

The Health of Women and Chronic Debilitating Conditions Clinical Application and Research Framework

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**School of Medicine
Greenville**

Disclosure

No relationship or financial conflicts of interests to disclose.

The statements and opinions expressed are those of the speaker and do not represent University of South Carolina or Prisma Health

An ad hoc committee of the National Academies of Sciences, Engineering, and Medicine will:

1. Review the existing literature on chronic debilitating conditions specific to women.
2. The review will consider:
 - The epidemiology of chronic debilitating conditions including gender and racial and ethnic differences in clinical presentation and outcomes
 - How the development and accumulation of chronic debilitating conditions in women are influenced by factors such as menopause, aging-related skeletal muscle dysfunction (loss of muscle mass, muscle strength, and muscle function), and frailty
 - Prevention, diagnosis, and treatment of female-specific gynecologic conditions
 - To the extent possible, the social and economic impact of chronic debilitating conditions
3. Assemble evidence-based findings on chronic debilitating conditions in women.
4. The findings should incorporate the influence of social determinants of health, including but not limited to gender, race and/or ethnicity, socioeconomic status, sexual and gender minorities, and underserved rural populations
5. Produce a report that describes current gaps in evidence and provides a suggested research agenda for the future

REVIEW THE EXISTING LITERATURE

ASSEMBLE EVIDENCE-BASED FINDINGS

- Not a universally accepted definition of gender
- Lack uniform knowledge of when science should utilize the terms sex and gender
 - recognition sex & gender are not interchangeable
- Limitations of literature search engine capabilities
- No mandatory reporting of sex and gender analysis and/or limitations to sex and gender analysis

> [Addict Biol.](#) 2022 Nov;27(6):e13236. doi: 10.1111/adb.13236.

Gender differences in cocaine-induced hyperactivity and dopamine transporter trafficking to the plasma membrane

Jing Deng ^{1 2}, Xirong Zheng ^{1 2}, Linyue Shang ^{1 2}, Chang-Guo Zhan ^{1 2}, Fang Zheng ^{1 2}

Affiliations + expand

PMID: 36301205 PMCID: PMC9625146 (available on 2023-11-01) DOI: [10.1111/adb.13236](#)

Abstract

As well known, cocaine induces stimulant effects and dopamine transporter (DAT) trafficking to the plasma membrane of dopaminergic neurons. In the present study, we examined cocaine-induced hyperactivity along with cocaine-induced DAT trafficking and the recovery rate of the dopaminergic system in female rats in comparison with male rats, demonstrating interesting gender differences.

> [J Chem Neuroanat.](#) 2022 Jul;122:102092. doi: 10.1016/j.jchemneu.2022.102092.

Epub 2022 Mar 29.

Gender differences in effects of prenatal and postnatal exposure to electromagnetic field and prenatal zinc on behaviour and synaptic proteins in rats

Burcu Acikgoz ¹, Nevin Ersoy ², Ilkay Aksu ³, Amac Kiray ⁴, Husnu Alper Bagriyanik ², Muge Kiray ⁵

Affiliations + expand

PMID: 35364275 DOI: [10.1016/j.jchemneu.2022.102092](#)

Gender differences pharmacokinetics, bioavailability, hepatic metabolism and metabolism studies of Pinnatifolone A, a sesquiterpenoid compound, in rats by LC-MS/MS and UHPLC-Q-TOF-MS/MS.

Peng W, Li Z, Cai D, Yi X, Yue Jeff Zhang J, Zhong G, Ouyang H, Feng Y, Yang S.

Phytomedicine. 2023 Jan;109:154544. doi: 10.1016/j.phymed.2022.154544. Epub 2022 Nov 13.

PMID: 36610155

This difference in **rat** genders may pertain to the **sex**-specific expression of hepatic enzymes as demonstrated in the metabolic stability evaluation in the present research; the male **rats** exhibited higher CL(int(mic)) (158.839.57 mul/min/mg protein) than female ...



Mary Ann Liebert, Inc. publishers

JOURNAL OF NEUROTRAUMA

Journals

Search

Alerts

[J Neurotrauma.](#) 2019 Jun 15; 36(12): 1974–1984.

Published online 2019 May 28. doi: [10.1089/neu.2018.6233](#)

PMCID: PMC6599384

PMID: [30489213](#)

Functional and Histological Gender Comparison of Age-Matched Rats after Moderate Thoracic Contusive Spinal Cord Injury



RESOURCES

These resources are freely available and are intended to facilitate the research, creation, and dissemination of sex and gender education information.

Announcements

Sex and Gender Education Materials

NIH Courses on Sex and Gender Influence on Health and Disease

Slide Set How-To Guides

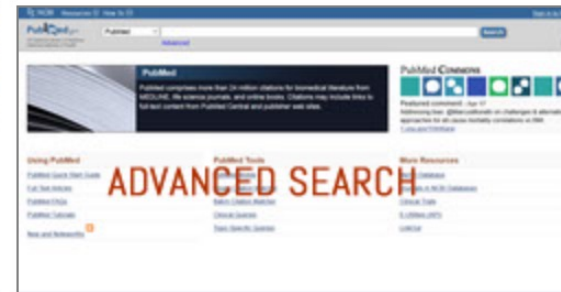
Learning Module Resources

Literature Search & Database Resources

LITERATURE SEARCH & DATABASE RESOURCES



PubMed Search Tool (Basic)



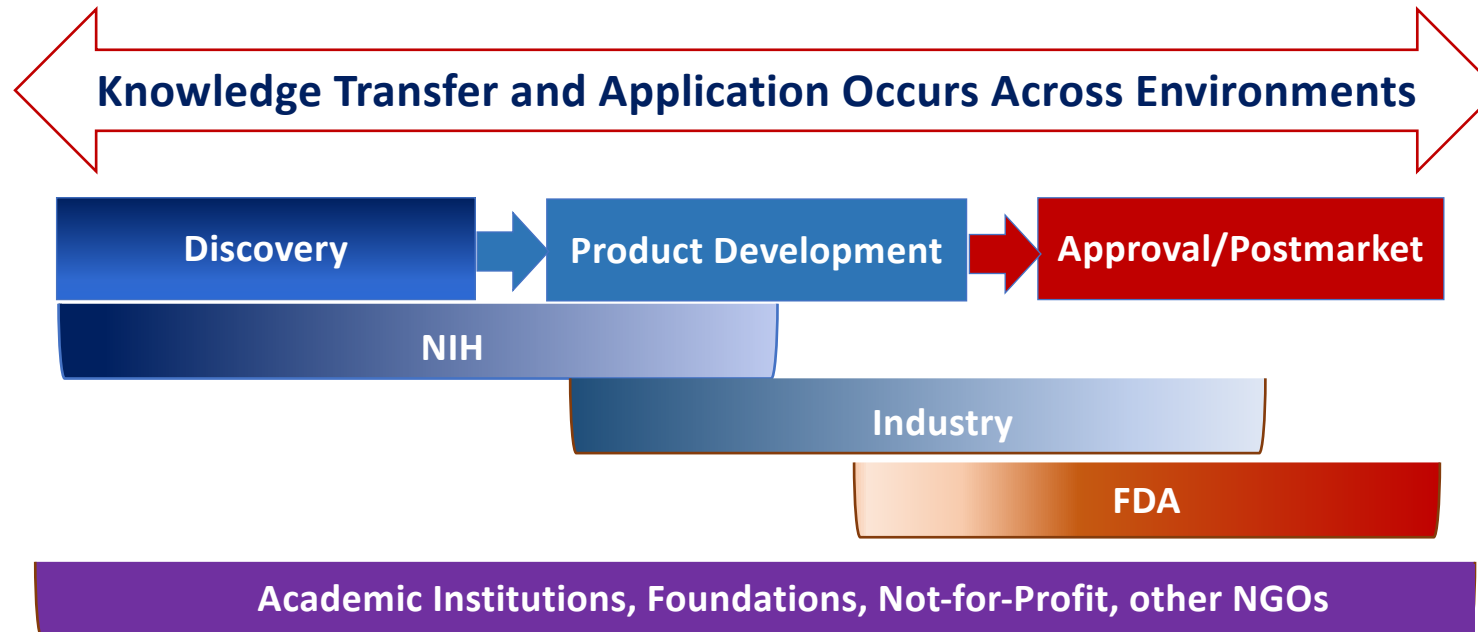
PubMed Search Tool (Advanced)

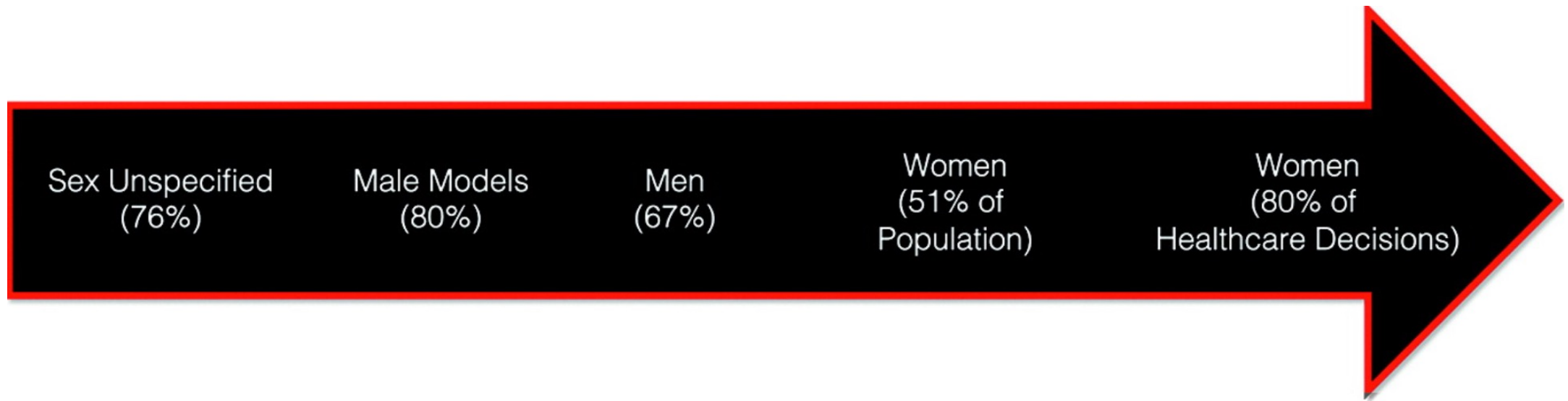
View [How to Guide](#) / [Article](#)



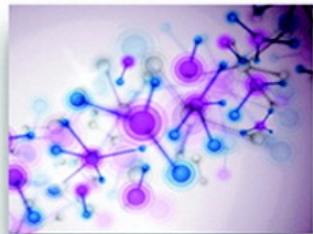
Opportunities

Traditional Research Environments

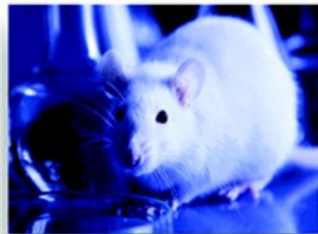




Cell-Based Research



Animal-Based Research



Human Trials



Population Health & Health Systems Research

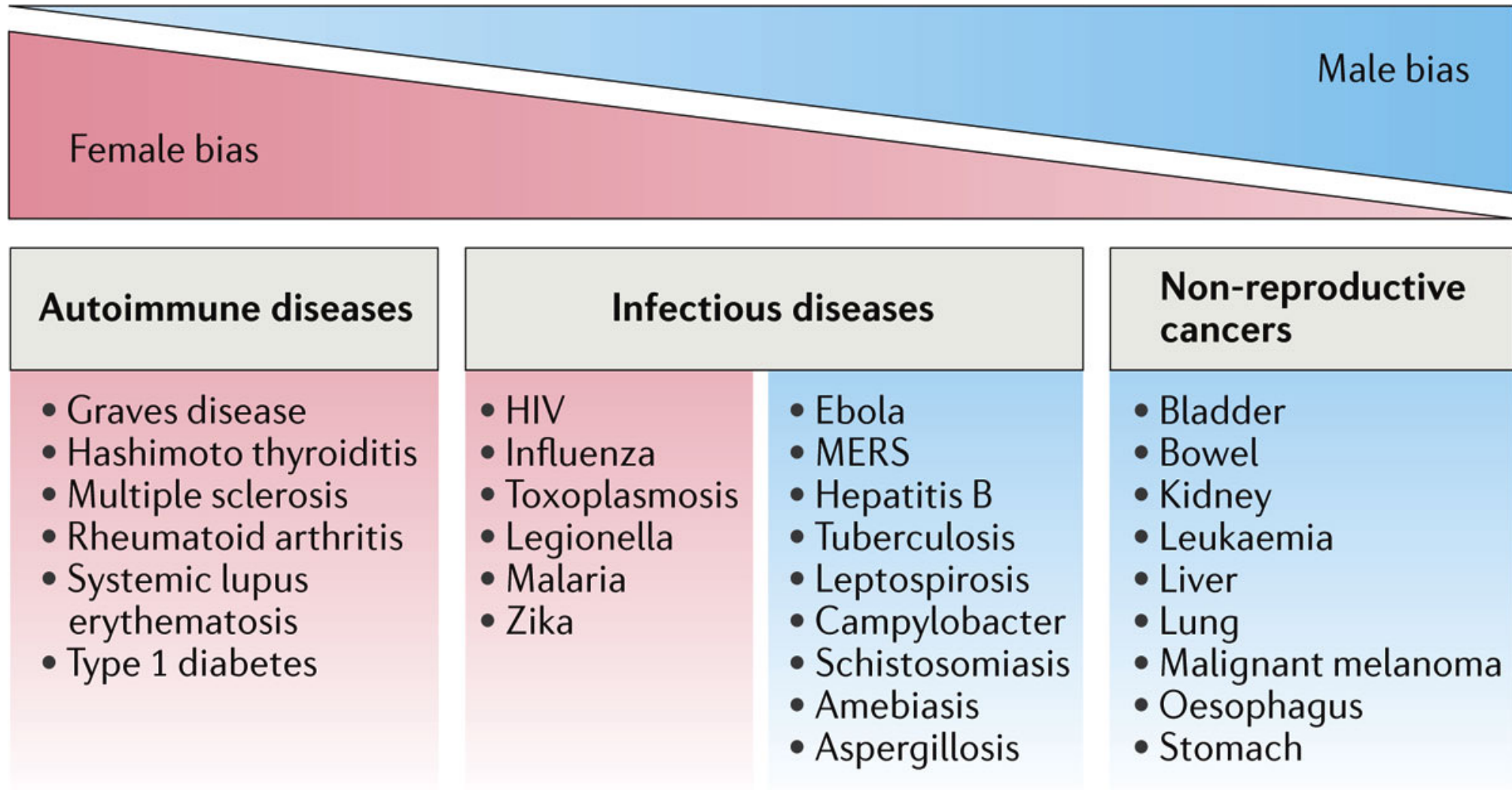


Clinical Care

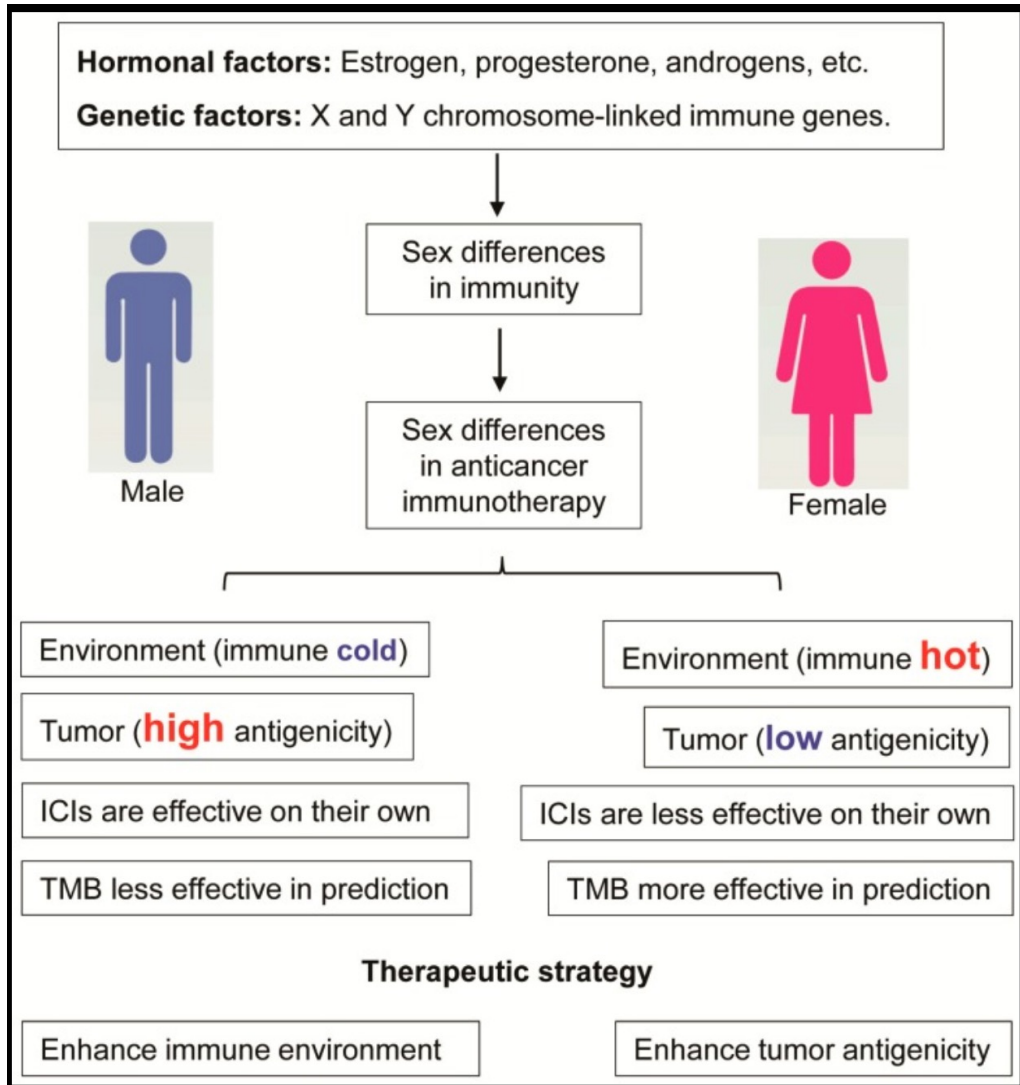


Image Source: M. Jenkins @ Laura W Bush Institute
Published: Development of a PubMed Based Search Tool for Identifying Sex and Gender Specific Health Literature
JWH 9 Feb 2016 <https://doi.org/10.1089/jwh.2015.5217>

Sex bias in infectious diseases, inflammatory diseases, and cancers

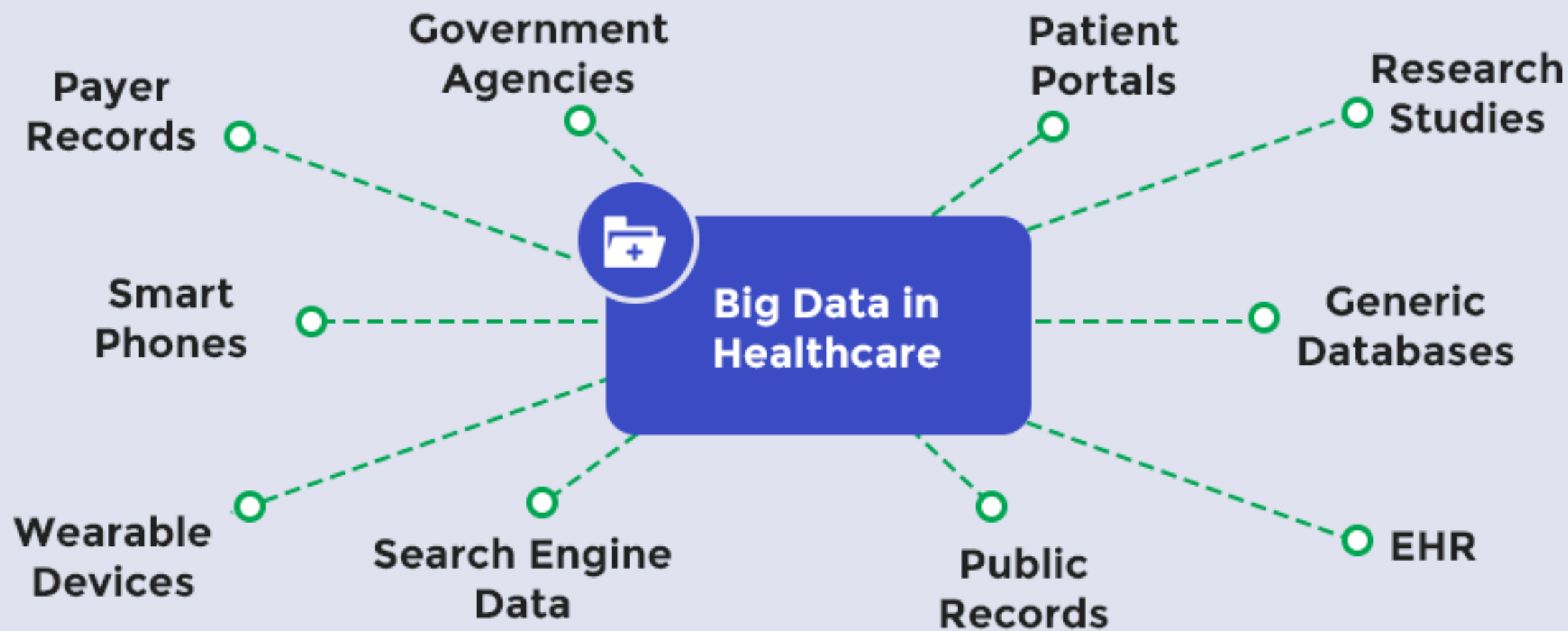


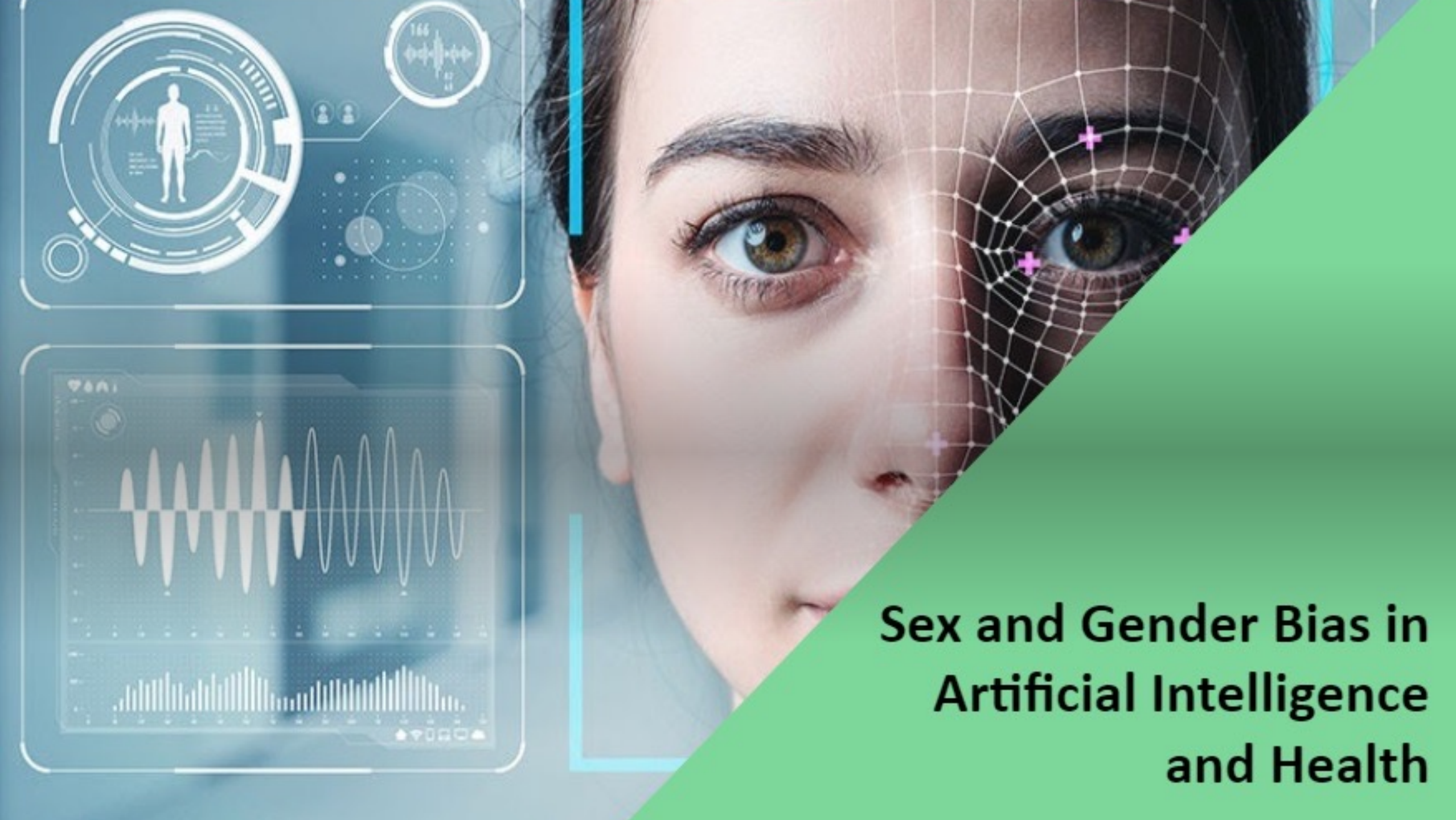
Concept of Biological Plausibility





Harnessing 21st Century Research Resources





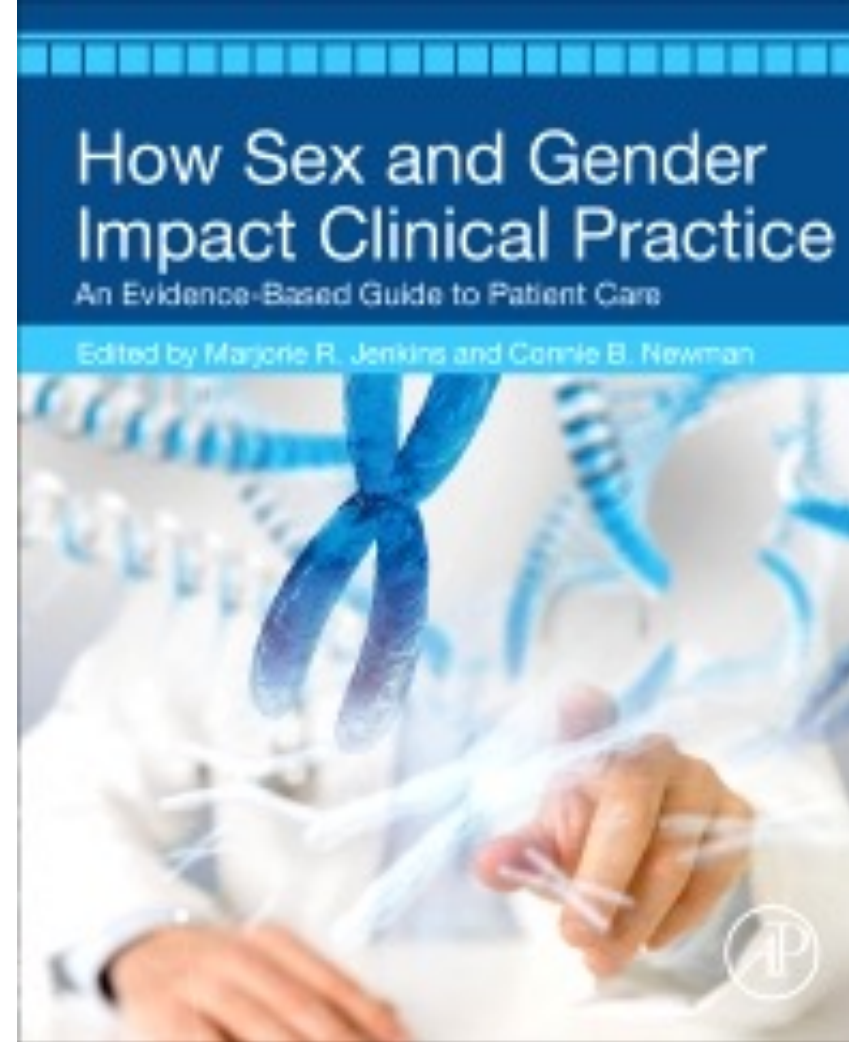
Sex and Gender Bias in Artificial Intelligence and Health



Opportunities

Develop Stronger Health Policy Mandates
Break Down Research Silos
Consider Biological Plausibility
Invest in Data Infrastructure
Critically Assess Research Investment

Lessons learned
through creating
an evidence-
based sex and
gender clinical
textbook for
primary care
physicians



Gender Bias in Medicine



BIAS IN MEDICINE
- AN UNTREATED
EPIDEMIC

Casey Quinlan

Research Focused on
Gender Bias

Validated Diagnosis And
Assessment Tools
In Populations For Which
They Will Be Utilized

Implement Objective
Algorithms for
Treatment of Diagnosed
Conditions

Medical Education
Research

Review > [Can J Cardiol.](#) 2022 Dec;38(12):1865-1880. doi: 10.1016/j.cjca.2022.09.009.

Epub 2022 Sep 15.

Sex and Gender Bias as a Mechanistic Determinant of Cardiovascular Disease Outcomes

Isabel Kim¹, Thalia S Field², Darryl Wan³, Karin Humphries¹, Tara Sedlak⁴

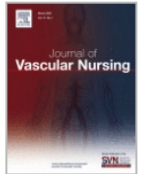
Affiliations: [+ expand](#)

PMID: 36116747 DOI: [10.1016/j.cjca.2022.09.009](#)



Journal of Vascular Nursing

Volume 15, Issue 4, December 1997, Pages 124-127



Perceived gender bias in the treatment of cardiovascular disease

Ruth Thureau BSN (RN)* 

JAMA
Network | **Open**

Original Investigation | Cardiology

Association of Gender and Race With Allocation of Advanced Heart Failure Therapies

Khadijah Breathett, MD, MS; Erika Yee, BS; Natalie Pool, PhD, RN; Megan Hebdon, PhD, DNP, RN; Janice D. Crist, PhD, RN; Ryan H. Yee, BS; Shannon M. Knapp, PhD; Sade Solola, MD; Luis Luy; Kathryn Herrera-Theut, BS; Leanne Zabala, MD; Jeff Stone, PhD; Marylyn M. McEwen, PhD, RN; Elizabeth Calhoun, PhD; Nancy K. Sweitzer, MD, PhD

JAMA Network Open. 2020;3(7):

> [Epilepsy Behav.](#) 2021 Jan;114(Pt A):107272. doi: 10.1016/j.yebeh.2020.107272. Epub 2020 Jul 8.

Gender differences in Epworth Sleepiness Scale revealed by paired patient-spouse scoring

[Andreja Packard](#)¹, [Ramon Bautista](#)², [Carmen Smotherman](#)³, [Shiva Gautham](#)³

Affiliations + expand

PMID: 32651121 DOI: [10.1016/j.yebeh.2020.107272](#)

STANDARD STEMI CARE in ER

490 men

233 women

Men

Women

Who received standard of care by clinical guidelines?

77%

69%

Door to cardiac catheterization balloon time

104 min

112 min

30-day mortality **6.1% higher** in women

INTERVENTION

378 men

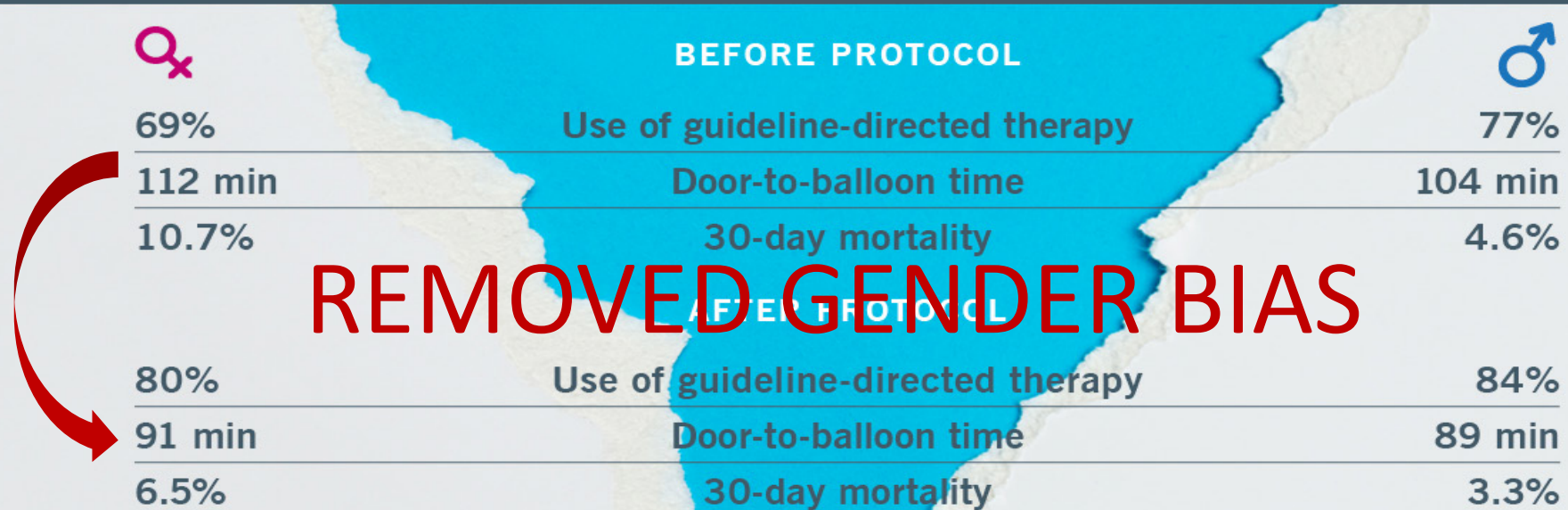
171 women

4-step protocol

1. ER Criteria do not require cardiology consult
2. Guideline based drug therapy
3. Immediate transfer to the cardiac cath lab
4. Initial radial approach for vascular access

Bridging the Gender Gap in STEMI Care & Outcomes

When Cleveland Clinic adopted a new care process for ST elevation myocardial infarction (STEMI), it did more than improve outcomes. It significantly shrank the well-established gender gap in STEMI care — to the benefit of women:

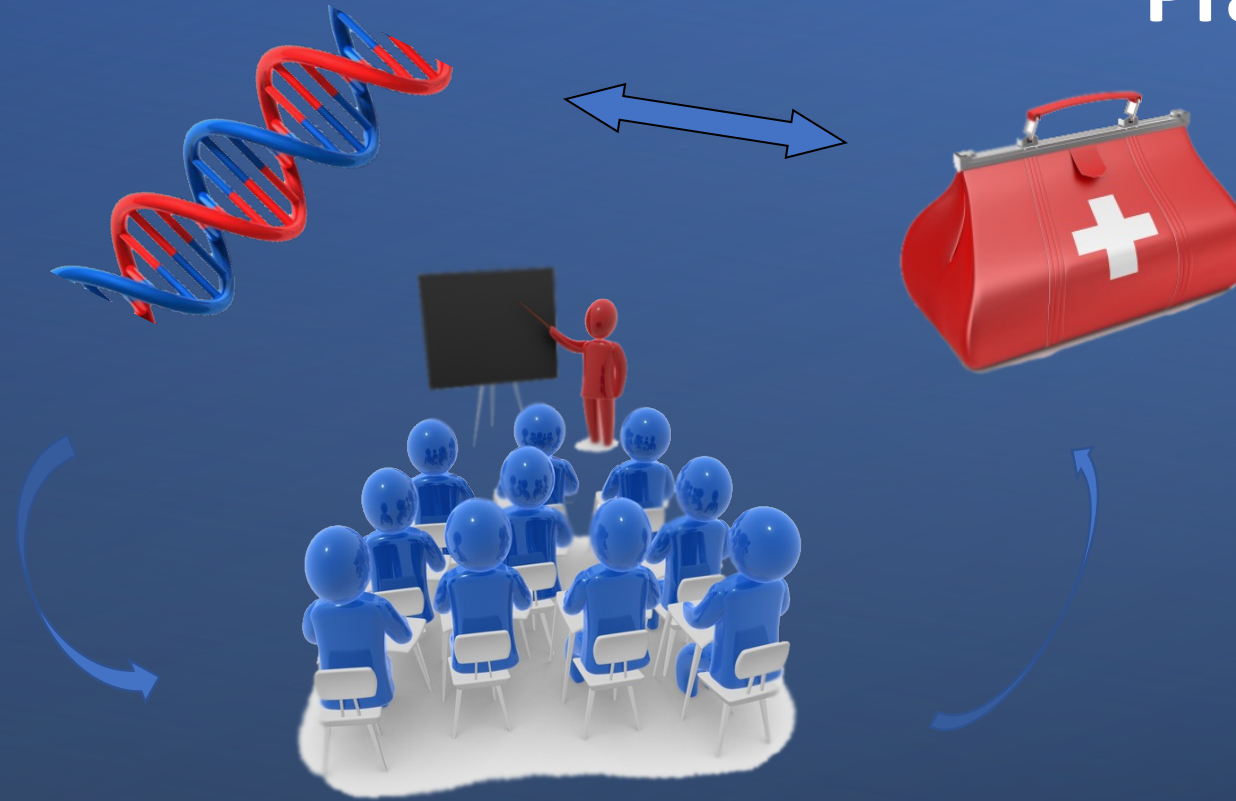


Education and the Hidden Curricula



**Sex and
Gender
Research**

**Translation to
Clinical
Practice**



Health Professions Education

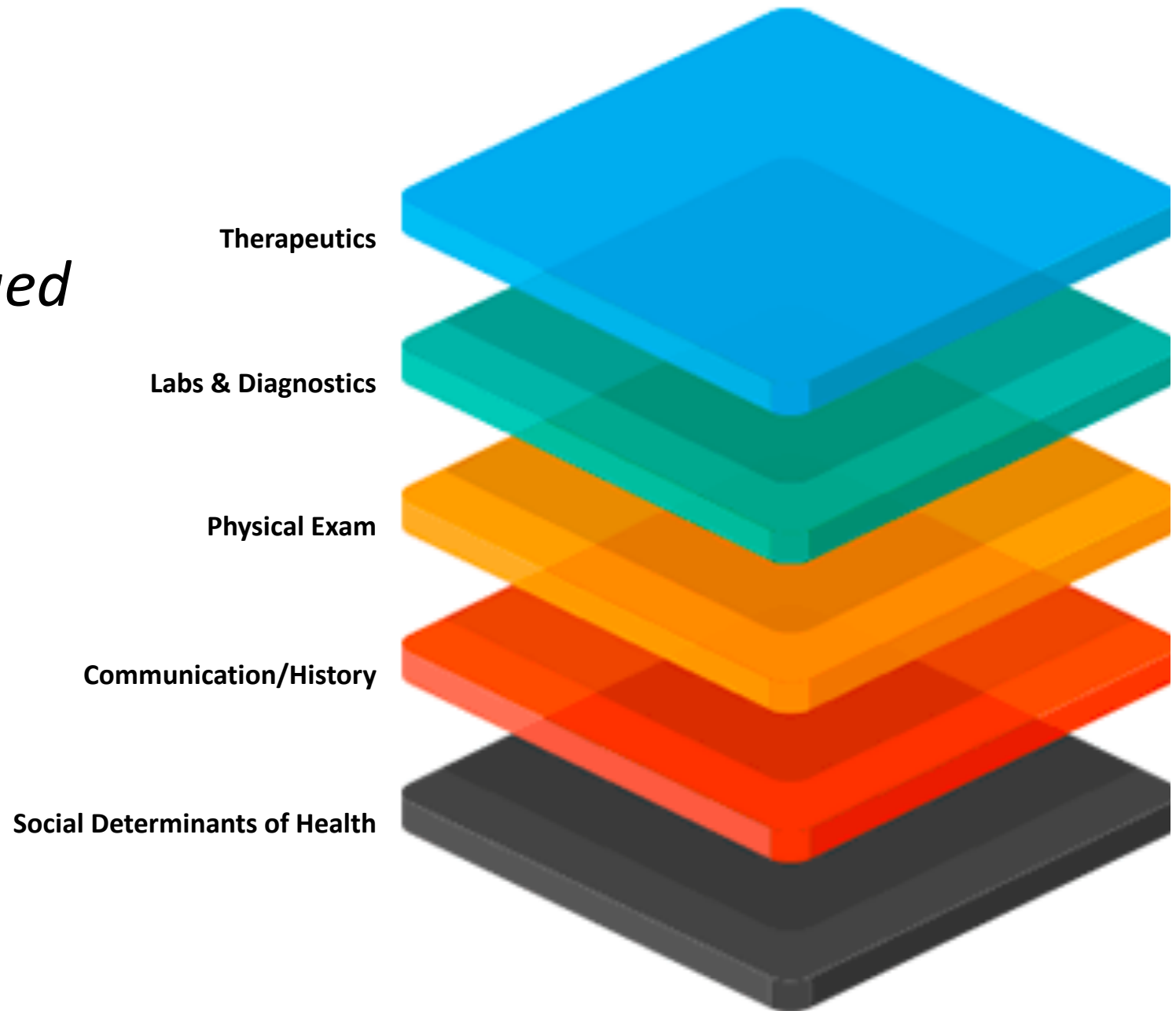
Uncovering the

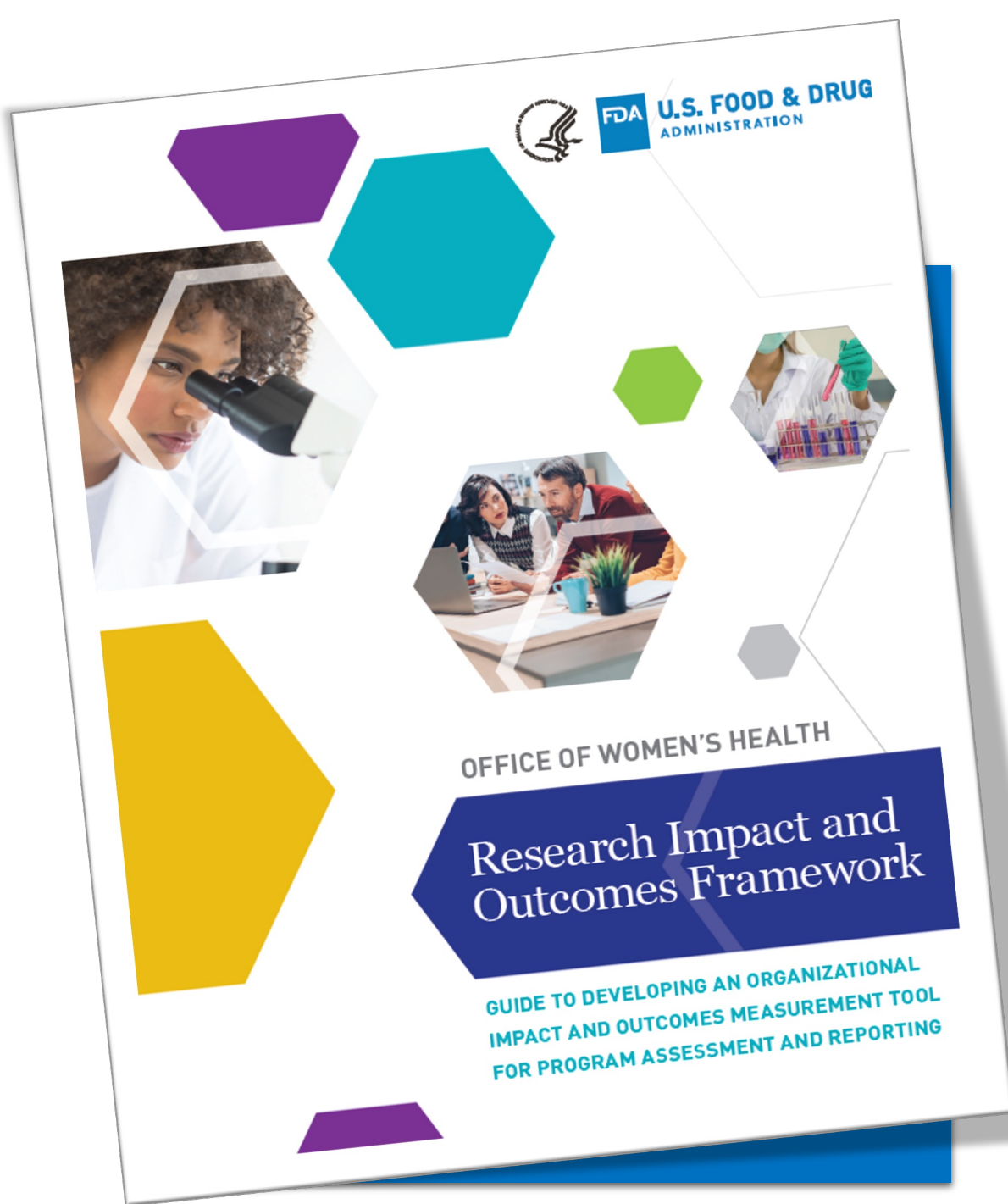
Hidden Curriculum

By John T. Brinkmann, MA, CPO/L, FAAOP(D)

Interesting Concept Emerged

“STACKING”
Sex & Gender
Impact
on
Health
Outcomes

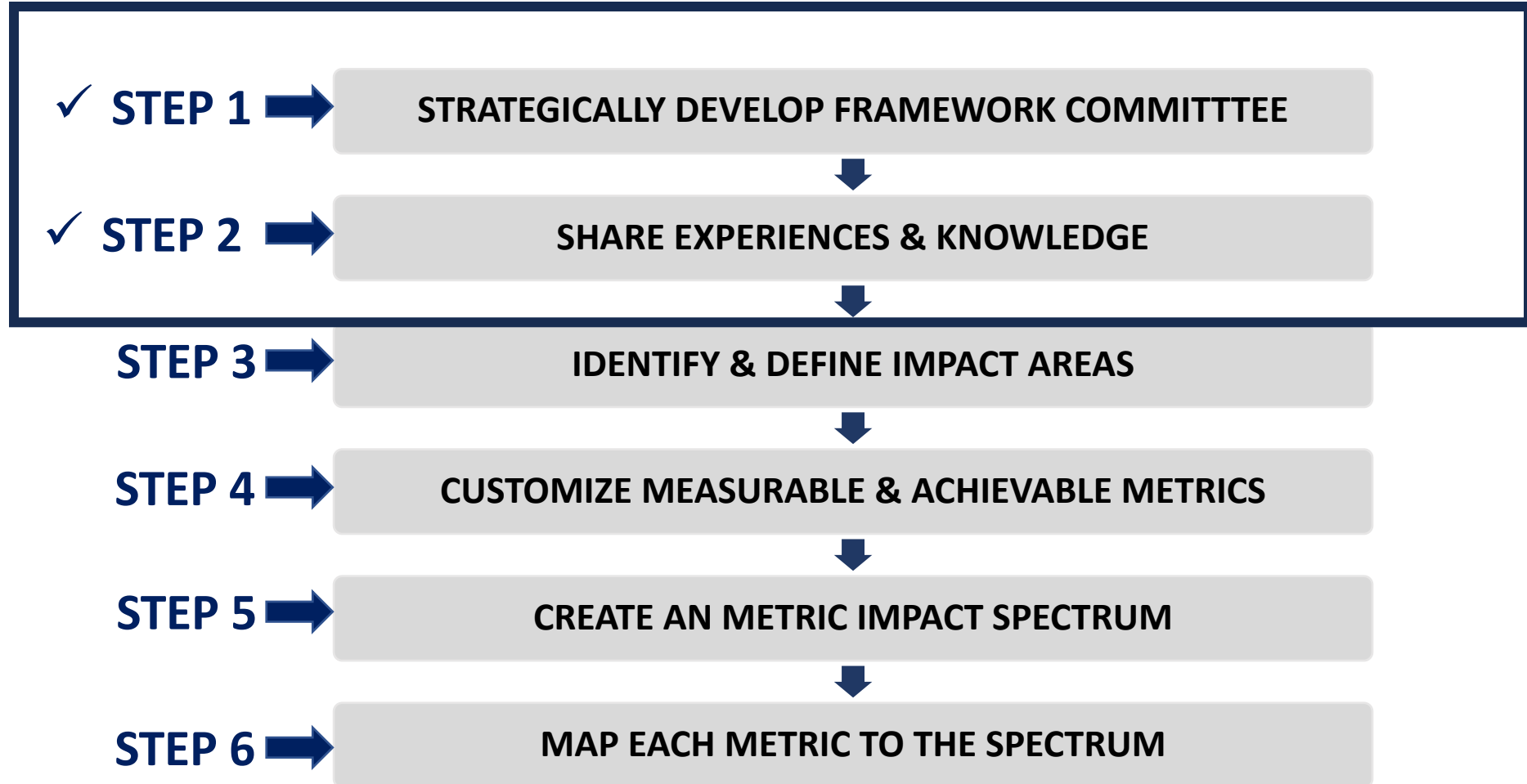




FDA Office of Women's Health Research Impact and Outcomes Framework

<https://www.fda.gov/files/science%20&%20research/published/FDA-Office-of-Women%E2%80%99s-Health--Research-Impact-and-Outcomes-Framework.pdf>

Framework Development





This Research Agenda will.....

What Will Drive Others To Progress This Research Agenda



- Knowledge Gaps
- Public Health Priorities
- Align with a Major Funding Agency or Partner
- Supports Institutional Mission
- Academics
 - Extramural Funding
 - Federal
 - Industry
 - Big Tech
 - Non-Profit
 - Faculty Development
 - K Awardees
 - Develop a National Reputation
- Community Awareness and Support
- Meet the The Healthcare Triple Aim
 - Improve Access, Lower Cost, Increase Quality,

STEP 3 → Impact Areas

Examples: Align and Define

Engagement

Harnessing appropriate expertise and capabilities, attracting key players to ensure the progress of the research agenda

Advocacy

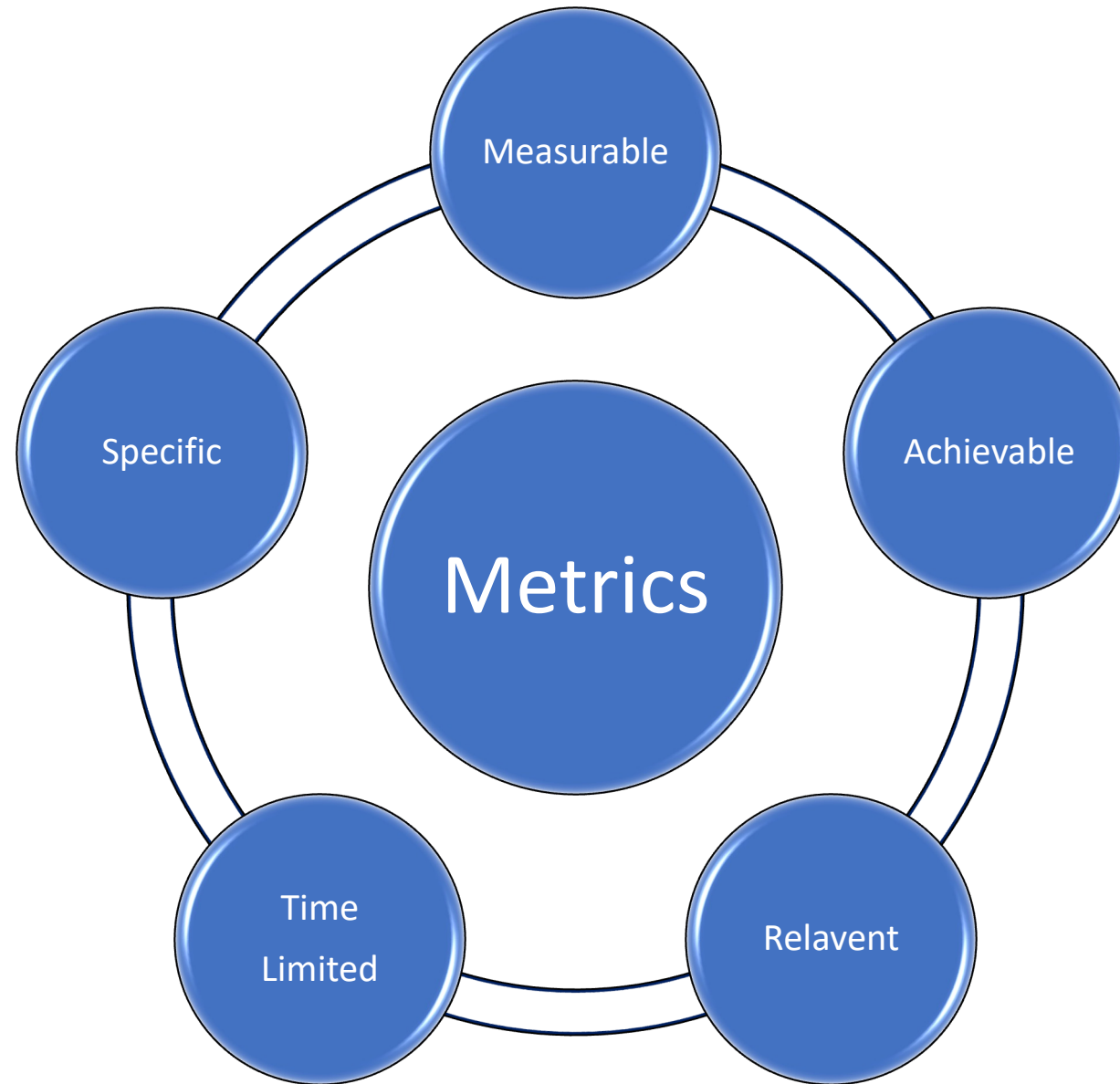
Increasing awareness to influence decisions and actions by stakeholders in progressing the research agenda and dissemination of discoveries

Significance & Alignment

Ensuring funding decisions and research outcomes progress the application of clinically meaningful evidence-based findings and improve health outcomes for women with chronic disease

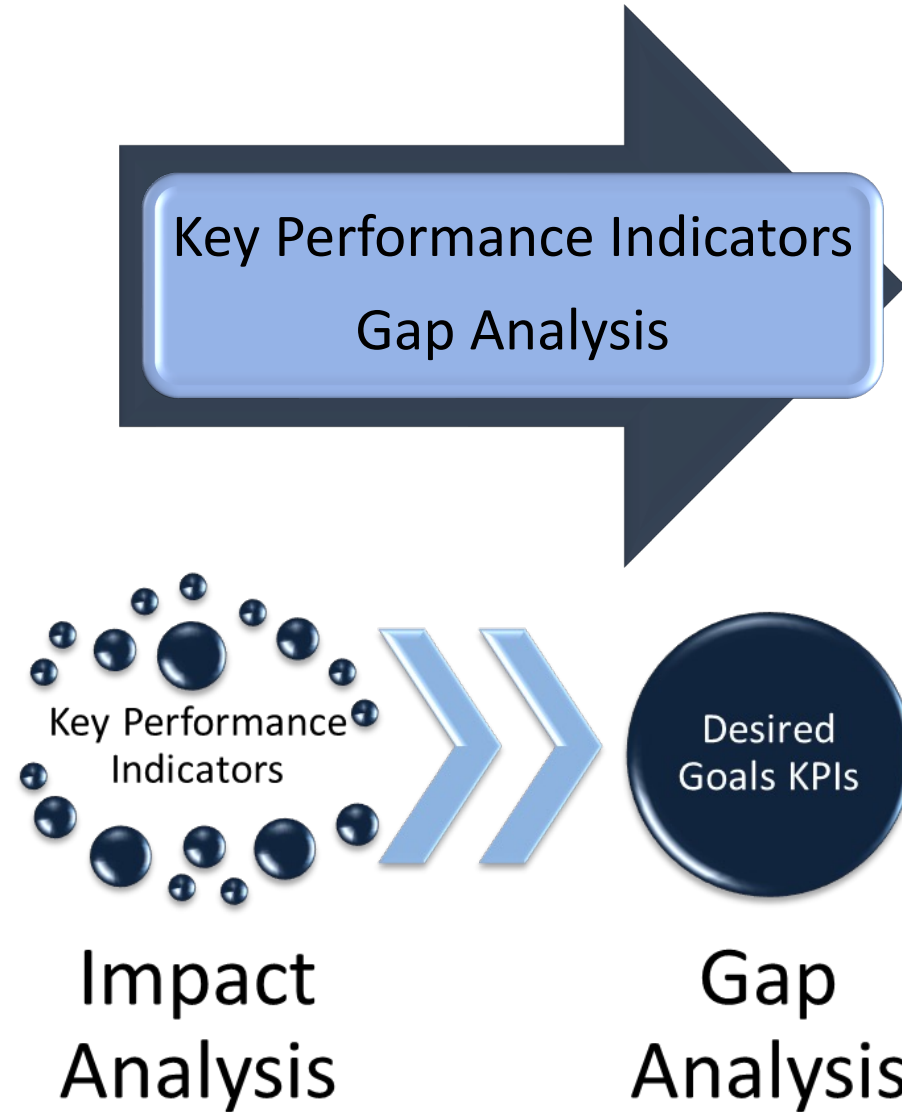
Innovation

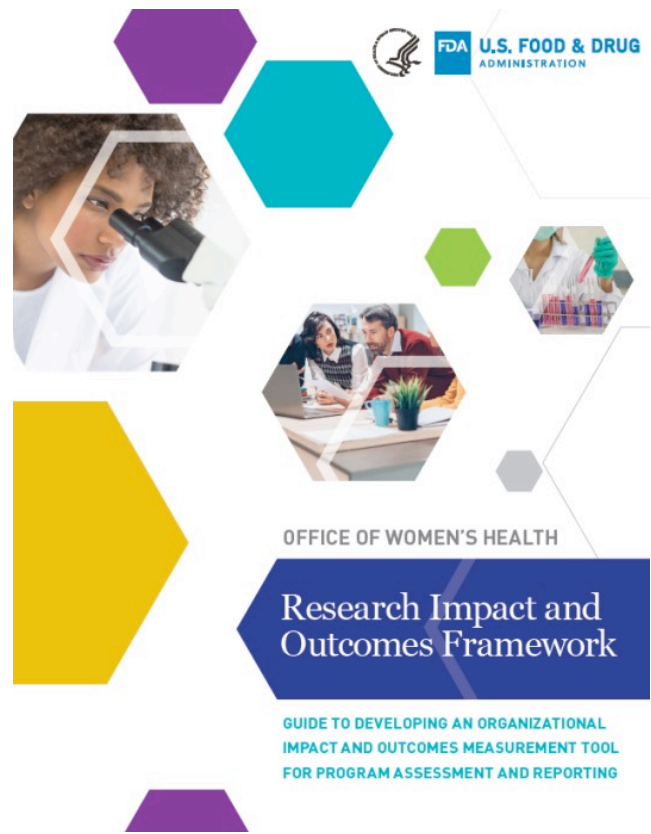
Producing a new and measurable shift in the landscape of chronic disease diagnosis, evaluation, treatment, and prognosis in women with chronic diseases



STEP 4 ➔ **Developing Metrics**

Plan to Measure Impact



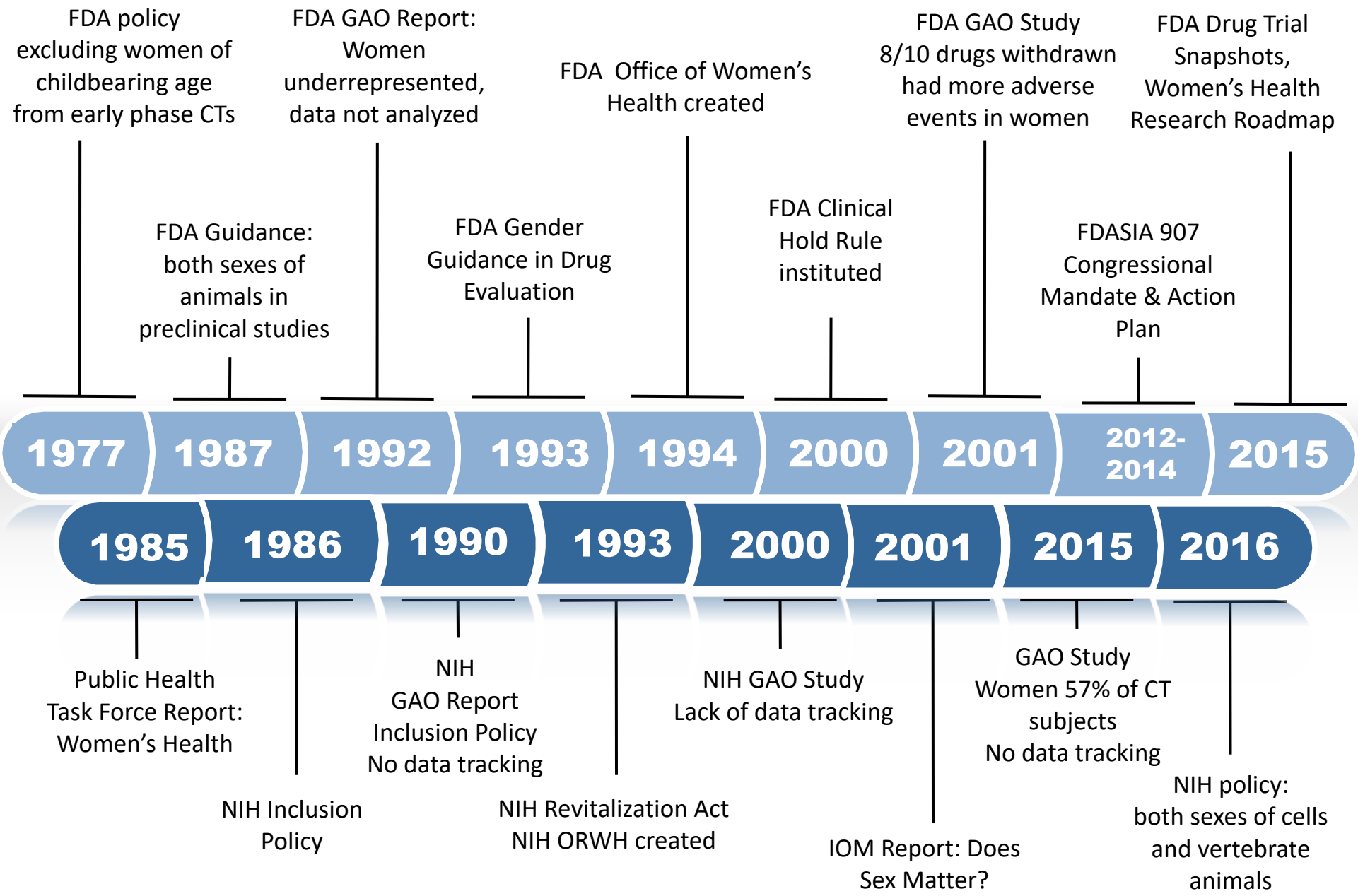


RIO Framework User Guide

<https://www.fda.gov/downloads/ScienceResearch/SpecialTopics/WomensHealthResearch/UCM603175.pdf>

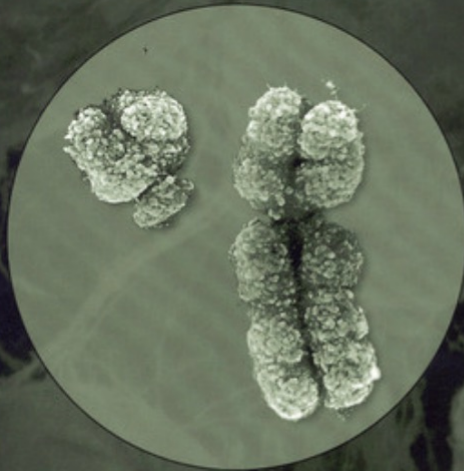


Acknowledging Decades
of
Foundational Work



Exploring the
Biological
Contributions
to Human Health

Does
Sex
Matter?



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PRINCIPLES
of
GENDER-SPECIFIC
MEDICINE

SECOND EDITION



Edited by
MARIANNE J. LEGATO, M.D.



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Public Priorities in Women's Health: Analysis of Request for Information Published to Inform "Advancing NIH Research on the Health of Women: A 2021 Conference"

Elizabeth Barr, PhD,¹ Samia Noursi, PhD,¹ Erik Roodzant, MA,^{1,2} Amelia Ubesie, DrPH, MPH,^{1,2}
Shilpa Amin, MD,¹ Nikeya Macioce, PhD,^{1,3} Damiya Whitaker, PsyD,¹
Janine A. Clayton, MD,¹ and Sarah M. Temkin, MD¹

“The NIH vision of a world where every woman receives evidence-based disease prevention and treatment tailored to her unique needs, desires, and circumstances.”

THANK YOU

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