faculty and educators on the importance of understanding and teaching about sex and gender influences on health and disease, and ensure they are aware of and utilize the developed teaching materials.
  - b. Identify groups and associations engaged in sex and gender research and education or those involved with developing curricula to identify potential areas of collaboration.
- C) Identify existing research agendas to which women’s health research can be added and integrate new information into curricular materials.

### Cross-Reference:

To see more on **training on sex- and gender-informed data collection and utilization**, see: Data and Modeling 1.2 and 1.5, Research Design and Methodologies 2.1.C, Regulatory and Science Policy 3.1.B, and Innovation Introduction 4.2.C.

### Key Stakeholders:





**Opportunity 6.2** | Advocate among educational policymakers and institutional decision-makers for the integration of women’s health and sex and gender considerations into education and training.

Sex and gender are infrequently included in health education or training at any level due to a variety of factors, including a lack of awareness that sex and gender differences exist, time constraints in existing curricula, and insufficient teaching or faculty development resources. While students and faculty can advocate for the inclusion of this material, greater integration of sex and gender ultimately requires in the commitment and support of decision-makers within educational institutions to allocate the necessary resources and ensure its incorporation. In addition, the likelihood of integration of sex and gender differences into curricula increases when regional and national accrediting organizations require it. Healthcare professional schools are held to accreditation standards, changes to which have prompted the inclusion of other topics in curricula, but no accreditation standards currently address sex and gender differences.

### Solution Strategies

- A) Develop an advocacy toolkit for the integration of women’s health and sex and gender considerations into education and training.
  - a. The toolkit should be free, open source, hosted on a user-friendly source platform, translated into core languages, and ready to be adapted to different settings.
  - b. It should be developed by a multistakeholder group (including academia, accrediting bodies, government, community, etc.) and funded by a collaboration of the private and public sectors.
  - c. The stakeholder group should develop metrics to track the integration of this content in curricula, and these metrics should be included in the toolkit.
- B) Implement the toolkit in educational institutions for studying and teaching sex- and gender-based health through a multi-pronged dissemination strategy convening education and institutional policymakers and communities of practice.
  - a. The dissemination and training strategy should include incentives for adapting the tools to different professional sectors, including through accrediting bodies, to underscore its importance. The strategy should address government officials, academic/research institutions, civil society organizations, and NGOs (e.g., UN Women).
- C) Measure impact and ensure sustainability of the toolkit by developing an impact measurement strategy, developing incentives for continuing use of the toolkit, and providing guidance for endowments of faculty positions dedicated to sex and gender-based health and acknowledgment of educators who include sex and gender considerations in their teaching materials.

### Key Stakeholders:





**Opportunity 6.3** | Investigate barriers and enablers for the participation, progression, and leadership of women in R&D, entrepreneurship, and healthcare careers, and use successful practices to create reference tools.

Structural inequities and challenges have long constrained women’s career participation, progression, and leadership in healthcare and R&D fields and institutions. These inequities affect women worldwide, particularly those from underrepresented backgrounds and those in LMICs. Despite constituting 70 percent of the health workforce globally, delivering healthcare to 5 billion people, and contributing approximately US\$3 trillion to global health each year—half in the form of unpaid work—women occupy only 25 percent of health leadership roles (Women in Global Health, 2023). Developing and supporting more women in the R&D workforce (and engaging more men in sex- and gender-based research) are necessary to increase the production of research that is beneficial to women or women’s health.

### Solution Strategies

- A) Identify and analyze initiatives and policies that have successfully enabled women’s career participation, progression, and leadership, including what processes and solutions have worked well for them.
  - a. Case studies can be developed of successful networking, mentorship, and sponsorship initiatives, as well as other initiatives that support and encourage women’s participation and career growth at all stages of their careers. Initiatives may span different levels, including organizational, regional, national, and international.
  - b. Success can be measured with metrics like representation of women in leadership positions or satisfaction and well-being of women.
- B) Promote a baseline standard for re-entry and family leave policies across countries.
- C) Launch campaigns to challenge the traditional division of labor and change stereotypical gender roles that expect girls and women to take on household or family caring responsibilities while sacrificing their training and careers.

### Key Stakeholders:





**Opportunity 6.4** | Establish safeguards for women’s rights within countries globally to receive STEMM education and pursue STEMM, R&D, and entrepreneurship careers and leadership positions.

A substantial contributor to women’s inability to fully participate and advance through career fields of their choice is the lack—or poor implementation of— policies to promote gender equity in education and the workplace. Indeed, women enjoy only 77 percent of the legal rights that men do worldwide, and gender equity policies vary considerably across geographic regions (World Bank, 2023). For example, only 20 percent of countries require employers to provide paid breaks and facilities for breastfeeding or expressing milk, and more than half a billion working women worldwide do not have essential maternity protections safeguarded by national law (WHO, 2023f). Policy and regulation are critical instruments that countries can use to close gender gaps in education and industries so that the world does not miss out on the potential women have to offer.

#### Solution Strategies

- A) Develop benchmarking standards for laws and regulations that safeguard opportunities for women to pursue STEMM, R&D, and entrepreneurship careers and leadership positions. Develop an inventory with a scorecard of laws and regulations across individual countries to inform the benchmarking.
- B) Create new laws supportive of women’s career advancement that are aligned and enforced at national, state, local, institutional, and organizational levels (e.g., following the example of US Title IX), based on gaps identified in the inventorying of laws and regulations.
  - a. In complement, stakeholders should increase public awareness of existing laws, such as laws protecting women from workplace discrimination, determine accountability activities (e.g., enabling environments, safeguarding measures, platforms for reporting), and train individuals on related policies and issues to nurture leaders at all levels, including men, women and girls, gatekeepers, and influencers.
- C) Develop milestones and timelines for implementation (e.g., “By 2030, there should be X women in X leadership positions who receive the support needed to succeed and thrive in these positions.”).

**Key Stakeholders:**   

**Opportunity 6.5** | Enhance men’s allyship to activate opportunities for women to pursue STEMM, R&D, and entrepreneurship careers and leadership positions.

Men traditionally hold more power than women in R&D and healthcare settings. Therefore, they are critical partners in dismantling privilege, expanding career opportunities for women, and broadening these fields’ understanding of sex and gender influences. To foster equitable professional environments that empower women to thrive and make full use of their skills, men must understand the effects of implicit and explicit bias, recognize systemic privilege, and be well-versed in practical steps they can take to support women and other underrepresented groups.

#### Solution Strategies

- A) Increase the number of men allies by assessing currently available programs around the globe and adapting successful ones to new settings (e.g., The Ohio State University Advocates & Allies for Equity program)
  - a. Develop training and incentives to enable stakeholders at all levels to participate. Organizations can institutionalize required training and provide incentives (e.g., educational grants, prizes, etc.).
- B) Programs should be adapted to specific cultural contexts in different countries, engaging grassroots organizations for support.

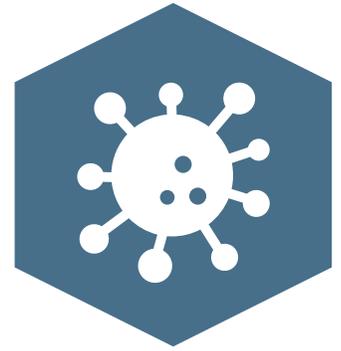
**Key Stakeholders:**   



# Issue-Specific Topics:

## Opportunities and Solution Strategies

# 7 | Communicable Diseases



Communicable diseases, also known as infectious diseases, are diseases caused by bacteria or viruses, transmitted between people either directly or indirectly through contact with animals or vectors. Biological factors and gender norms can increase women’s exposure risks and lead to disparities in disease outcomes and socio-economic consequences. Limited gender-specific interventions exist to address women’s unique needs; the intersection of pregnancy and infectious disease adds an additional layer of complexity. Sex-related differences in local and systemic immune responses to infections are particularly important in determining differential susceptibility and outcome risks. An opportunity exists to enhance understanding of sex differences in responses to vaccines, preventive measures, and treatments. A comprehensive awareness of the interplay between infectious diseases, sex, and gender will enable the development of suitable, acceptable, and impactful interventions for women’s health.

Women in low- and middle-income countries (LMICs) face heightened vulnerability to infectious diseases due to geographic, socio-economic, and political factors that increase exposure and limit access to prevention and treatment. They experience disproportionately high burdens of HIV and sexually transmitted infections (STIs), along with high rates of malaria and other infectious diseases such as upper respiratory infections, skin infections, and leishmaniasis (Rashid et al., 2004). The impact of these diseases extends beyond years of disability and lives lost; they can also lead to economic losses from reduced workforce participation and unpaid caregiving, primarily undertaken by women (Boutayeb, 2010; Ferrant et al., 2014).

The stark contrast between the volume of new products in the R&D pipelines for infectious diseases compared to non-communicable diseases highlights the healthcare inequities faced by LMICs, which bear the burden of most infectious diseases. While communicable diseases account for 17 percent of disability-adjusted life-years (DALY) globally, this figure surges to 26 percent in low- and lower middle-income countries (WHO, 2020a). Yet only 13 percent of the health products currently in development target communicable diseases (WHO, 2023b). Pregnant women may be more vulnerable to emerging infectious diseases (Jamieson et al., 2006). Maternal immunizations—vital to prevent transmission from mother to fetus—face numerous barriers that impede development, including limited data on safety and efficacy, liability concerns, and limited delivery and monitoring capabilities in health systems.

Despite hard-won advancements in disease control, health systems must prepare to address the growing need for infectious disease prevention and treatment. Climate change and movement of animals to new regions increase the potential spread of infectious diseases (NCEZID, 2022). Governments and the private sector must act now to prepare for higher transmission rates and the emergence of novel infectious diseases and build on the past R&D achievements, such as the rapid development of vaccines for COVID-19 and Ebola, pre-exposure prophylaxis for HIV, vector control products for mosquito-borne diseases, and maternal vaccines for COVID-19, tetanus, and pertussis. Stakeholders across the R&D ecosystem should all mobilize to advance R&D for infectious conditions, that affect women differently or disproportionately and that are understudied in women.

## Key Stakeholders

-  Communities and Community Organizations
-  Researchers and Academia
-  Health Care Workers and Systems
-  Public and Philanthropic R&D Funders
-  Private Sector
-  Payors and Insurers
-  Regulatory and Standard-Setting Agencies



**Opportunity 7.1** | Assess the burden of disease and costs resulting from infections that affect women disproportionately or differently, including reproductive tract infections, infections in pregnancy, and pathogens with outbreak potential.

Sex and gender influence disease incidence, duration, and severity through differences in vulnerability to infection, exposure to pathogens, and response to illness (Lawry et al., 2023). For example, an individual's immune system and pregnancy status both influence their vulnerability and response to illness (Robinson & Klein, 2012). Gender influences on social norms or access to resources may also influence exposure to pathogens and illness progression through differences in the ability to access or utilize treatments.

To effectively identify and address gaps in prevention and treatment measures that meet women's needs, stakeholders must first understand the burden of infection, disease consequences, and socio-economic costs of key communicable diseases in women. Improving the availability and accuracy of data that captures the sex-specific burden and costs of key communicable diseases in women will enable R&D agenda-setting efforts to prioritize the highest need areas for women.

### Solution Strategies

- A) Evaluate sex-disaggregated data across infections, including emerging and outbreak pathogens, to determine which affect women disproportionately or differently.
- B) Map available data and evaluate data gaps for the burden of infection, disease, and costs; link existing datasets for pooled analyses; and ensure sex-disaggregation of data for infectious conditions affecting women disproportionately or differently.
  - a. Utilize machine learning to stimulate data mining to examine large data sets to assess the disease burden in sub-populations of women, especially from disinvested communities.
  - b. Leverage existing surveys and previously collected data (e.g., STI data from HIV prevention studies).
  - c. Develop improved methodologies for estimating the burden of disease, costs, and quality of life impacts of common infections in women at the regional, national, and global levels.
- C) Strengthen laboratory and surveillance systems to contribute to estimations of the burden of infection and related diseases that affect women disproportionately and/or differently.
- D) Conduct selected studies on infection and disease prevalence, incidence, and economic and social costs, and studies of infectious etiologies of disease outcomes (e.g., the proportion of infertility that is tubal factor), in strategically chosen locations.

### Cross-Reference:

To see more on **burden of disease assessment**, see: Data and Modeling 1.3 and Female-Specific Conditions 9.10.A.

To see more on **leveraging artificial intelligence and machine learning (AI/ML) to improve women's health**, see Data and Modeling 1.5.B, Research Design and Methodologies 2.3, Non-Communicable and Chronic Conditions 8.1.B, 8.2.B, 8.3.B, and 8.5.C, and Female-Specific Conditions 9.3.D and 9.6.B.

### Key Stakeholders:





**Opportunity 7.2** | Stimulate R&D to explore associations between microbes (pathogens, commensals) and conditions that primarily or disproportionately affect women.

Infections not only present direct risks and symptoms but can also impact the development and prognosis of longer-term diseases, such as chronic gynecologic conditions and immune-mediated disorders, which disproportionately affect women. For example, understanding the link between human papillomavirus (HPV) and cervical cancer has revolutionized prevention efforts for this deadly cancer. Studies suggest that infectious agents may contribute to a range of conditions as varied as like irritable bowel syndrome, endometriosis, and Alzheimer's disease (Muraoka, 2023; Gargano & Hughes, 2014). However, the links between infectious agents and chronic diseases require further investigation (O'Connor et al., 2006). Focusing investments on research to identify the role of microbes as potential underlying causes of chronic conditions can unveil innovative opportunities for prevention and treatment interventions for women.

### Solution Strategies

- A) Undertake a global audit of research agendas aiming to explore the association between microbes and conditions that primarily and disproportionately affect women.
  - a. Leverage databases to assess associations between microbes and health conditions in women, involving geospatial and modeling experts.
  - b. Assess and develop bio-databases to explore links between conditions.
  - c. Ensure that the local disease environment is considered, e.g., which neglected tropical diseases are endemic in the area that could be causing illness.
- B) Research the etiology and role of pathogenic infection in the development of autoimmune conditions that disproportionately affect women, such as lupus, multiple sclerosis, and celiac disease.
- C) Research the potential role of pathogenic infection in the development of other gynecologic conditions, such as endometriosis, abnormal uterine bleeding, polycystic ovary syndrome (PCOS), and fibroids.

### Cross-Reference:

To see more on **data sharing and biobanks**, see Research Design and Methodologies 2.4.A, Innovation Introduction 4.1.B, Non-Communicable and Chronic Conditions 8.1.A, and Female-Specific Conditions 9.1.A and 9.5.

### Key Stakeholders:





**Opportunity 7.3** | Develop and evaluate vaccines and other prevention interventions for infections that disproportionately impact women and evaluate maternal immunization to protect the mother-infant dyad.

Women are affected disproportionately or differently by several infectious diseases—such as HIV, STIs, and tuberculosis—that could be prevented through vaccination and other prevention interventions (UN Women, 2018; Van Gerwen et al., 2022; Humayun et al., 2022). Pregnancy can enhance the risks of severe presentation of infectious diseases, so prevention is essential to help control adverse outcomes. Pregnancy also presents a unique opportunity to pass disease protection to the growing fetus through maternal immunizations. Clinical trial enrollment has historically excluded pregnant women which has led to limited knowledge of vaccine safety during pregnancy upon initial licensure. However, greater interest in developing maternal immunizations presents an opportunity to accelerate the development of vaccines and prevention interventions that can preserve the health of both women and their infants.

### Solution Strategies

- A) Evaluate existing data and conduct studies that evaluate differences by sex and gender in acquisition and transmission risk, disease progression, and immune responses to infection.
- B) Develop and evaluate vaccines and other prevention measures, including those that can be used in pregnancy, that prevent:
  - a. High-burden infectious conditions (e.g., tuberculosis (TB), malaria, HIV);
  - b. New and emerging pathogens with outbreak potential;
  - c. Major causes of neonatal and infant illness and/or death (e.g., group B strep, respiratory syncytial virus (RSV), Klebsiella, Acinetobacter).
- C) Develop and evaluate vaccines, monoclonal antibodies, and other preventive therapies for HIV and other STIs, such as:
  - a. Prophylactic approaches for HIV, herpes simplex virus (HSV), gonorrhea, chlamydia, and syphilis
  - b. Therapeutic approaches for HSV, HPV, and HIV
  - c. Multipurpose prevention technologies that can dually prevent pregnancy and infections
- D) Evaluate women's preferences and perspectives in different communities early in product development to encourage prevention interventions that are suitable, deliverable, and acceptable to women in both LMIC and HIC settings.

### Cross-Reference:

To see more on **solutions for pregnant women**, see: Communicable Diseases 7.5 and Female-Specific Conditions 9.3 and 9.5.

### Key Stakeholders:





**Opportunity 7.4** | Develop improved diagnostic tests for STIs and other reproductive tract infections, including affordable point-of-care and self-testing products.

Over one million STIs are acquired every day globally (WHO, 2023d). Most STIs are asymptomatic, but if left untreated, they can lead to a range of adverse female reproductive tract outcomes, including infertility, chronic pelvic pain, ectopic pregnancies, stillbirths, and preterm births (Van Gerwen et al., 2022). Convenient and affordable rapid STI diagnostic tests are lacking in much of the world, particularly in LMICs, where the use of syndromic management (treating based on symptoms without lab tests) misses most STIs given their asymptomatic nature. However, the STI innovation pipeline is rich and numerous platforms exist to develop improved STI diagnostics (Murtagh, 2019). Increased attention is needed to bring these products through licensure, WHO prequalification, and implementation in LMICs.

### Solution Strategies

- A) Advance, develop, and accelerate the uptake of accurate, feasible, and affordable rapid point-of-care tests (PoCTs) for STIs and other reproductive tract infections (RTIs), including:
  - a. PoCTs for gonococcal and chlamydial infections;
  - b. PoCTs that can distinguish active syphilis from latent or prior infection;
  - c. PoCTs for HPV suitable for screening in low-resource settings;
  - d. PoCTs for identifying gonococcal antimicrobial resistance (AMR);
  - e. Improved tests for other STIs/RTIs, e.g., bacterial vaginosis, trichomoniasis, HSV, genital schistosomiasis.
- B) Evaluate acceptability, feasibility, effectiveness, and cost-effectiveness of existing PoCTs and near-care tests for STIs in LMICs.
- C) Develop new diagnostic tools for upper genital tract infections and associated diseases (e.g., biomarkers, radiologic tools).
- D) Develop self-testing and self-sampling tools and strategies for reproductive tract infections.

### Key Stakeholders:





### Opportunity 7.5 | Expand therapeutic options for infections in women, including during pregnancy and breastfeeding.

As noted under Opportunity 7.1, sex and gender influence disease acquisition and progression. As a result, treatments may have a differential impact on men versus women, exacerbated by the fact that the male body historically represented the standard and women were largely underrepresented in clinical trials. Furthermore, drug safety in pregnancy is often obscure, with limited data on factors like the effects of gestational timing of exposure to medication (Pisa et al., 2015). Increased investment in the development of new or improved therapeutics with sex and gender considerations can ensure that women's needs are being met.

#### Solution Strategies

- A) Develop new or improved therapies for infectious conditions that may disproportionately affect women, for which current treatment is sub-optimal or presents a difficult therapeutic challenge (e.g., curative treatment for HSV, Hepatitis E, treatment for AMR gonorrhea).
- B) Given the frequency of urinary tract infections (UTIs), recurrent UTIs, and UTIs with AMR organisms in women, develop new or improved therapies for UTIs, including exploring non-antibiotic approaches and re-evaluating evidence for existing antibiotics.
- C) Address unique therapeutic challenges during pregnancy and breastfeeding, including re-evaluating evidence of new and old antibiotics/antivirals. Areas of focus could include:
  - a. Develop oral alternatives to benzathine penicillin for syphilis treatment;
  - b. Develop options for treatment of AMR infections (e.g., pyelonephritis w/ resistant Klebsiella);
  - c. Evaluate therapeutics for high-burden diseases (HIV, TB, malaria, hepatitis) and neglected tropical diseases in pregnant and breastfeeding women;
  - d. Create frameworks to ensure the safe early consideration and inclusion of pregnant and breastfeeding women when studying therapies for existing and emerging pathogens with outbreak potential to ensure equitable access.

#### Cross-Reference:

To see more on **solutions for pregnant women**, see: Communicable Diseases 7.3 and Female-Specific Conditions 9.3 and 9.5.

#### Key Stakeholders:



# 8 | Non-Communicable & Chronic Conditions



Non-communicable and chronic conditions are diseases that are not transmitted between people, persist or recur over time, and are often not curable. Amid the growing burden of non-communicable and chronic conditions in high-income (HIC) and low- and middle-income (LMIC) countries, researchers must work to develop new medicines and products that can increase women’s life expectancy and quality of life. Globally, non-communicable and chronic conditions are estimated to cost over US\$30 trillion between 2010 and 2030 (Bloom et al., 2011). Further, particularly in LMICs, the potential market size for chronic condition medications and diagnostics far outweighs measured market expenditures, indicating an unmet need for affordable and scalable solutions in low-resource settings (Defeat-NCD Partnership, 2021). All partners should collectively commit to driving sex- and gender-specific approaches to R&D for chronic conditions.

Chronic conditions frequently affect women both differently and disproportionately, yet existing research insufficiently addresses how women experience these conditions, such as biological and hormonal differences; social and structural factors; and biological embedding—which refers to the impact of life experiences, such as gender inequity, on biology. For example, despite cardiovascular disease (CVD) being the leading cause of global female mortality, women represent just one-third of CVD clinical trial participants, which greatly limits information available about the disease in and appropriate treatments for women (Jin et al., 2020; Woodward, 2019). This underrepresentation is even more significant because CVD symptoms and progression present differently in women than men. Additionally, many diseases that disproportionately impact women are historically underfunded. For example, migraines—which disproportionately affect women—received less funding than would be commensurate with the burden of disease (Mirin, 2021). Similarly, gynecologic cancers are underfunded compared to prostate cancer in the US based on lethality (Spencer et al., 2019). Mental health also lags behind physical health in attention, funding, and action (WHO, 2021a). Researchers estimate that 20 to 25 percent of women in LMICs experience perinatal depression; this poses significant and lasting implications for women’s health and well-being (Prom et al., 2022).

Inadequate attention to the unique, women-centric attributes and needs in research and policy has enduring downstream effects. Women may delay treatment due to limited awareness of how diseases present differently. Additionally, therapeutic drugs may enter the market without sufficient testing in women, which can compromise efficacy and safety in women. Prioritizing personalized care, including precision medicine, in R&D can bring technologies and products to market that meet the diverse needs of women. A more equitable R&D agenda will require 1) defining women’s health beyond reproductive and maternal health to include the broad array of non-communicable and chronic conditions throughout the life course and 2) building the evidence base for sex and gender differences in disease risks, symptoms, and treatment response.

## Key Stakeholders

-  Communities and Community Organizations
-  Researchers and Academia
-  Health Care Workers and Systems
-  Public and Philanthropic R&D Funders
-  Private Sector
-  Payors and Insurers
-  Regulatory and Standard-Setting Agencies



**Opportunity 8.1** | Evaluate sex- and gender-related differences in the evolution and presentation of cardiometabolic diseases and responses to available therapies to inform the development of optimal prediction, prevention, screening, diagnosis, monitoring, and treatments for women, with a specific focus on ischemic heart disease, diabetes, and obesity.

Ischemic heart disease, which is caused by narrowed heart arteries that limit blood and oxygen flow to the heart, is the leading cause of death among women worldwide and diabetes ranks eight; obesity is contributing factor for both conditions (IHME, 2023). Multiple studies have documented differences in the incidence, prevalence, morbidity, and mortality related to cardiometabolic conditions between men and women worldwide (Khan et al., 2020; Huebschmann et al., 2019).

Despite recent strides made in understanding sex and gender differences in cardiometabolic disorder risk factors, more research is needed to explore the mechanisms explaining differences in disease presentation and progression, which could lead to more personalized prediction, prevention, diagnostics, monitoring tools and treatments (Peters et al., 2019; Strack et al., 2022).

### Solution Strategies

- A) Leverage ongoing longitudinal studies on cardiometabolic conditions with a consortium-based approach to:
  - a. Share and pool existing data and biospecimens to enable research on life stage onset, preclinical and clinical manifestation of these conditions, risk of long-term complications, protective factors, access to and quality of timely identification of risk factors, diagnosis and healthcare delivery, response to treatment, incidence of fatal and non-fatal events, and additional stratification or cross-country comparisons, including natural experiments on the relationship of these conditions and changes in healthcare and public policies, for example;
  - b. Conduct meta-analyses in instances where data or biospecimen sharing is not possible;
  - c. Stimulate and support the proposal of new studies based on innovative research questions, novel biomarkers, emerging risk factors, implementation science, or underrepresented populations not included in the scope of work of established longitudinal studies; and
  - d. Share best practices and cross-collaborate for establishing long-term and sustainable research programs and research capacity building that respond to local health needs and are supported by local governments and public and private partners.
- B) Develop an artificial intelligence/machine learning (AI/ML) pilot prototype with the assurance of robust and comprehensive data that represent women from diverse health, personal and social trajectories, and conduct prospective trials to develop, test, and evaluate a clinical decision support tool for diagnosing ischemic heart disease in women.
- C) Research genotypes and phenotypes utilizing datasets that comprehensively document women's diverse health, personal and social backgrounds to further understand the risk for developing type 2 diabetes, to enable more precise risk stratification and optimize screening, prevention, diagnosis, monitoring, and treatment regimens.

### Cross-Reference:

To see more on **leveraging artificial intelligence and machine learning (AI/ML) to improve women's health**, see Data and Modeling 1.5.B, Research Design and Methodologies 2.3, Communicable Diseases 7.1.B, Non-Communicable and Chronic Conditions 8.2.B, 8.3.B, and 8.5.C, and Female-Specific Conditions 9.3.D and 9.6.B.

To see more on **data sharing and biobanks**, see Research Design and Methodologies 2.4.A, Innovation Introduction 4.1.B, Communicable Diseases 7.2.A, and Female-Specific Conditions 9.1.A and 9.5.

### Key Stakeholders:





**Opportunity 8.2** | Evaluate sex- and gender-related differences in outcomes and responses to medications (including chemoprevention, chemotherapy, immunotherapy, and targeted therapy) to inform the development of prevention strategies, screening and diagnostic tools, and treatments for lung, colorectal, and gynecological cancers.

Understanding sex- and gender-related differences in oncology treatment response is critical to ensuring patients receive therapies with the highest chance of success. Studies of several existing therapies have found significant differences in side effects and outcomes between men and women. For example, although immune checkpoint inhibitors have improved outcomes for patients certain types of melanoma and lung cancer, women are more likely to experience immune-related adverse events than men (Duma et al., 2019). Women also experience a higher rate of hematologic toxicity from chemotherapy. For example, women experienced higher rates of anemia and leukopenia than men when receiving a common chemotherapy regimen for lung cancer (Singh et al., 2005).

On the other hand, studies have found that certain therapies elicit better outcomes for women than men. One meta-analysis, for example, found that women experienced better responses than their male counterparts to a regimen of anti-programmed cell death protein 1 (anti-PD1) or anti-programmed death-ligand 1 (anti-PD-L1) agents plus chemotherapy compared to anti-PD1 or anti-PD-L1 alone (Conforti et al., 2019). Additionally, men and women may have distinct risk factors; for example, 15–20 percent of lung cancer cases in men globally are not associated with smoking, while over 50 percent of cases in women are not associated with smoking (Parkin et al., 2005). Discovering and exploiting these critical differences in disease and treatment response is an opportunity to further personalize oncology treatment and improve the chances of better patient outcomes. A critical factor will include adequate inclusion of women in cancer clinical trials, as data shows women are underrepresented in clinical trials of anti-cancer therapies (Babcook, et al., 2022)

### Solution Strategies

- A) Establish a cross-functional consortium of academic researchers, patient advocacy groups, and oncology research and institutional groups to investigate sex- and gender-related differences in efficacy and safety in the treatment of lung, colorectal, and cervical cancer, as well as new tools for diagnosis and screening of women for lung cancer. Build upon these analyses to produce consensus documents to support a greater understanding of these differences and potential next steps to improve outcomes in women living with these cancers. This includes strategies to ensure that clinical trials in these diseases include women patients across races and ethnicities in representative numbers according to epidemiology.
- B) Work with real-world evidence platforms that include both national and global data to compare the incidence of adverse events and outcomes (e.g., progression-free survival) due to treatment with PD-1 inhibitors (e.g., pembrolizumab, nivolumab) in the treatment of males vs females with non-small cell lung cancer and advance AI/ML-based prediction models to better identify individuals who are at elevated risk for lung cancer.
- C) Prioritize research to support the development, evaluation of efficacy, and implementation of self-collection mechanisms for cervical cancer screening to improve screening rates.
- D) Establish global, multi-organizational collaborations to evaluate sex- and gender-related differences in the microbiome, both before and during the treatment of colorectal cancer. Determine whether any microbiome elements correlate with differences in patient outcomes after treatment.

### Key Stakeholders:





**Opportunity 8.3** | Evaluate sex- and gender-related differences in the evolution and presentation of neurological disorders and responses to available therapies to inform the development of prevention strategies, screening, diagnostics, monitoring, and treatments for women, with a specific focus on dementia, migraine, and pain.

Women are disproportionately impacted by dementia, migraines, and pain (IHME, 2023). Women not only have a higher incidence rate of dementia but also experience faster disease progression and cognitive decline (Rosser & Cosentino, 2023). As the population of older adults continues to grow, the market for diagnostic, monitoring, and treatment innovations for dementia and chronic pain will also expand (WHO, 2022).

The global incidence of migraine is also increasing, having jumped 40 percent between 1990 and 2019 (Fan et al., 2022). The burden of migraine, dementia, and pain syndromes is significant. Migraine (16.3 percent) and dementia (10.4 percent) alone were the second and third largest contributors of neurological DALYs globally in 2016, with migraine causing more burden in females than males (GBD 2016 Neurology Collaborators, 2019).

Expanding the current evidence base of the mechanisms driving sex and gender differences for these prevalent neurological conditions can enable the development of tools and therapies to improve outcomes for women.

### Solution Strategies

- A) Investigate risk and protective factors for dementia, migraine, and chronic pain, including environmental and social determinants, genetic links to autoimmune disorders, phenotypes at risk, and genetic protections.
- B) Augment current efforts by existing consortia to include sex and gender considerations in the design of diagnostic, monitoring, and treatment tools, including digital ones, that use novel imaging, biomarkers, and AI strategies for women with dementia and their caregivers.
- C) Apply research on migraine pathogenesis to the development of innovative treatments and develop affordable tools for diagnosis and monitoring of neurological disorders, such as using a smartphone app for monitoring migraine or pain onset and severity.
- D) Research nuances in women with migraine with and without aura, specifically measuring hormonal levels across the menstrual cycle (e.g., progesterone, estrogen) to determine the potential impact on pharmacodynamics and medication efficacy.
  - a. Study the biological underpinnings of pharmacokinetics, pharmacodynamics, and pharmacotoxicity of medicines for treatment of migraine and pain as they relate to pregnancy and breastfeeding.

### Key Stakeholders:





**Opportunity 8.4** | Develop prevention interventions, screening and diagnostic tools, and treatments that account for sex- and gender-specific elements in mental health disorders across diverse settings and across the life course, with a specific focus on post-traumatic stress disorder (PTSD), depression, and anxiety.

Women are at a higher risk of developing a mental health disorder in their lifetime than men. Researchers attribute higher risk in women to numerous factors, including socio-cultural factors, such as gender inequities leading to limited agency, high workloads, and domestic violence, and biological factors, including the impact of hormones on mood modulation (Bezerra et al., 2021). The perinatal period is a particularly critical time to identify and address mental health concerns in women because prevalence is higher during this period (Fekadu et al., 2020). Due to several biological factors, women and men respond differently to psychotropic drugs, but research into these nuances is nascent (Jacobson, 2014). Women in low-income countries face additional barriers to receiving culturally sensitive care, as many interventions are not adapted to their unique contexts. If a broader evidence base can be established, an opportunity exists to develop new therapies or dosing guidelines and context-specific tools to prevent and manage mental health disorders in women.

### Solution Strategies

- A) Research nuances in women receiving psychotropic therapies, specifically measuring hormonal levels across the menstrual cycle (e.g., progesterone, estrogen) and life course to determine the potential impact on pharmacodynamics and medication efficacy.
- B) Fund local academic and community-based advocacy groups to develop culturally- and gender-sensitive diagnostic and monitoring tools for PTSD, depression, and anxiety for use in low-resource settings by community health workers or individuals.
- C) Conduct implementation research on how psychological interventions can be scaled up within a stepped-care approach by engaging with the existing healthcare systems and the communities to address the treatment gap for perinatal depression in resource-limited settings.

### Key Stakeholders:





**Opportunity 8.5** | Evaluate sex- and gender-related differences in the evolution and presentation of autoimmune disorders and responses to available therapies to inform the development of prevention, screening, diagnosis, and treatment options for women, with a specific focus on systemic lupus erythematosus (lupus), rheumatoid arthritis, osteoporosis, and autoimmune thyroid diseases.

Women disproportionately bear the burden of autoimmune conditions; approximately 80 percent of people diagnosed with an autoimmune disease are women (Angum et al., 2020). Lupus, rheumatoid arthritis, and autoimmune thyroid diseases are highly prevalent among women and have limited availability of screening tools, diagnostics, and treatments. Given the overwhelming predominance of autoimmune diseases in women, sex- and gender-specific R&D is critical. An opportunity exists to continue expanding investment into autoimmune disease R&D, such as that of the NIH, to support the development of screening, diagnostic, monitoring, and treatment tools and therapies that could reach a market of millions of women.

### Solution Strategies

- A) Extend studies on the impact of sex hormones on autoimmunity to clinical and translational efforts to bring new treatment technologies to market, such as cellular genomic and protein-based technologies currently in development.
- B) Develop guidelines for early detection of autoimmune diseases in girls and young women with high-risk, familial autoimmune disease history.
- C) Develop AI/ML tools to serve as a first-line risk assessment strategy for lupus to support patients and doctors in determining whether further testing or monitoring is warranted.
- D) Design and develop inflammation surveillance and autoimmune disease management monitoring solutions using wearable sensors to capture patient data and wearable devices, such as smartwatches. Developed prototypes could allow for a cost-effective means of monitoring autoimmune conditions in pre-, during-, and post-inflammatory crises.

### Key Stakeholders:



# 9 | Female-Specific Conditions



Immense unmet need and untapped market potential exist for innovations that address reproductive, maternal, gynecological, and life stage conditions. For example, menopause—a life stage that 1 billion women experience worldwide each year—presents an estimated US\$600 billion opportunity for innovations to manage symptoms (Hinchcliffe, 2020). However, women’s reproductive and gynecological health suffers from a vicious cycle of deprioritization and underfunding in the broader R&D ecosystem, leading to a stagnant landscape of products. This costs society billions yearly, including health expenditures, productivity losses from missed work hours, reduced productivity and advancement, and unemployment linked to these conditions. In the US, annual healthcare spending on reproductive, maternal, perinatal, and gynecological conditions is estimated at US\$195 billion (Dieleman et al., 2020). Although these estimates begin to reveal the burden of reproductive and gynecological health conditions, the overall societal cost remains largely unknown.

Globally, women face risks of maternal morbidity and mortality and unmet needs for contraception, diagnostics, and treatments for a wide variety of conditions. Maternal mortality remains unacceptably high as rates continue to rise worldwide, particularly in LMICs, where 95 percent of maternal deaths occur (WHO, 2023e). In the US, maternal mortality has doubled in the last decade; researchers have observed significant racial and ethnic disparities, particularly among Black and American Indian/Alaska Native women (Fleszar et al., 2023). In addition to maternal conditions, gynecological and life stage conditions such as uterine fibroids, endometriosis, pelvic floor disorders, and menopause are common and often debilitating conditions that represent substantial unmet need for innovations.

Despite demonstrated need, few innovative treatments and diagnostic tools have emerged in recent decades. Notably, no disease-modifying therapies are available for any gynecological condition. Additionally, the pipeline for obstetric therapies is sparse compared to conditions of similar health burdens. The incidence of pre-eclampsia is comparable to that of Inflammatory Bowel Disease (IBD), but trials focused on IBD outnumber those for pre-eclampsia by eightfold (National Library of Medicine, 2023). Even compared to the pipeline for a single rare disease such as Amyotrophic Lateral Sclerosis (ALS), the pipeline for obstetric drugs lags—34 versus 17 drugs, respectively (Fisk & Atun, 2008).

Greater investment at all stages—from basic research funding and innovation development to ensuring purchasing eligibility and insurance coverage for new medications and tools—will diminish stigma and underestimation of women’s health conditions. Developing diagnostic and therapeutic solutions to empower women to have greater autonomy over their health will require increased funding, incentives, and partnerships, as well as close engagement of women throughout the R&D process.

## Key Stakeholders

-  Communities and Community Organizations
-  Researchers and Academia
-  Health Care Workers and Systems
-  Public and Philanthropic R&D Funders
-  Private Sector
-  Payors and Insurers
-  Regulatory and Standard-Setting Agencies



**Opportunity 9.1** | Investigate the biological and external mechanisms of female gynecological health conditions and develop tools and therapies for prevention, diagnosis, treatment, and non-invasive monitoring of conditions, including normal menstruation and disorders such as polycystic ovarian syndrome (PCOS), endometriosis, adenomyosis, and fibroids.

Female gynecological health conditions, such as PCOS, endometriosis, adenomyosis, fibroids, and heavy menstrual bleeding, affect a significant portion of the population worldwide. Endometriosis alone is estimated to affect 10 percent of women and girls of reproductive age globally, or 190 million people (WHO, 2023a). These conditions are poorly understood (Hudson, 2021; Aninye & Laitner, 2021). At the same time, the diagnosis and treatment of gynecological conditions cost billions due to high prevalence and expensive interventions—often long-term medication use or invasive surgery (Pynnä et al., 2021; Simoens et al., 2007). An opportunity exists to advance the basic science for gynecological conditions and to support the development of less invasive, more effective, and higher-medical value options for diagnosis, monitoring, and treatment.

### Solution Strategies

- A) Establish consortia for public-private partnerships to enable cross-industry, academia, and government collaboration and knowledge-sharing on non-clinical models, biomarkers, datasets, trial designs, and novel endpoints. Focus areas could include:
  - a. Support for the development of biobanks for menstrual blood, endometrial or other tissue and biospecimens;
  - b. Identification of new biomarkers or establish ranges for existing biomarkers for diagnosis, treatment, and monitoring leveraging existing databases;
  - c. Development of in-vitro models which are 3D/on a chip to de-risk clinical studies and shorten clinical trials;
  - d. Identification of opportunities to collect samples for multiple conditions to expand the understanding of the basic science, for example, across endometriosis and fibroids;
  - e. Development of non-invasive endpoints to measure disease modification in diseases like endometriosis and adenomyosis that would be acceptable for approval;
  - f. Development of target product profiles.
- B) Support more efficient development and regulatory approval of diagnostics and therapeutics by:
  - a. Conducting a landscape analysis to map products in development by stage;
  - b. Funding and providing technical assistance to organizations with promising products to help them navigate validation and regulation requirements in different countries.
- C) Develop non-invasive diagnostic and monitoring tools and disease-modifying therapies for PCOS, endometriosis, adenomyosis, fibroids, and heavy menstrual bleeding, for example:
  - a. Development of androgen assays specifically for women and across age ranges to support diagnosis of PCOS that are appropriate for low-resource settings;
  - b. Development of non-invasive diagnostic tests for endometriosis and adenomyosis;
  - c. Development of modalities to deliver therapies directly to endometriotic lesions;
  - d. Development of innovative strategies to target stem cell transformation leading to fibroids.

### Cross-Reference:

To see more on **data sharing and biobanks**, see Research Design and Methodologies 2.4.A, Innovation Introduction 4.1.B, Communicable Diseases 7.2.A, Non-Communicable and Chronic Conditions 8.1.A, and Female-Specific Conditions 9.5.

### Key Stakeholders:





**Opportunity 9.2** | Stimulate R&D on the role of the vaginal microbiome in health and illness and develop interventions to address vaginal dysbiosis and foster a low-risk vaginal microbiome.

The vaginal microbiome is a dynamic community of microorganisms that is crucial to a woman's overall health. The vaginal microbiome not only serves as a critical line of defense against the negative impacts of infections on the reproductive tract, but can also impact well-being when an abnormal vaginal microenvironment causes discomfort, odor, or unusual discharge (Amabebe & Anumba, 2018). Stigma and limited investment in vaginal health research have posed barriers to developing prevention, diagnostic and therapeutic strategies to support the vaginal microbiome. Prioritizing research in this field could lead to improved diagnostics, personalized treatments, and preventive strategies that could benefit billions of women worldwide.

### Solution Strategies

- A) Expand strategic partnerships between stakeholders like research institutions, healthcare providers, patient advocacy groups, policymakers, and funders to ensure the translation of research findings into clinical practice. Focus areas could include:
  - a. Development of an R&D agenda focused on understanding the determinants of a healthy vaginal microbiome and of vaginal dysbiosis (microsome, bacteria, viruses, fungome, metagenomics, host genetics and immune response, exposures, gut microbiome, sexual practice, diet);
  - b. Establishment of bi-annual meetings with these stakeholders to translate the collected data and leverage it to improve health outcomes.
- B) Invest in basic and clinical research to better understand the vaginal microbiome's composition, function, and relationship with various health conditions. This could include:
  - a. Expanding cytology biobanks and developing new biobanks for vaginal secretions;
  - b. Large-scale longitudinal studies across diverse populations to understand variations and the influence of factors like diet, lifestyle, and ethnicity.
- C) Foster collaboration with pharmaceutical companies, biotech startups, academia, and regulatory bodies to develop novel therapeutics that can help restore and maintain a healthy vaginal microbiome. This might include approaches to reducing or eliminating high-risk anaerobic bacteria in the vagina and uterus and the development of probiotics, prebiotics, or microbiome transplants.

### Key Stakeholders:





**Opportunity 9.3** | Increase research on prenatal, intrapartum, and postpartum conditions and risk factors associated with adverse maternal health outcomes (e.g., postpartum hemorrhage, pre-eclampsia, and preterm labor) to enable the development of diagnostics, treatments, and prevention, including artificial intelligence/machine learning (AI/ML) tools.

Maternal morbidity and mortality, stillbirths, and adverse neonatal outcomes are all interconnected. Thus, investing in maternal health positively impacts the range of adverse perinatal outcomes. Global progress in reducing maternal and newborn deaths as well as stillbirths has slowed down in the past decade; the rate of progress achieved between 2000 and 2010 exceeded the pace observed in subsequent years (WHO, 2023e). Increased investment and research into developing new drugs, devices, and tools is required to address the significant factors that contribute to adverse maternal outcomes, as limited research exists to date into medicines or techniques for prevention and control. Maternal and perinatal conditions cause 7 percent of the global disease burden, but innovations for obstetrics only account for an estimated 1 to 5 percent of the drug pipeline (David et al., 2015). An opportunity exists to increase knowledge of the risk factors and causes of adverse maternal health conditions and develop new tools and treatments to improve maternal and infant health.

### Solution Strategies

- A) Establish a consortium of researchers, manufacturers, product developers, and regulatory bodies working on early detection, non-clinical models, biomarkers, datasets, trial designs, novel endpoints, prediction tools and new diagnostics and therapeutics for postpartum hemorrhage (PPH), pre-eclampsia and preterm labor, coordinated by a global steering committee.
- B) Accelerate innovation in novel therapeutics and in diagnostic technologies, including point-of-care options, to predict and diagnose risk factors associated with adverse maternal health outcomes like pre-eclampsia, PPH, infections, gestational diabetes, and anemia that contribute to maternal morbidity and mortality.
- C) Support more efficient development and regulatory approval of diagnostics and therapeutics by:
  - a. Identifying products in the early phases of development via a landscape analysis;
  - b. Funding and providing technical assistance to organizations with promising products to help them navigate validation and regulation requirements in different countries.
- D) Develop AI/ML risk prediction tools for pregnancy, intrapartum, and postpartum monitoring and management, through:
  - a. Data Collection and Integration: Establish a comprehensive data collection system that incorporates various data sources, such as electronic health records, wearable devices, and mobile applications. This system should enable seamless integration and analysis of diverse data types, including physiological parameters, medical history, and patient-reported information.
  - b. Machine Learning Algorithms: Develop and train machine learning algorithms to analyze the collected data and identify patterns, trends, and potential complications during pregnancy, labor, and postpartum phases. These algorithms can be trained to enable risk stratification for referral and to predict outcomes such as preterm birth, pre- and postpartum pre-eclampsia, gestational diabetes, and postpartum depression.
  - c. Addressing Existing Silos: Foster collaboration among various groups working in AI/ML tools with practitioners and communities.
  - d. Prioritizing Inclusive and Respectful Maternity Care: Include women, especially from groups marginalized by discrimination, as experts and thought leaders in the development of AI/ML tools.

### Cross-Reference:

To see more on **solutions for pregnant women**, see: Communicable Diseases 7.3 and 7.5 and Female-Specific Conditions 9.5.

To see more on **leveraging artificial intelligence and machine learning (AI/ML) to improve women's health**, see Data and Modeling 1.5.B, Research Design and Methodologies 2.3, Communicable Diseases 7.1.B, Non-Communicable and Chronic Conditions 8.1.B, 8.2.B, 8.3.B, and 8.5.C, and Female-Specific Conditions 9.6.B.

### Key Stakeholders:





**Opportunity 9.4** | Investigate evidence gaps in understanding the role of micronutrients, including iron and folic acid, and their formulation for improving maternal outcomes.

Women of reproductive age in LMIC and low-resource settings often have concurrent deficiencies of multiple micronutrients due to inadequate dietary intake and limited choices in fruits, vegetables, animal proteins, and fortified foods (WHO, 2004). In pregnancy and lactation, the burden and severity of micronutrient deficiencies are worsened by the increased demand, leading to potentially adverse effects on both the mother and baby (Bailey et al., 2015). To address the issue of multiple and concurrent micronutrient deficiencies, the United Nations Children’s Fund, United Nations University, and the WHO developed a multiple micronutrient tablet called UNIMMAP (United Nations International Multiple Micronutrient Antenatal Preparation). However, the WHO does not yet universally recommend multiple micronutrient supplements for pregnant women over the current practice of prenatal supplementation with iron and folate, except in the context of rigorous research. As such, WHO recommends further research on the use of multiple micronutrient supplementation over iron and folic acid supplementation alone for pregnant women in low-resource settings (WHO, 2020b).

### Solution Strategies

- A) Synthesize global evidence on a) dose, b) dosing regimen, c) formulation, and d) duration of use of multiple micronutrients for all women and girls of reproductive age through a meta-analysis or systematic review of existing literature.
- B) Synthesize global evidence, including private sector data, on the risk and benefits of food fortification, including home fortification with micronutrients for women of reproductive age group, and help decide best possible mechanism to deliver fortified food to women most in need.
- C) Identify and expedite the development of promising products currently in the development or pre-production stages to bring to market diagnostics for anemia that are affordable, do not require invasive procedures, and can be used at the point-of-care.

### Key Stakeholders:





**Opportunity 9.5** | Create and support biobanks with diverse, linked milk and blood samples that can be accessed for research, including assessing the safety of prescription and over-the-counter medication use during pregnancy and breastfeeding.

Information about the impact of medication use in pregnancy on babies is often lacking; even less information is available on the transfer of medication from mother to child when breastfeeding. Closing this knowledge gap will promote the protection of mothers' and babies' health and ensure timely post-market updates about drug safety are disseminated to patients. Globally 200 million women get pregnant each year. A study of pregnant women in 28 countries found that 81 percent reported taking medication during pregnancy (Lupattelli et al., 2014). Breastfeeding women face a comparable situation, where many suffer from a chronic disease as well as postnatal health issues that require medication use. A study observed that of newly FDA-approved drugs, one-third of medications were not adequately labeled for safety during pregnancy and lactation and less than 20 percent included human data on pregnancy and lactation (Byrne et al., 2020). New biobanks with linked milk and blood samples could enable knowledge generation of interactions between medications and pregnancy and breastfeeding. They could also be used in a variety of other research, such as nutritional or immunologic studies focused on pregnancy and breastfeeding. Safe, ethical inclusion of pregnant and lactating women in these biobanks will require strict adherence to local regulations, consent processes, and cultural norms.

#### Solution Strategies

- A) Develop a global maternal and infant Blood and Breastmilk network, expanding upon Innovative Medicines Initiative ConCePTION's Breastmilk Network.
  - a. Set up and sustain the systematized collection and handling of blood and milk samples at regional and international levels;
  - b. Set up and sustain a federated network of milk biobanks that would comply with quality standards and that could enable the pooling of samples;
  - c. Globalize the efforts; this could include the identification of pilot opportunities to enable diverse population research in regions where breastmilk banks are sparse, such as Sub-Saharan Africa and South Asia, with care taken to ensure the pilots are culturally acceptable.

#### Cross-Reference:

To see more on **data sharing and biobanks**, see Research Design and Methodologies 2.4.A, Innovation Introduction 4.1.B, Communicable Diseases 7.2.A, Non-Communicable and Chronic Conditions 8.1.A, and Female-Specific Conditions 9.1.A.

#### Key Stakeholders:





**Opportunity 9.6** | Develop improved, accessible contraceptive technology with fewer side effects and more prolonged efficacy.

From a business perspective, the contraceptive market appears robust—a market research firm estimated the market size at US\$28 billion in 2022 and growing at 6 percent annually (Grand View Research, 2022). Yet, innovations in contraceptive technology have slowed within the pharmaceutical industry; most recent industry-funded clinical trials focus on incremental revisions to existing hormonal products (Callahan et al., 2020). New partnerships between academic institutions, nonprofits, small biotechnology companies, philanthropy, and government could help fill the gap in contraception innovation.

Many women choose not to use available methods of contraception, often to avoid unwanted side effects or due to cost. In the US for example, approximately 50 percent of contraceptive options on the market are not fully covered by insurance, despite federal mandates that insurers cover contraception at no cost (Committee on Oversight and Reform, 2022). These barriers to contraceptive use drive high rates of unplanned pregnancies and lead more women to die unnecessarily from pregnancy and childbirth. Lack of contraception access also decreases women's educational attainment, workforce participation, and autonomy. Women need more and better options to ensure parenthood is a choice, including more options available for male partners. With payors and innovators in place, potential exists for millions of women to uptake new methods that elicit fewer side effects.

**Solution Strategies**

- A) Fund methods currently in preclinical and clinical trials to bridge the gap in early and late-stage investments, including:
  - a. Male contraceptives;
  - b. Novel intrauterine devices (IUDs) with fewer side effects, including less pain during insertion and less bleeding while inserted;
  - c. Novel methods that precisely indicate critical days of ovulation;
  - d. Longer-acting options beyond IUDs, such as sustained-release oral contraceptives or self-injectables or implants;
  - e. Peri-coital (“on demand”) contraception options beyond spermicide, diaphragms, or condoms.
- B) Develop AI/ML tools to help physicians and patients identify the best contraception methods (highest efficacy and fewest side effects) based on patient profiles and medical histories.

**Key Stakeholders:**





**Opportunity 9.7** | Understand how policies that influence reproductive care impact women's health to support the development of new modalities for the full range of reproductive care.

Increased advocacy and funding for research on reproductive care policy in diverse settings can broaden the evidence base for potential implications of these policies on women's quality of life and how policies may hinder or support the development of new reproductive care methods. Key focus areas for development include safe and effective methods for facilitating completion of non-viable pregnancies that preserve the health of the pregnant individual due to complications or worsening disease, or when the embryo or fetus has lethal anomalies; these include inevitable or incomplete miscarriage—particularly those in the second trimester, ectopic pregnancies, preterm premature rupture of the membranes, and stillbirths.

The incidence of pregnancy loss in the second trimester is not well known and estimates range from 0.4 percent to 3 percent (Odendaal et al., 2019). While strong evidence exists supporting methods for managing pregnancy loss in the first trimester, data is limited for treatment options for pregnancy loss in the second trimester. For example, one systematic review of medical treatments for incomplete miscarriage found no randomized control trials that specifically studied the treatment of miscarriage between 13- and 24-weeks gestation (Kim et al., 2017). Research is needed to generate evidence on the best treatment modalities for second trimester miscarriages to guide improved care for women.

Ectopic pregnancies—which occur in one to two percent of pregnancies—are pregnancies outside of the uterus, which are nonviable and risk the mother's health without prompt treatment (Brady, 2017). The most common treatments for ectopic pregnancies—surgical intervention and provision of methotrexate—are associated with unwanted side effects and adverse outcomes. Alternative pharmacological methods are promising, but additional research is needed to test these methods to ensure safety and efficacy across the array of presentations and patient populations.

### Solution Strategies

- A) Increase funding allocations for mixed-methods research in diverse settings studying the impact of reproductive health policies on women's health, incorporating leading reproductive health research institutions, providers, and patient advocates.
- B) Develop new modalities for pregnancy termination in cases of incomplete miscarriage and ectopic pregnancy.
  - a. Investigate management of incomplete miscarriage in second trimester pregnancies to identify best practices or inform the development of new methods.
  - b. Investigate new medical approaches for the treatment of ectopic pregnancy.

### Key Stakeholders:





### Opportunity 9.8 | Optimize fertility potential, including in males, by developing new, affordable diagnostic tools and treatments.

Family planning is more than pregnancy prevention—fertility care is a key component that can help families have children when they want them. The global lifetime prevalence of infertility is estimated to be 17.5 percent; inequities in fertility care exist due to limited availability of services and high costs (WHO, 2023c). In 2009 a panel of experts estimated that only 24 percent of the need for assisted reproductive technologies, including in-vitro fertilization (IVF), in the US was being met (Ethics Committee of the American Society for Reproductive Medicine, 2021). Unmet need for infertility treatment may be significant in other countries as well. In China, for example, the number of assisted reproductive technology centers per citizen is estimated to be 1 for every 7.5 million people, compared to 1 for every 700,000 in the US (Qiao & Feng, 2014). Equity and ethical concerns also abound, as those with the fewest resources are the least likely to have access to fertility care. A market research firm forecasts that the global infertility treatment market will grow by 8 percent annually (Future Market Insights, 2021). Industry should be ready to meet demand with innovations that can be applied in both high- and low-resource settings.

#### Solution Strategies

- A) Research causes of, evaluation methods, and treatments for poor ovarian reserve and male infertility in diverse populations.
- B) Expand options for fertility evaluation, including in low-resource settings, focusing on alternative samples (e.g., use of menstrual blood, saliva, urine, endometrial tissue, etc.).
- C) Simplify the IVF process to decrease costs and increase accessibility while retaining or improving efficacy. Options include:
  - a. Oral ovulation induction agents;
  - b. Home urinary/salivary testing to decrease travel costs;
  - c. The use of simplified, more affordable pain control and anesthesia approaches during egg retrieval;
  - d. Simplification of laboratory techniques (e.g., intravaginal embryo culture).

#### Key Stakeholders:





**Opportunity 9.9** | Develop self-administered solutions and new biomaterials such as mesh products and stem cells to support safe and effective treatment options for conditions such as urinary incontinence and prolapse in women.

Stress urinary incontinence (SUI) and pelvic organ prolapse (POP) are conditions with growing burden and negative impacts on the overall health and quality of life for millions of women globally. POP is estimated to affect 40 percent of women at some point in their lives, and SUI is estimated to affect up to 35 percent (Wang et al., 2022; Luber, 2004). Pessaries are a non-surgical method to manage female POP and SUI. Traditionally placed in the vagina for extended periods of time, pessaries have few side effects but may be difficult for the patient to insert and remove (Jones & Harmanli, 2010). Issues with comfort and convenience may also limit widespread use of the devices. Although surgical solutions such as the placement of mesh can ameliorate symptoms associated with SUI and POP, they present risks of complications. Some biomaterials, including pelvic mesh implants, were recalled because of poor patient outcomes.

Most in-vitro biomaterials studies do not report the sex of the cells, which leads to a gap in understanding of sex-specific cell interactions with biomaterials (James et al., 2021). Efforts to ensure SABV is applied across R&D efforts and modalities (i.e. therapeutics, devices, and digital platforms), are critical first steps to improving the value of findings and innovations, and globalizing these efforts is vital. Greater knowledge about critical differences in response to devices between sexes, such as the immune or biomechanical responses to biomaterials, will support development and scaling of devices that fit the needs of women.

### Solution Strategies

- A) Globalize guidelines for biomaterials research and testing that require:
  - a. Transparency from vendors of the sex of cells in primary cell cultures;
  - b. Inclusion and reporting of sufficient numbers and types of male and female cells to draw conclusions about the long-term safety and efficacy of the biomaterials according to sex, age, and hormonal status (pre- or post-menopause);
  - c. Manufacturer reporting of biomaterial safety profiles according to sex, age, and hormonal status.
- B) Support the continuation of innovations currently in development, including:
  - a. Self-fit and administered mechanical devices vaginally inserted to improve stress incontinence or prolapse that do not require assistance from a medical professional;
  - b. Self-administered vaginal inserts for SUI and POP that may simultaneously be used to collect & analyze vaginal discharge, microbiome, and/or menstrual blood flow and/or deliver drugs to the vagina;
  - c. Tissue engineering using stem cell strategies to treat and prevent POP.

### Cross-Reference:

To see more on **inclusion of sex and gender considerations in regulatory and science policy frameworks**, see topic 3, Regulatory and Science Policy.

### Key Stakeholders:





**Opportunity 9.10** | Develop novel, evidence-based, and specific diagnostics and treatments for symptoms of menopause, such as hot flashes, insomnia, joint pain, mental health disorders, and genitourinary syndrome.

Women's health research has traditionally focused on maternal and reproductive health, even though women aged 50 or over account for 26 percent of all women and girls globally (United Nations, 2022). Millions of women, typically between the ages of 45 and 55, experience menopause each year (NIH National Institute on Aging, 2021). The burden of menopause symptoms represents significant personal and societal costs. Globally, vasomotor symptoms are responsible for over US\$800 billion in healthcare costs and productivity losses (Das, 2019). Perceptions of menopause as an inevitable unpleasant physiological process contribute to limited help-seeking behaviors and a dearth of innovation. However, FemTech companies are emerging to revolutionize peri- and post-menopause care (Das, 2019). The growing, multi-billion dollar menopause market has the potential to increase understanding of risk factors for menopause symptoms and develop new tools and treatments for early detection, symptom prevention, and alleviation (Hinchcliffe, 2020).

### Solution Strategies

- A) Close the data gap by including menopause in global burden of disease estimates.
- B) Support the development of therapies, diagnostics, and digital tools in the pipeline, including:
  - a. Innovations in the long-term release of vaginal estrogen and/or progesterone;
  - b. Non-hormonal and non-pharmaceutical options for hot flashes and other menopausal symptoms;
  - c. Tools for predicting menopause onset, including early detection of premature ovarian failure.

### Cross-Reference:

To see more on **burden of disease assessment**, see: Data and Modeling 1.3 and Communicable Diseases 7.1.

### Key Stakeholders:





## Cross-Sector Partnership for Women's Health Innovation



# 10 | Cross-Sector Partnership for Women’s Health Innovation

Partnerships—among funders, researchers, clinicians, payors, the private sector, communities, community organizations, and others—are a critical component in many of the opportunities and solution strategies outlined in this report. New or strengthened partnerships are needed to activate these solutions, building off the momentum of efforts to raise awareness, close data and funding gaps, and innovate to meet specific women’s health needs.

**There is a key gap—and opportunity—within the partnership landscape for a partnership model that spans the full scope of women’s health R&D.**

Women’s health R&D is under-resourced and under-prioritized across the broader health ecosystem due to lack of awareness, bias, and data gaps. Existing partnerships play a critical role in addressing these gaps for specific issues, but these efforts are often fragmented, siloed by condition or discipline. Building from the work done to date by the Innovation Equity Forum, a cross-sector partnership could unify these fragmented efforts toward a robust, well-funded, and equitable<sup>9</sup> women’s health R&D ecosystem.



**Current State:**  
Nascent, under-resourced, and siloed field(s)

**BARRIERS:**

- Lack of awareness
- Bias
- Lack of funding
- Siloed sectors
- Lack of data
- Inequitable partnerships
- Ineffective accountability

**A partnership that spans the full scope of women’s health R&D could unify fragmented approaches to addressing these barriers:**

- 1.** Convene stakeholders across women’s health R&D to advance the opportunities laid out in this report
- 2.** Position women’s health R&D as a priority within existing R&D partnerships and the broader health ecosystem
- 3.** Define, implement, and share models, incentives, and accountability approaches for equitable R&D partnerships



**Future State:**  
Robust, well-funded, and equitable ecosystem

**ATTRIBUTES:**

- More researchers, investors, funders
- Plentiful public and private funding
- Gender equity integral to health R&D
- Women and girls central as equal partners, representative of geographies and demographics
- Balanced and equitable distribution of power and resources
- More innovations introduced & scaled

<sup>9</sup> Equity as used in this report is defined in the key terms section. Equitable partnerships are structured to address the implications of power and resourcing disparities under the values of fairness, respect, care, and honesty to ensure effective research collaborations. For examples of equitable partnerships standards, see The Swiss Commission for Research Partnerships with Developing Countries (2018) and the TRUST Global Code of Conduct for Equitable Research Partnerships (2018).



**Opportunity 10.1** | Create a partnership with the objective to strengthen the R&D ecosystem across the full scope of women's health.

The 2023 Innovation Equity Forum (IEF) was unique in its scope, bringing together stakeholders across geographic regions to tackle the holistic topic of women's health R&D, including issues of both sex and gender; conditions that only impact women, disproportionately impact women, and affect women differently; and health and well-being across the life course. This 2023 Women's Health Innovation Opportunity Map is a tremendous milestone that we hope spurs innovation, investment, and partnerships to bring critical, accessible, life-improving, and life-saving solutions to women and girls. Yet this report alone will not achieve the intended level of impact without a dedicated partnership and forum to advance it.

The IEF showcased the potential of a coordinated effort across stakeholders, sectors, and geographic regions. We call for this momentum to be accelerated by **an inclusive and equitable multistakeholder partnership covering the full scope of women's health R&D under the auspices of a credible neutral convener**. Key roles for the partnership include:

**1. Convene stakeholders across the full scope of women's health R&D to advance the opportunities laid out in this report.** The primary role of the partnership will be to continue the work started through the IEF. This partnership should unite diverse stakeholders from different disciplines, sectors, issues, and geographic regions to work together under a shared goal and strategy to drive measurable progress and strengthen the overall ecosystem for women's health R&D. *Key activities include:*

- Identify and convene stakeholders<sup>10</sup> with global representation, both within and beyond the R&D space.
- Establish an equitable governance structure for shared and balanced decision-making across stakeholder groups.
- Establish a collaboration and coordination model for co-creating strategic priorities and implementing activities to advance the opportunities outlined in this report.
- Define goals and measurable indicators to monitor progress on this Opportunity Map, including how innovations are translated into healthcare in low-resource settings and the strength of the ecosystem for women's health R&D.

**2. Position women's health R&D as a priority within existing R&D partnerships and the broader health ecosystem.** There is growing awareness of the importance of ensuring health research and development is sex- and gender-intentional. However, prioritization of women's health is often notably absent from large-scale global health R&D efforts, such as epidemic preparedness, vaccine research, or non-communicable disease forums. A central role of the partnership will be to **activate a coordinated network of champions to center women's health R&D across the health ecosystem**. *Key activities include:*

- Define a collective advocacy, resource mobilization, and communication approach, including compelling narratives tailored to engage different stakeholders.
- Compile a compelling evidence base for advocacy demonstrating the financial, health, and societal return on investment for women's health R&D.
- Develop advocacy and activism tactics to motivate enabling policies, pledges, commitments, and scorecards to assess how well women's health R&D is embedded in other R&D partnerships.
- Identify and equip champions to advocate at global, regional, national, and product-and disease-specific forums for legislative action, political mandates, and accountability mechanisms for prioritizing women's health R&D.

**3. Define, implement, and share models, incentives, and accountability approaches for equitable R&D partnerships.** Inequity within health R&D is a pervasive issue that transcends women's health. This partnership cannot on its own solve the broader issues of equity, but it can work to **ensure that women's health R&D partnerships are intentional**

<sup>10</sup> See Stakeholders in the women's health R&D ecosystem, page 20.

**models for equitable partnerships.** With its deliberate focus on ensuring broad geographic representation and participation by civil society organizations, the IEF demonstrated an initial starting point for this objective. *Key activities include:*

- Identify and develop approaches for equitable R&D partnerships, addressing key drivers of inequity<sup>11</sup> and building on positive examples and lessons learned.
- Implement equitable R&D principles and practices in this partnership’s governance and actions, ensuring active leadership by patient advocate and women’s rights groups and equity across settings with different resource levels.
- Develop metrics and mechanisms to hold partners accountable to expectations<sup>12</sup> for equitable partnerships.

**Activating this partnership is a critical first step** in activating the opportunities laid out in this report. This effort requires a broad coalition of stakeholders — working together under a co-created and collaborative plan of action — to elevate women’s health R&D across their respective networks. A secretariat with dedicated execution capacity should support the partnership, and it should be resourced to provide participation support to civil society organizations, LMIC stakeholders, and other under-resourced entities. To achieve the ambition outlined in this report, **the partnership and effort must be funded proportionally to the aspiration for impact and scaled accordingly.**

#### Key Stakeholders:



#### Key Stakeholders

-  Communities and Community Organizations
-  Researchers and Academia
-  Health Care Workers and Systems
-  Public and Philanthropic R&D Funders
-  Private Sector
-  Payors and Insurers
-  Regulatory and Standard-Setting Agencies

<sup>11</sup> For more information, see Emanuel et al. (2004), Swiss Commission for Research Partnerships with Developing Countries (2018), and TRUST(2018)

<sup>12</sup> The Swiss Commission for Research Partnerships with Developing Countries (2018) and the TRUST Global Code of Conduct for Equitable Research Partnerships (2018) establish principles and values to guide equitable partnerships



# Conclusion

# Conclusion

This Opportunity Map outlines a bold and actionable plan to address critical priorities for advancing women's health innovation

The opportunities highlighted in this report have high potential for impact, readiness to scale, innovation feasibility, ability to improve health equity, and focus on women's unmet health needs. Each opportunity is scoped to be scalable and feasible, can advance within 1-5 years, and has the potential to improve women's health and well-being within 15 years. **Now is the time to reimagine the potential for women's health innovations and to work collectively to advance the health of all women equitably.**

Each opportunity and solution strategy serves as a call to action; we urge funders, innovators, researchers, and community partners to utilize this report as a guide for their own priority-setting efforts. While the central focus is on innovation, the opportunities also directly or indirectly address access, availability, and training to collectively contribute to improving health for women globally. Many opportunities and solution strategies are interconnected and cannot be pursued in isolation. **The entire R&D ecosystem, not just those focused on women's health, will benefit by working as a field to achieve the full ambition outlined in this Opportunity Map.**

## Looking Ahead

Publishing the Opportunity Map—and engaging over 250 experts from diverse sectors, geographic regions, and identities to develop these opportunities—marks the first step to gather stakeholders in the women's health R&D ecosystem and coalesce around potentially impactful investments to improve women's health. In the long term, the ambition of this work is to improve the health and well-being of women everywhere—by broadening and deepening the women's health innovation space, enabling larger and more targeted funding investments, and fostering inclusive, participatory partnerships. As more partners join the effort and propose innovations, the leading opportunities outlined here will continue to evolve. **Strengthening alignment among key stakeholders and sectors will be vital to advancing more equitable innovation for women's health.**

Investing in women's health innovations offers substantial benefits to women and their communities. Improved women's health contributes to stronger, healthier communities, increased economic productivity, and greater gender equity, thereby unlocking the full potential of half the world's population. **We can collectively foster a healthier and more equitable society through aligned efforts and a shared vision for a future of strengthened innovation, increased funding, and improved well-being for women worldwide.**

We call all innovators, influencers, and advocates from across the women's health R&D ecosystem to work together to realize the opportunities presented in this report, including:

**1 | Commit to equitable inclusion, participation, and funding of women** across the R&D continuum, including embedding sex and gender considerations at all stages.

**2 | Invest in the areas of women's health innovation** highlighted in this report that address critical needs for diverse groups of women and have high return on investment potential, including financial returns and health and social benefits.

**3 | Create a partnership** with the objective to strengthen the R&D ecosystem across the full scope of women's health.



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# Appendices

# Appendices

## Appendix 1: Methodological Detail

### About the CHNRI Method

Originally developed by the Child Health and Nutrition Research Initiative in 2007, the CHNRI method is a systematic yet flexible approach designed to set priorities in health research investments, which researchers have since adapted to broader applications (Rudan et al., 2008; Rudan et al., 2017). The method is led by process managers who systematically pool research ideas from a wide range of experts. The experts then score the ideas against predefined criteria. Strengths of the CHNRI method include its rigor, flexibility, transparency, and replicability.

CHNRI approaches typically apply the following steps:

1. Process managers specify the context, scope, and criteria for the exercise
2. Experts list a large number of proposed health research options
3. Synthesis and consolidation of proposed research options into a systematic list
4. Experts score the research options using the chosen set of criteria
5. Calculation of priority scores and criterion sub-scores for each research option

The Women’s Health Innovation Opportunity Map adapted the CHNRI method to generate and assess opportunities—including but not limited to research questions—that advance women’s health innovation from various stakeholder perspectives across the R&D ecosystem. The process is presented in **Figure 3** below.



### 1. Selecting topics and criteria (January–February 2023)

The Opportunity Map topics represent broad categories for advancing women’s health R&D within which specific needs and actions can be articulated. At the virtual kickoff Innovation Equity Forum meeting in January 2023, members contributed ideas for broad topics and selection criteria to guide opportunity generation. Following the meeting, the process managers<sup>13</sup> categorized members’ suggestions into nine topics, including cross-cutting and issue-specific themes. Forum members also volunteered to serve as sub-committee co-leads to oversee the opportunity generation by topic; **Figure 4** depicts the sub-committees formed around each topic and the appointed co-leads.

<sup>13</sup> The process managers comprised Maike Scharp of the Gates Foundation and Jamie White of NIH ORWH, who served as the Co-Chairs for the IEF and provided oversight on the Opportunity Map development process, and four consultants from Camber Collective, who provided strategic oversight, analytical and writing support, and project management support to the Forum and Co-Chairs.

**Figure 4: Topics and Co-Leads**

Cross-Cutting Topics	Issue-Specific Topics
<p><b>1 Data and modeling</b> Co-Leads: Monica Mallampalli, Zainab Samad</p>	<p><b>7 Communicable diseases</b> Co-Leads: Nkem Chukwueme, Sami Gottlieb, Jaishree Raman</p>
<p><b>2 Research design and methodologies</b> Co-Leads: Glenda Ernst, Michelle Oyen</p>	
<p><b>3 Regulatory and science policy</b> Co-Leads: Jerin Jose Cherian, Nada Hanafi</p>	<p><b>8 Non-communicable and chronic conditions</b> Co-Leads: Mariam Hassan, PK Morrow, Varun Renjen</p>
<p><b>4 Innovation introduction</b> Co-Leads: Brittany Barreto, Milly Nanyombi Kaggwa, Shirshendu Mukherjee</p>	
<p><b>5 Social and structural determinants</b> Co-Leads: Beth Garner, Sabrina Rasheed, Nyasha Sithole</p>	<p><b>9 Female-specific conditions</b></p> <p><b>Reproductive and maternal health</b> Co-Leads: Lisa Halvorson, Hrishikesh Pai</p> <hr/> <p><b>Gynecology and life stage conditions</b> Co-Leads: Rishma Pai, Stephanie Sassman</p>
<p><b>6 Training and careers</b> Co-Leads: Farah Asif, Leon McDougale, Mercedes Rumi</p>	
<p><b>10 Cross-Sector Partnership for Women’s Health Innovation</b> Co-Leads: Metin Gülmezoglu, Michael Santos</p>	

## 2. Developing opportunities (February–April 2023)

Forum members were invited to self-select their top three choices for one of eleven sub-committees to develop the scope, define the problem, and identify and score opportunities relevant to a specific topic. Individuals were placed in sub-committees based on their preferences, expertise, country of origin, and affiliation to ensure diverse perspectives and representation on all sub-committees. For the female-specific conditions topic, two sub-committees focused on reproductive and maternal health and gynecology and life stage conditions, respectively. An additional sub-committee focused on partnerships to advance women’s health innovation. Two to three members served as co-leads for each sub-committee, with co-leads representing both high- and low-resource settings.

From February through April, members submitted opportunity ideas through an online form and interactive whiteboarding sessions during sub-committee meetings. Members contributed to a long list of potential opportunities by drawing on their subject matter expertise to propose ideas that fill critical gaps and address key challenges. Members also reviewed existing resources and priority lists to include relevant opportunities in this exercise, and where additional expertise was needed, members consulted external experts.

The process managers logged all ideas in Microsoft Excel and filtered (ensuring alignment with project and topic scope) and synthesized (removing duplicates, combining similar options, rephrasing for clarity and consistency) the ideas to produce a systematic list.

### 3. Evaluating opportunities against the PRIME criteria (May 2023)

In May, sub-committees reviewed the long lists of opportunities for their topic to select no more than 15 per sub-committee that would move forward for scoring based on 1) alignment with the topic's scope and 2) likelihood to score favorably across all PRIME criteria. From May 26 – June 4, Forum members completed a scoring form administered with Qualtrics to independently evaluate opportunities by the PRIME criteria. Scorers leveraged their expertise to evaluate how each opportunity fulfills each of the PRIME criteria along a 7-point Likert scale, in which 1 represented "Very low," 4 represented "Moderate," and 7 represented "Very high." Scorers could optionally skip topics or criterion assessment questions to which they did not feel sufficiently informed to respond. They were also invited to assess whether each opportunity primarily applies to the US only, high-income countries (HICs), low- and middle-income countries (LMICs), or both HICs and LMICs. They could leave open-ended feedback on each topic, including questions, suggestions for rephrasing or clarity opportunities, or additional opportunity ideas.

### 4. Calculating Opportunity Scores and analyzing results (June–August 2023)

For each opportunity and each of the five PRIME criteria, the process managers calculated Criterion Scores, representing the mean score across all respondents. Composite Opportunity Scores were also calculated, combining two or more of the PRIME Criterion Scores to highlight different risk categories and help members consider the tradeoffs across opportunities. Sub-analyses also included examining the Criterion Scores by scorer characteristic, including by country income level, gender identity, and sector. Process managers calculated and analyzed the Criterion Scores and composite Opportunity Scores using Microsoft Excel. All respondents' data were kept confidential throughout the analysis. All scores and analyses are presented in Appendices 3-4.

Upon reviewing the Criterion Scores and composite Opportunity Scores, sub-committee members selected up to 10 opportunities to move forward for discussion and development at the IEF. At the IEF and in follow up discussions, members reviewed the scores and leveraged this information, along with previous discussions at sub-committee meetings, to select the top five opportunities to highlight in this report. They articulated and refined approximately three solution strategies per opportunity that offer specific actionable steps for different stakeholders.

Sub-committees were encouraged to keep the following lenses in mind as they developed opportunity ideas:

- **Serving the underserved:** Ensuring that opportunities do not overlook traditionally underserved populations
- **Sex and gender influences:** Considering both sex as a biological variable (SABV) and gender as a social construct
- **Life course perspective:** While much work in this space focuses on women of reproductive age, girls at an early age and women later in life should also be considered
- **Quality of life and well-being:** Not only focusing on reducing morbidity and mortality, but also ensuring that years lived are years in wellness

## The Innovation Equity Forum Convening: July 6–7, 2023 in Bethesda, Maryland

The Gates Foundation and NIH organized the IEF with the objectives to:

- Convene a **global community of key stakeholders** and gatekeepers of health innovation around women's health R&D
- Mobilize and accelerate innovations to improve women's health through shared **understanding of select critical women's health R&D priorities**
- Foster **cross-sector multinational partnerships** to advance R&D efforts in women's health innovation through enhanced coordination and collaboration

The IEF, which all Forum members were invited to attend, consisted of a series of plenaries, panels, and breakout discussions to advance specific solution strategies for each opportunity. The IEF, which all Forum members were invited to attend, consisted of a series of plenaries, panels, and breakout discussions to develop specific solution strategies for each opportunity. 148 people joined in-person and approximately 77 joined virtually.

### Limitations and mitigation

The results presented in this report should be considered in light of several limitations. First, the primary focus of this report is on research and product development for women's health. As such, the scope does not comprehensively address barriers to health care access or availability, patient education, or provider training on specific health care needs of women, all of which have a large impact on women's health. Nevertheless, many opportunities presented in the Opportunity Map will directly or indirectly improve access, availability, and training.

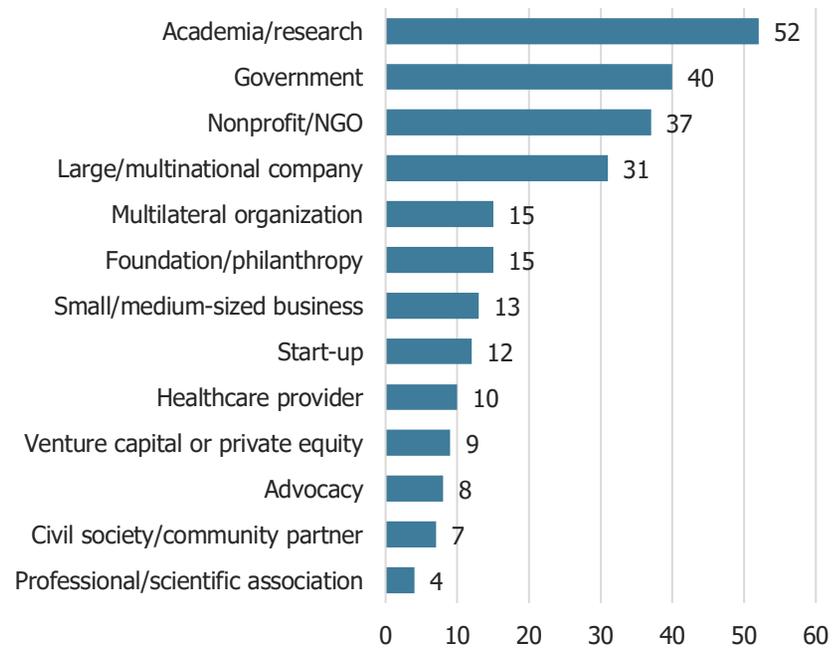
Second, the report may reflect biases of the authors. The project team utilized a tiered approach to stakeholder engagement to allow members to contribute to the project in a manner sustainable for them. While some members attended every meeting and contributed significantly to the Opportunity Map, others participated largely as observers, which may have influenced sub-committee decisions and the opportunities included in the report.

Similarly, while the Opportunity Map is intended to be reflective of global issues and values, the process was not fully representative given time and resource constraints. The Forum comprised members across sectors, geographic regions, and identities (see Appendix 2), but representation varied. For example, fewer participants represented publishers and regulatory agencies than other sectors, such as pharmaceuticals, academia, and philanthropy. Additionally, the power dynamics and inequities that exist in society may have influenced the input and participation of members, leading to biases in the results. As such, the full spectrum of interests and needs of all stakeholders may not be represented.

To mitigate these limitations, the Forum engaged in multiple iterations of brainstorming and feedback, including both in-person and virtual participatory meetings, asynchronous report reviews, and anonymous surveys. Additionally, the leadership team of each sub-committee included at least one Co-Lead representing a low- or middle-income country, to enable elevation of key issues that are pertinent to lower-resource settings.

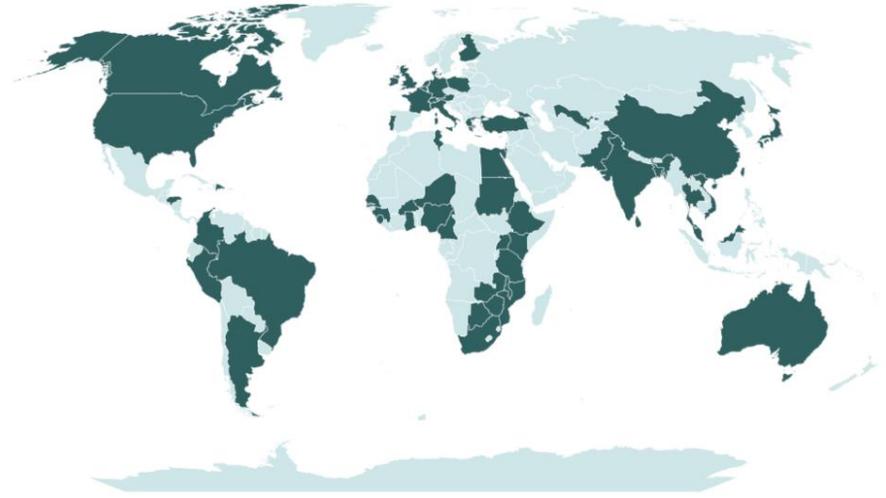
## Appendix 2: Innovation Equity Forum demographics

**Figure 5. Forum members' organizational sectors**

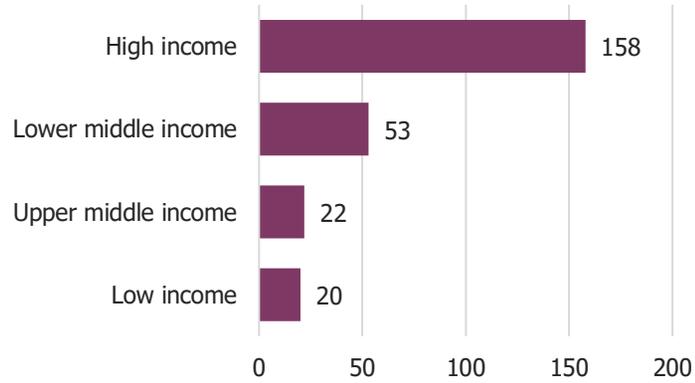


**Figure 6. Forum members' countries of origin**

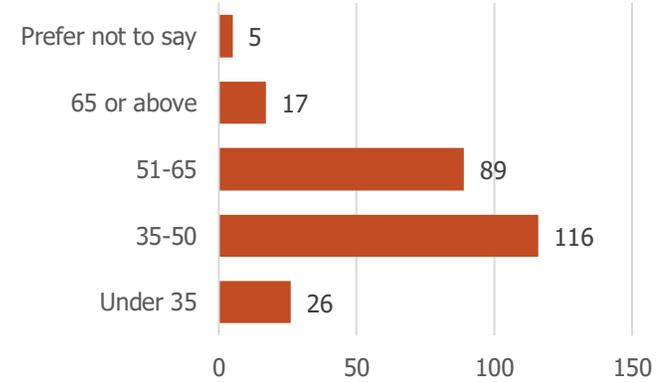
Many of the organizations represented by members have a regional or global mandate.



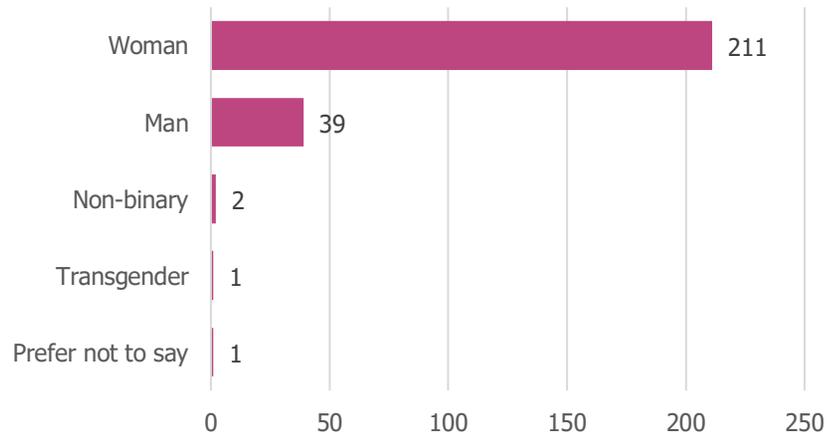
**Figure 7. Forum members' country of origin income level**



**Figure 9. Forum members' age ranges**

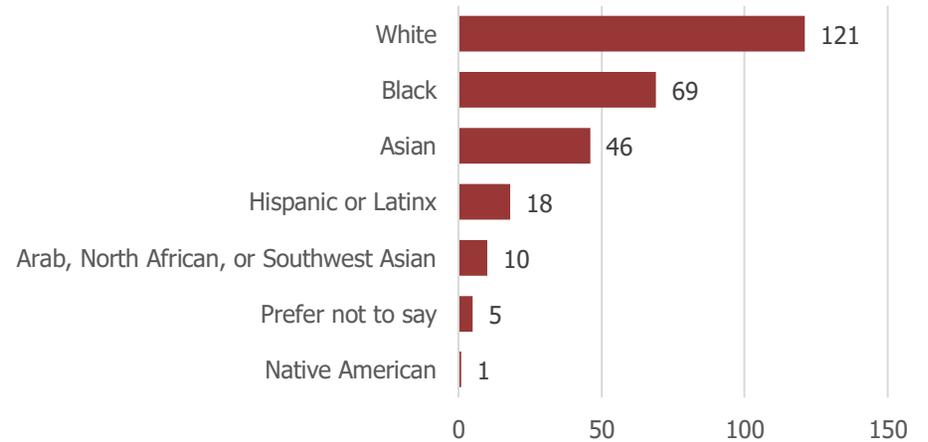


**Figure 8. Forum members' gender identity**



*Total exceeds 253 as some members selected more than one gender identity.*

**Figure 10. Forum members' racial and ethnic backgrounds**



*Total exceeds 253 as some members selected more than one racial and ethnic background.*

## Appendix 3: Summary of Criterion Scores by Topic and Criterion

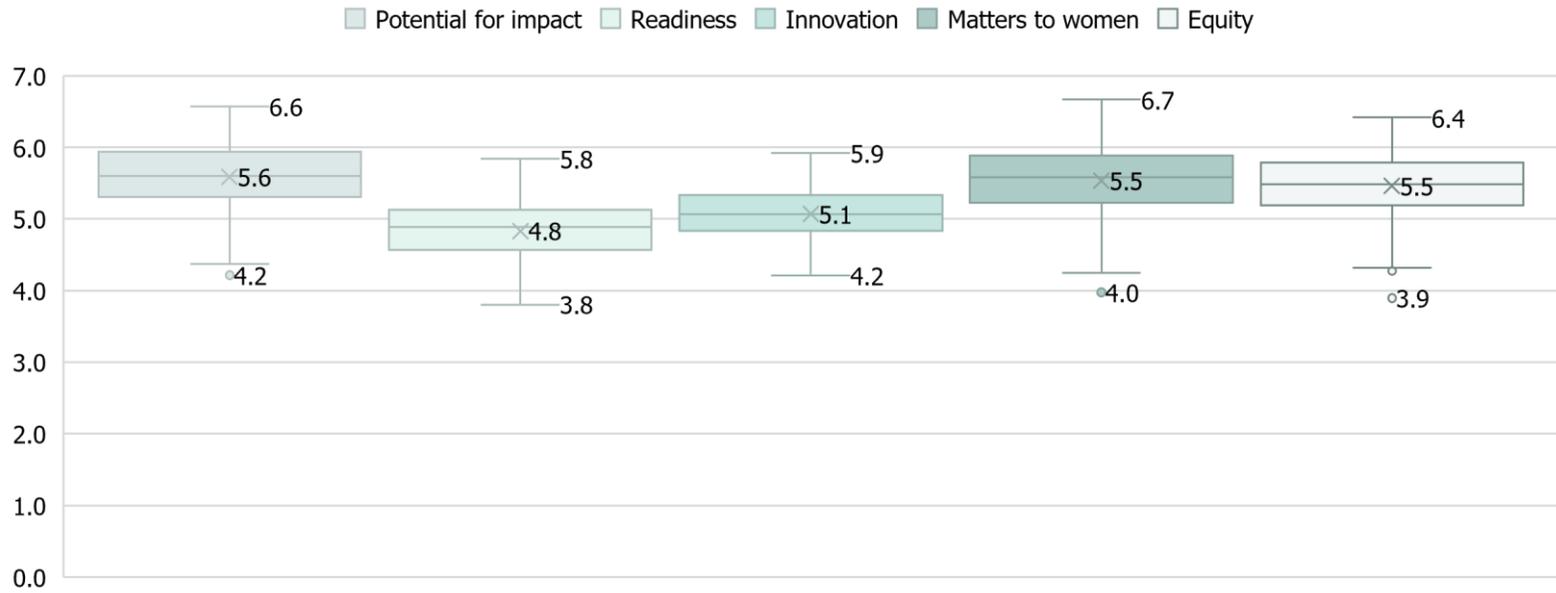
### Summary of Criterion Scores by Topic

Topic	Opportunities		Respondents		Average Criterion Scores				
	n	Min	Max	P	R	I	M	E	
<b>Data and Modeling</b>	13	44	55	5.3	4.6	4.9	5.1	5.1	
<b>Research Design and Methodologies</b>	11	36	46	5.6	4.9	5.3	5.2	5.2	
<b>Regulatory and Science Policy</b>	13	52	60	5.8	4.7	5.0	5.7	5.6	
<b>Innovation Introduction</b>	15	43	50	5.6	4.7	5.0	5.4	5.4	
<b>Social and Structural Determinants</b>	13	39	49	5.8	5.2	5.3	5.8	5.8	
<b>Training and Careers</b>	10	35	40	5.9	5.2	5.3	5.9	5.7	
<b>Communicable Diseases</b>	12	27	34	5.7	4.8	5.2	5.7	5.6	
<b>Non-Communicable and Chronic Conditions</b>	14	21	30	5.6	4.9	5.0	5.6	5.6	
<b>Reproductive and Maternal Health</b>	14	35	48	5.4	4.8	5.0	5.5	5.4	
<b>Gynecology and Life Stage Conditions</b>	13	30	40	5.4	4.7	4.9	5.5	5.4	
	128			5.6	4.8	5.1	5.5	5.5	

*Minimum and maximum respondents refers to the minimum and maximum who scored any criterion for any opportunity within the specific topic, as participants were able to skip any criterion assessments that they did not feel sufficiently informed to complete.*

*Average Criterion Scores are the mean of the criterion score across all opportunities with a topic.*

### Distribution of Criterion Scores by Criterion



*Minimums, averages, and maximums of Criterion Scores for each PRIME criterion: Potential for Impact, Readiness, Innovation, Matters to Women, and Equity.*

## Appendix 4: Criterion Scores by Topic

Criterion scores are presented for each of the opportunities evaluated against the PRIME criteria (up to 15 per topic).

\* Opportunities that are highlighted in this report are starred, including where multiple of the opportunities below were combined into a final opportunity or solution strategy as phrased in the body of the report.

### 1. Data and Modeling

#	Opportunity	P	R	I	M	E
1*	Update and expand burden of disease metrics to better account for sex- and gender-related conditions, long-term sequelae, and socio-cultural gender biases (e.g., input data gaps, disability weighting, duration assumptions, etc.)	5.5	4.9	5.0	5.6	5.8
2*	Generate more granular data on disease occurrence and determinants to inform prioritization, models (baseline and training data), and product development (including real-world evidence) for women's health across the life course	5.4	4.6	4.9	5.4	5.6
3	Increase digital wearable device data collection with a sex and gender lens (e.g., masks, spirometers)	4.5	4.5	4.8	4.4	4.0
4*	Build capacity for sex- and gender-sensitive data collection among researchers, local health workers, community leaders, and women themselves to ensure women's needs and voices are represented	5.6	4.6	4.9	5.6	5.4
5	Increase representation and identification of women in bio-repositories for women's health, including blood and urine samples	5.4	4.7	5.0	5.2	5.2
6*	Fill data gaps needed to calculate return on investment (ROI) in women's health R&D, including economic models and ROI for disease-specific areas	5.5	4.5	4.8	5.0	5.2
7*	Create an international data and modeling community of practice across sex, gender, and social determinants of health stakeholders to establish recommendations for standardized methods of collecting, reporting, analyzing, and disseminating health data in a sex- and gender-specific way; to ensure implementation; and to engage in continuous learning	5.8	4.7	5.0	5.3	5.7
8*	Develop study networks for research and data harmonization to ensure adequate and appropriate data collection for women across the life course – from pre-puberty through post-menopause	5.6	4.7	4.9	5.3	5.4
9	Understand how data standards frameworks (like FAIR data principles: findability, accessibility, interoperability, reusability) are used and what gaps need to be filled in the ethical governance of data	4.5	4.5	4.2	4.3	4.6
10	Develop complex benefit and risk prediction models specifically to examine women's health outcomes and behaviors across the life course (through longitudinal studies), including by integrating sex and gender into models	5.4	4.2	4.9	5.4	5.2
11*	Develop approaches for incorporating qualitative information and proxy indicators – including unstructured narrative data – into models	4.2	4.0	4.4	4.4	4.3
12	Develop simulation models of diseases and disorders relevant to women, ensuring sex and gender are considered in the design	5.1	4.3	4.8	4.7	4.7
13	Promote ethics and standards development for big data, artificial intelligence (AI), machine learning (ML), and other critical and emerging technologies relevant to women's health, e.g., ensuring bias mitigation across the development and implementation of structured and unstructured models	5.9	4.9	5.4	5.7	5.7

## 2. Research Design and Methodologies

#	Opportunity	P	R	I	M	E
1*	Advance gender- and sex-intentional study design during all stages of research (at cell, animal, and in-vitro level and in trials) and at all ages, to generate endpoints, outcome measures, and evidence relevant for women, and to evaluate heterogeneity of treatment effect by sex and gender	6.3	5.5	5.9	6.0	6.0
2	Feature and draw from best practices and exemplars in promoting the inclusion of women throughout the research and data lifecycle, including culture shifting practices	5.5	5.4	5.0	5.8	5.6
3*	Promote knowledge- and resource-sharing on the preclinical and clinical research landscape in LMICs and other under-resourced settings to strengthen research activities and promote collaborations	5.5	5.0	5.0	5.1	5.4
4*	Design trials to accommodate the unique needs of women both in and out of the formal workplace (e.g., remote trial participation options, satellite sites, wearables) and increase representation of traditionally underrepresented demographics	5.7	5.0	5.3	5.8	5.9
5	Develop or expand pregnancy registry studies and other study designs for robust data collection to answer key questions about use of treatments in pregnancy	5.9	5.3	5.2	6.1	5.7
6*	Apply community engagement good practices for the co-production of user-focused research questions and study design	5.3	5.2	5.0	5.4	5.5
7	Investigate how to optimize personalized medicine (e.g., genetics, imaging data, phenotypes) for women's health	5.6	4.6	5.4	5.2	4.9
8*	Improve machine and deep learning approaches to better understand the biological underpinning of disease and inform product development, risk identification, and treatment approaches, including by leveraging existing data sets and non-biased common data elements	5.7	4.7	5.4	4.9	4.9
9*	Strengthen use of computational and bioinformatics modeling (and reduce use of animal models)	5.0	4.1	5.1	4.0	3.9
10*	Support in-vitro translational model development – such as organoids and organ-on-a-chip systems – to ensure more extensive clinical/translational characterization of disease and differences by sex and gender	5.2	3.8	5.3	4.6	4.5
11*	Encourage open science and open innovation to enhance transparency and accelerate R&D, including collaboration, re-using data, making use of routinely collected data, and promoting uniform standards for data labeling and sharing	5.9	5.0	5.1	4.7	5.1

### 3. Regulatory and Science Policy

#	Opportunity	P	R	I	M	E
1*	Ensure sex- and gender-intentional science policy frameworks covering all aspects of the R&D lifecycle for medical products and health care innovations	6.1	4.9	5.2	6.2	6.1
2	Ensure harmonization and collaboration mechanisms between funders, researchers, publishers, regulatory agencies, and civil society to accelerate the development of innovations that improve women's health	6.1	4.6	5.0	5.7	5.7
3*	Assess and implement regulatory and policy incentives to increase the pace and volume of development, market authorization, and access to innovations that improve the health of women	6.0	4.6	4.8	5.6	5.6
4*	Develop policy and regulatory instruments to ensure new products coming to market have sex- and gender-inclusive evidence at all stages of product development	5.9	4.5	5.2	5.8	5.6
5	Synthesize and increase adoption of guidance for the responsible and equitable inclusion of pregnant and lactating women in different stages of research, and address outstanding barriers to conducting clinical trials in these populations	6.0	4.9	5.2	6.2	5.9
6	Synthesize and increase adoption of guidance for the appropriate inclusion in research of all women throughout the lifecycle – including women of reproductive age, elderly women, and pre- and post-menopausal women	6.2	5.3	5.4	6.2	6.2
7	Promote engagement and collaboration among regulatory decision-makers on their role in ensuring sex and gender considerations throughout the regulatory and policy lifecycle	5.4	4.6	4.6	5.3	5.5
8*	Require legal and/or regulatory frameworks covering all aspects of the R&D lifecycle for medical products and health care innovations to systematically apply sex- and gender-intentional approaches	5.7	4.4	4.8	5.5	5.5
9*	Promote regulatory reforms to ensure clinical studies capture differences in disease trajectory and outcomes across sex and gender, including novel endpoints, to improve the development of sex- and gender-specific treatment options	5.9	4.6	5.0	5.7	5.6
10*	Develop flexible regulatory paradigms that balance pre- and post-market requirements for innovations that improve the health of women, including the use of real-world evidence	5.2	4.6	4.8	5.2	5.1
11*	Drive sex-, gender-, and age-disaggregated post-market surveillance (pharmacovigilance, medical device reporting) and standardized indicators specific to women's health (e.g., interactions between interventions and menstrual cycles) to improve confidence around safety and uncover sex- and gender-related differences in safety outcomes	5.9	5.1	5.4	5.9	5.8
12*	Require reporting of sex- and gender-specific outcomes in health care product labeling and package inserts (e.g., efficacy cutoffs and pharmacokinetic/pharmacodynamic (PK/PD) differences by sex)	5.6	4.7	5.0	5.7	5.3
13	Align regional, national and/or subnational regulatory policies to promote product authorization and introduction	5.2	4.1	4.7	5.0	5.2

#### 4. Innovation Introduction

#	Opportunity	P	R	I	M	E
1*	Encourage market-shaping approaches (e.g., joint funding, pooled procurement, advance purchase orders, procurement guarantees) that enable suppliers to develop innovations accessible in LMIC settings, by incentivizing payors and market entry and addressing demand and scale issues	5.8	4.7	5.2	5.4	5.5
2	Establish joint marketplaces for the delivery of women's health innovations, with opportunity to build supply chain and distribution synergies	5.3	4.4	4.7	5.2	5.2
3*	Develop the community of entrepreneurs that want to provide access to innovations in LMICs – including strengthening networks of venture capitalists and angels, educating on LMIC market entry and commercialization strategies, and building shared availability of market information and data	5.6	5.0	5.2	5.6	5.7
4*	Develop innovative funding opportunities, including from untraditional bodies and collaborations between public sector, academia, global/regional entities, and industry to accelerate innovation (e.g., regional innovation hubs, issue-specific challenges)	5.9	5.1	5.3	5.5	5.5
5	Coordinate philanthropic, public, multilateral, and private capital to increase and harmonize women's health R&D investments	5.5	4.6	4.9	5.4	5.3
6	Develop dedicated, long-term, sustainable funding opportunities with components that allow for learning adaptations (e.g., milestone-based financing), and coordinate among funders to prevent fragmentation of long-term funds	5.6	4.5	4.9	5.2	5.2
7*	Incentivize the payment of women's health services or products within diverse reimbursement infrastructures, including for private, commercial, and government payors – e.g., by inventorying and fast-tracking billing codes, understanding metrics for consideration of coverage, and promoting accountability for coverage of women's health solutions	5.5	4.2	4.7	5.6	5.6
8*	Develop stronger mentorship, incubation, and acceleration for founders of companies improving women's health (catering to different needs of HIC and LMIC settings)	5.8	5.3	5.3	5.6	5.3
9*	Establish principles and operational mechanisms for transparency and collaboration along the women's health R&D value chain, including for technology transfer, intellectual property, and information and data sharing	5.3	4.7	4.9	5.2	5.2
10	Ensure that sex, gender, and social determinants of health are considered in the initial design and across the product development lifecycle, by designing products with the explicit goal of providing end-user value (not just clinical or economic value)	6.0	5.0	5.5	5.8	5.9
11	Develop products and solutions that address access challenges for underserved populations, e.g., products that are low-cost, accessible at the point-of-care, and independent of health system constraints	6.3	5.3	5.7	6.2	6.4
12*	Improve the availability and collection of data on user needs, product requirements, and effective delivery approaches, and strengthen scientific rigor in data analysis	5.5	5.0	5.1	5.3	5.2
13	Build medical affairs capabilities specific to women's health in order to align clinicians on the most important clinical endpoints and indicators, as well as definition of clinical success	5.3	4.6	4.8	5.2	5.0
14	Reduce media censorship of women's health products	5.3	4.4	4.8	5.5	5.2
15	Uncover/establish exits for companies working in this space	4.6	4.1	4.5	4.7	4.3

## 5. Social and Structural Determinants

#	Opportunity	P	R	I	M	E
1*	Ensure that national and global research agendas are guided by women's needs and voices through broad representation and reflection of different communities (i.e. representation in policy decisions impacting women's health)	6.6	5.3	5.5	6.7	6.4
2*	Develop equitable standards for inclusion of social determinants of health considerations for women's health research	6.0	5.1	5.4	6.1	6.1
3	Demonstrate investment cases in developing products that address social determinants of health in both general and vulnerable populations of women and de-risk investment of new funders	5.6	4.9	5.2	5.8	5.7
4*	Include sexual and gender minority representation in review panels for research grants in women's health R&D	6.0	5.2	5.3	5.8	6.0
5	Measure data on community and network effects, both beneficial and harmful, from women's health R&D interventions (e.g. change in household income levels, community literacy)	5.5	5.0	5.1	5.5	5.5
6	Conduct observational research on novel social determinants of health interventions through natural experiments	5.2	5.0	5.3	5.4	5.3
7	Research women's health R&D with a syndemic approach through simultaneous exploration of diseases and their social contexts	5.6	5.0	5.4	5.6	5.6
8	Close the digital divide by enabling contextually appropriate and accessible data collection from women (e.g., through cellphones, non-Wi-Fi enabled devices)	5.6	5.2	5.1	5.3	5.6
9*	Research the impacts of gender roles and economic agency (e.g., decision-making, unpaid work) on women's health	5.8	5.2	5.4	5.7	6.0
10	Investigate occupational impacts on women's health (e.g., caregiving role, structural policies such as family leave)	5.8	5.4	5.3	6.0	5.9
11*	Conduct a global review of social determinants of health interventions with an emphasis on those that focus on vulnerable populations of women (in low-resource settings, unhoused, rural, immigrants/refugees)	5.8	5.3	5.4	5.9	6.1
12*	Research traditional and cultural practices that promote women's health outcomes and well-being	5.6	5.5	5.1	5.6	5.6
13	Investigate the complex interplay between economic factors, climate, and diseases/conditions affecting women	5.7	5.1	5.3	5.5	5.7

## 6. Training and Careers

#	Opportunity	P	R	I	M	E
1*	Develop and integrate sex and gender considerations into educational content for health and R&D fields at all levels, ensure its inclusion, and assess its impact	6.0	5.3	5.3	5.9	5.7
2*	Develop and integrate sex- and gender-considerations into educational content for entrepreneurial and related fields – including finance, information systems, bioethics, etc.	5.5	4.8	4.9	5.4	5.4
3*	Train educational policymakers and institution decision-makers on integrating sex- and gender considerations into education and training	5.9	5.1	4.9	5.8	5.4
4	Develop incentives and support within educational institutions to study and teach sex- and gender-based health	5.6	4.9	5.1	5.4	5.4
5*	Investigate barriers to women’s career participation, progression, and leadership in R&D fields and institutions	6.1	5.6	5.6	6.2	6.1
6*	Investigate how successful organizational policies and practices have overcome barriers to women’s career progression, and share guidance and actionable learnings	6.1	5.6	5.5	5.9	5.7
7	Strengthen equitable family leave and re-entry policies for women at all stages of their R&D-related careers, and build upon the evidence base for effectively implementing such policies to enable harmonization	6.0	4.9	5.2	6.3	5.8
8*	Develop objective assessments for legal provisions and policy reforms that enable women’s equitable career progression	5.6	4.7	5.0	5.7	5.5
9	Foster networking, mentorship, sponsorship, and capacity-building opportunities for women science and entrepreneurial leaders that are accessible for institutions to use and adapt	6.2	5.8	5.9	6.3	5.9
10*	Enhance men's allyship to activate opportunities for women and girls to pursue STEMM, R&D, and entrepreneurship careers and leadership positions	5.9	5.1	5.2	5.9	5.7

## 7. Communicable Diseases

#	Opportunity	P	R	I	M	E
1*	Evaluate sex- and gender differences in infections, particularly emerging pathogens and outbreak diseases, in terms of burden, modes of transmission, clinical presentations, antimicrobial resistance, and long-term outcomes, to inform appropriate prevention and treatment measures for women	5.9	4.9	5.6	5.7	5.7
2*	Develop and evaluate vaccines and other prevention interventions for infections that have a disproportionate impact on women (e.g., HIV, and selected STIs, outbreak pathogens, and neglected tropical diseases)	6.2	4.8	5.3	5.9	5.9
3	Develop innovative methods for preventing UTIs, e.g., non-antimicrobial methods	5.0	4.3	4.5	5.3	4.9
4*	Develop improved diagnostic tools for STIs and other reproductive tract infections, including affordable point-of-care and self-testing products	6.3	5.2	5.6	6.1	5.9
5	Explore sex and gender differences in immune responses to infections and vaccines, including autoimmune responses, that can be exploited to improve prevention and treatment measures for women	5.2	4.2	5.0	5.0	4.9
6*	Investigate interactions between chronic or co-morbid conditions that disproportionately affect women with infectious conditions to improve prevention and management	5.6	4.6	5.2	5.7	5.4
7	Test effectiveness of sex- and gender-intentional* m-Health and telemedicine strategies, with a focus on women living in remote areas, to increase treatment follow-up rates, especially for long-term treatment such as tuberculosis and HIV	5.7	5.1	5.5	5.7	5.7
8*	Develop and evaluate improved therapies for infections in women, including during pregnancy	6.2	4.9	5.2	5.8	5.9
9	Ensure evaluations of health interventions for infectious conditions (e.g., diagnostics, therapies, prevention measures) involve women, including pregnant and lactating women, from the earliest stages	6.0	5.1	5.5	6.1	6.3
10*	Test the efficacy/effectiveness, safety, and feasibility/acceptability of maternal vaccination for common infectious diseases and outbreak pathogens (e.g., COVID-19, RSV, malaria, group B strep, Ebola, Zika)	5.9	4.7	5.1	5.9	5.6
11	Stimulate R&D on the role of the vaginal microbiome in health and the prevention, diagnosis, and treatment of bacterial vaginosis	5.5	4.6	5.0	5.4	5.1
12*	Investigate the burden and costs of infertility and other adverse reproductive tract outcomes due to infectious conditions (e.g., gonorrhea/chlamydia, BV, genital schistosomiasis, TB)	5.3	5.2	5.3	5.9	5.5

## 8. Non-communicable and Chronic Conditions

#	Opportunity	P	R	I	M	E
1*	Evaluate sex-related differences in responses to cardiometabolic medications and consequent implications for development of future treatments for women	5.6	5.1	5.2	5.8	5.7
2	Research non-invasive, accessible and reliable testing for NCDs at the point-of-care to increase early detection and connection to treatment	6.1	5.4	5.6	5.9	5.9
3	Investigate how chronic pain is experienced differently across sexes and genders to create disaggregated measurement	4.9	4.6	4.4	5.1	5.1
4*	Evaluate sex- and gender-related differences in responses to oncology medications (including immunotherapy, targeted therapy, and chemotherapy) and consequent implications for development of future treatments for oncology diseases for women, such as for lung, cervical, and other cancers	5.6	4.9	5.2	5.9	5.4
5	Research mechanisms to improve the diagnosis and treatment of cancer during pregnancy in women	4.9	4.5	4.5	5.6	5.3
6*	Develop diagnostic tools and treatments that are able to take gender-specific elements into account for mental health disorders – including their impact on NCD control – across diverse contexts and across the life course	6.0	5.3	5.2	6.1	5.8
7	Develop or improve tools/equipment that take into account women's anatomy and physiology and will help to address musculoskeletal disorders (e.g., osteoporosis, osteoarthritis) and prevent injuries that become chronic conditions and long-term sequelae	5.2	4.4	4.6	5.4	5.2
8	Research impacts of gender-based violence/sexual assault on women's physical and mental health to inform interventions	6.1	5.5	5.5	6.3	6.2
9	Research prophylactics and treatments for victims of sex trafficking and rape, e.g., to prevent pregnancy and transmission of diseases and to treat pain, PTSD, etc.	5.5	4.8	5.0	5.8	5.8
10*	Evaluate sex- and gender-related differences in responses to autoimmune disorder medications and consequent implications for development of future treatments for autoimmune diseases for women	5.4	4.7	4.7	5.2	5.4
11*	Evaluate sex- and gender- related differences in responses to neurodegenerative medications and consequent implications for development of future treatments for neurodegenerative diseases for women	5.2	4.7	4.8	5.2	5.3
12	Research diagnostics for neurodegenerative disorders for use in low-resource settings	5.3	4.5	4.9	5.1	5.3
13	Develop digital tools to help improve diagnosis of chronic diseases that affect women disproportionately or differently	5.7	5.1	5.1	5.6	5.4
14	Develop evidence-based guidelines on available low-cost solutions for NCDs that can be used in low-resource settings (e.g., off-patent cancer drugs or immune-modulators)	6.2	5.3	5.4	6.0	6.0

## 9. Reproductive and Maternal Health

#	Opportunity	P	R	I	M	E
1	Conduct robust clinical lactation studies	4.8	4.5	4.6	5.1	5.0
2*	Increase the quantity and diversity of blood and breast milk samples to enable research	4.5	4.1	4.5	4.5	4.4
3	Conduct research to develop a publicly accessible knowledge bank for up-to-date information about best practices and safety for prescription and over-the-counter (OTC) medication use during pregnancy and breastfeeding	5.5	4.9	5.0	5.5	5.3
4*	Develop improved, accessible contraceptive technologies with fewer side effects and longer efficacy	6.1	5.5	5.4	6.3	6.0
5	Research pain prevention and management strategies related to reproductive and maternal health conditions (e.g., IUD insertion, pain management during labor)	5.4	4.9	4.9	5.7	5.4
6*	Understand the implications of policies related to safe abortion access on the ability to conduct sexual and reproductive health research (including requirements imposed by international funders)	6.0	5.0	5.4	6.1	6.2
7*	Investigate infertility etiology, including in males, to develop new, less expensive diagnostic tools and treatments	5.3	4.3	4.7	5.4	5.2
8	Investigate fertility preservation strategies	4.6	3.9	4.4	4.8	4.3
9	Develop tools – including AI/ML prediction – for pregnancy, intrapartum, and postpartum monitoring and management	5.6	5.0	5.5	5.5	5.5
10	Develop pre-conception and pregnancy-related point-of-care diagnostics to assess nutrition status, anemia, infections, gestational diabetes, etc.	5.8	5.0	5.6	5.7	5.8
11*	Increase research on prenatal, intrapartum, and postpartum conditions and risk factors associated with adverse maternal health outcomes (e.g., PPH, pre-eclampsia) to enable development of diagnostics, treatments, and prevention	6.4	5.6	5.7	6.4	6.3
12	Develop treatment for women in spontaneous preterm labor	5.7	4.7	4.9	5.8	5.7
13*	Investigate evidence gaps in understanding of the role of micronutrients, including iron and folic acid, and their composition for improving maternal outcomes, with a particular focus on LMICs	5.4	5.1	4.7	5.2	5.3
14	Investigate the role of the microbiome during pregnancy and lactation to improve maternal and infant health	5.1	4.6	4.8	4.7	4.9

## 10. Reproductive and Maternal Health

#	Opportunity	P	R	I	M	E
1*	Investigate the biological mechanisms that drive the development of female gynecological health conditions – such as polycystic ovary syndrome (PCOS), endometriosis, adenomyosis, fibroids, and heavy bleeding – and how understanding these mechanisms can be leveraged for prevention	5.9	4.9	5.0	5.9	5.9
2	Develop tools and therapies to improve diagnosis, treatment, and non-invasive monitoring of female gynecological health conditions – such as PCOS, endometriosis, adenomyosis, fibroids, and heavy bleeding – including by developing novel endpoints, biomarkers, and non-clinical models of disease to de-risk product development	6.2	5.1	5.4	6.1	5.9
3*	Conduct research on the vaginal microbiome and broad reaching effects relevant to gynecologic conditions	5.0	4.5	4.6	5.0	4.7
4	Develop tools suitable for low-resource settings for screening (including self-screening) and monitoring of cervical, uterine, and ovarian cancers, fibroids, and endometriosis	6.4	5.3	5.5	6.4	6.1
5	Conduct research to improve understanding of exposures and risks of developing pelvic pain and vaginal tension and how they present across gynecological conditions, to develop novel non-invasive diagnostics and therapies for pelvic floor disorders	4.9	4.1	4.5	5.3	5.3
6*	Develop novel treatment options for different types of urinary incontinence	5.4	4.6	4.6	5.7	5.4
7	Develop more eco-friendly choices for women to relieve involuntary urine loss, vaginal discharge, and menstruation	5.1	4.6	5.0	5.2	5.1
8*	Develop and test in women new biomaterials for gynecological conditions (such as mesh products) to ensure safety and efficacy	4.4	3.9	4.4	4.6	4.6
9	Investigate the biological mechanisms driving pre-menstrual syndrome (PMS) and novel solutions to mitigate adverse impacts it has on the women's lives	4.7	4.2	4.5	5.2	5.1
10	Conduct research to understand the implications of hormones (endogenous and exogenous) over the course of a woman's lifecycle on the incidence, progression, and treatability of diseases	5.2	4.6	4.6	5.5	5.4
11*	Investigate the pathophysiology of menopausal symptoms to support development of novel, evidence-based, specific treatments for symptoms of menopause (e.g., hot flashes, night sweats, and insomnia)	5.8	4.9	5.0	5.9	5.5
12	Develop comprehensive estimates of the epidemiology, health impacts, and burden/cost to society of gynecological and life stage conditions	5.6	4.9	5.1	5.5	5.4
13	Promote collaboration between researchers and companies focused on gynecological conditions	5.8	5.4	5.6	5.3	5.3

# Online Supplemental Appendices

## Supplemental Appendix 1: Innovation Equity Forum membership

The full roster of Innovation Equity Forum members can be found via the link below.

<https://orwh.od.nih.gov/resources-training>

## Supplemental Appendix 2: Detailed PRIME scores

The detailed PRIME scores can be found via the link below. Criterion scores are presented for each of the opportunities evaluated against the PRIME criteria (up to 15 per topic).

Geographic applicability indicates the percentage of respondents indicating that the opportunity is primarily applicable to: the US only, HICs, LMICs, or both HICs and LMICs.

Tables also display scores by scorer demographic, including gender identity, HIC/LMIC country of origin, and sector. For sector, respondents' primary organizations we categorized into three groupings:

1. "Funders and innovators:" Multilateral, government, foundation/philanthropy, VC or private equity, startups, small/medium businesses, large/multinational companies
2. "Academics and health professionals:" Academia/research, healthcare provider, professional/scientific association
3. "Community partners:" Nonprofit/NGO, civil society/community partner, advocacy

<https://orwh.od.nih.gov/resources-training>

