

Advancing Science for the Health of Women

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NIH Associate Director for Research on Women's Health
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National Institutes of Health

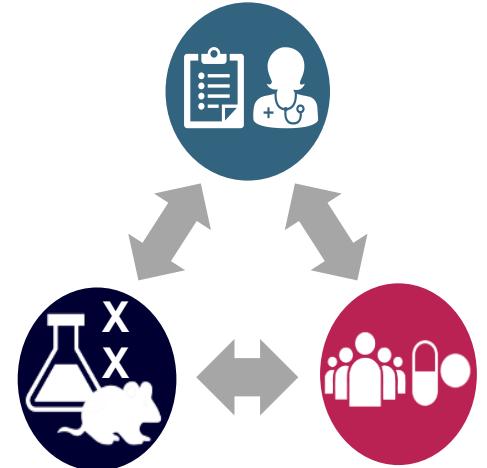
Government-University-Industry Research Roundtable Webinar
National Academies of Sciences, Engineering, and Medicine
March 23, 2018



National Institutes of Health
Office of Research on Women's Health

orwh.od.nih.gov | #SABV | @NIH_ORWH

NIH Office of Research on Women's Health (ORWH)



Our Mission:

1. Enhance and expand women's health research
2. Include women and minority groups in clinical research
3. Promote career advancement for women in STEM



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NIH Office of Research on Women's Health (ORWH)



1990



2010



2012

March is
Women's
History
Month



Rep. Louise Slaughter (D-NY)
August 14, 1929 –
March 16, 2018

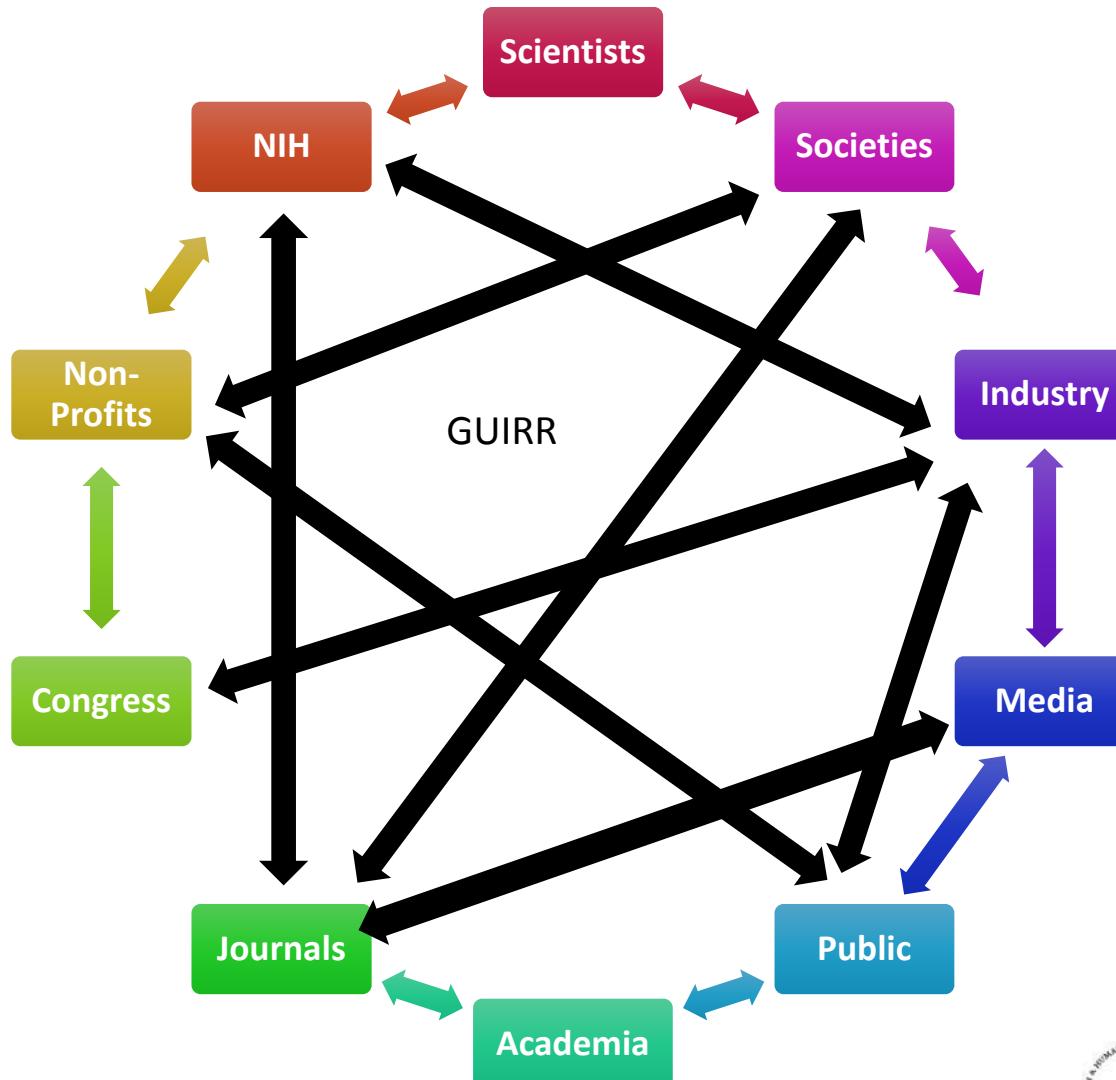
- Co-authored the Violence Against Women Act
- Dedicated first \$500 million in funds to breast cancer research
- First female Chair of the House Rules Committee

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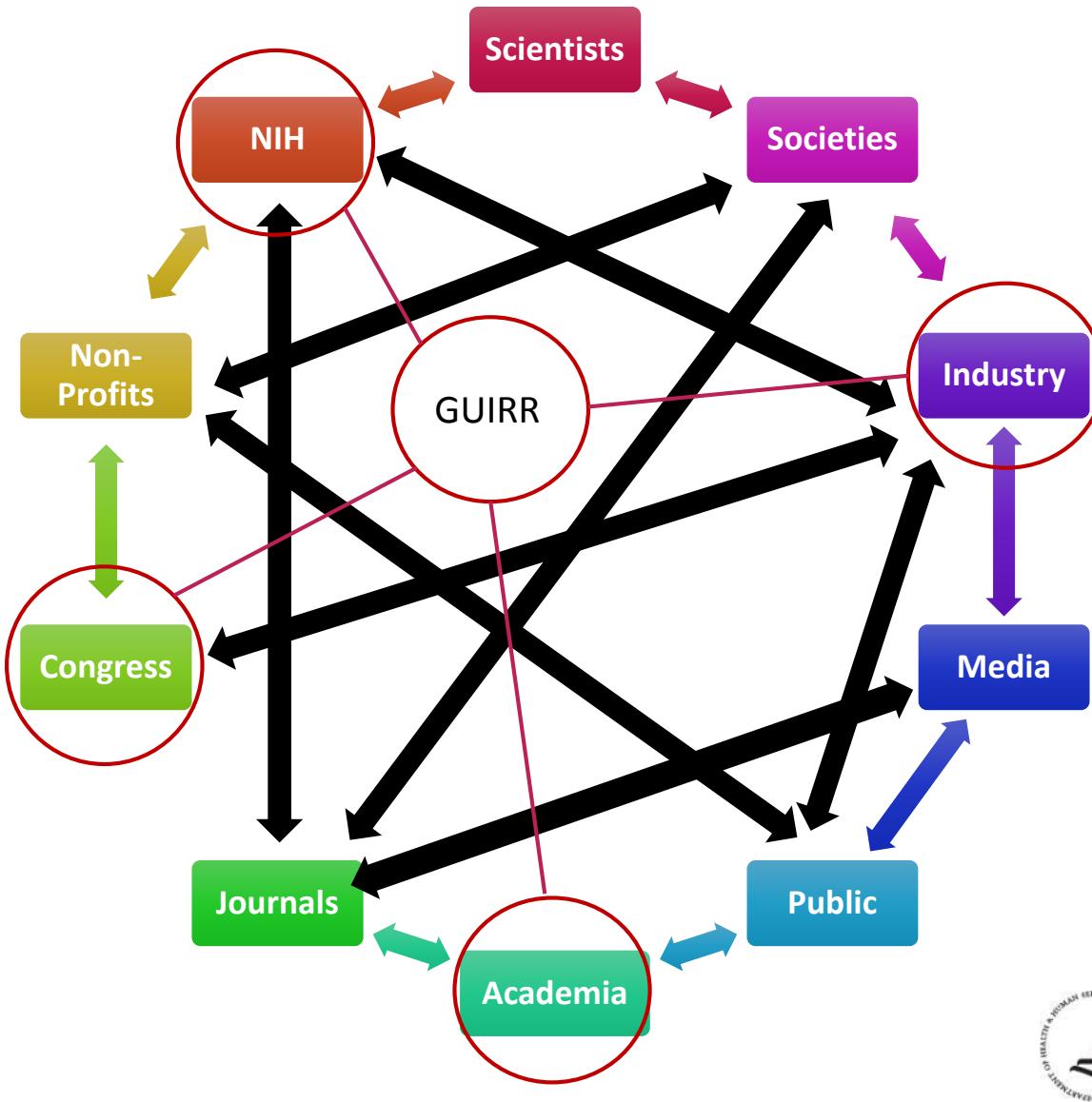


Circle of Partners in Human Health



NIH
National Institutes of Health
Office of Research on Women's Health

Circle of Partners in Human Health





Outline

- Women's Health: U.S. vs. Peer Countries
- Mission-based Solutions
 - Enhance and Expand Women's Health Research
 - Policy, Programs, and Partnerships
 - Inclusion of Women and Minority Groups in Clinical Research
 - Promote Career Advancement for Women in STEM
 - Strategic Plan for the Future—21st Century Cures



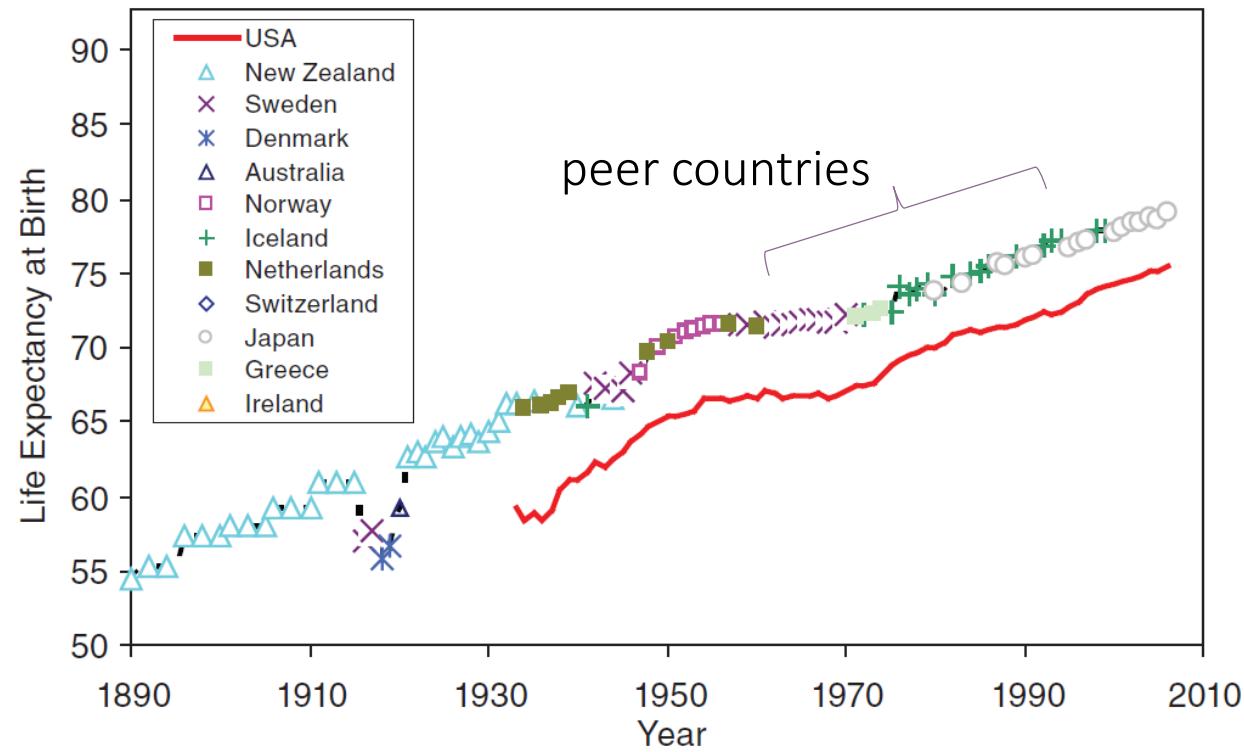
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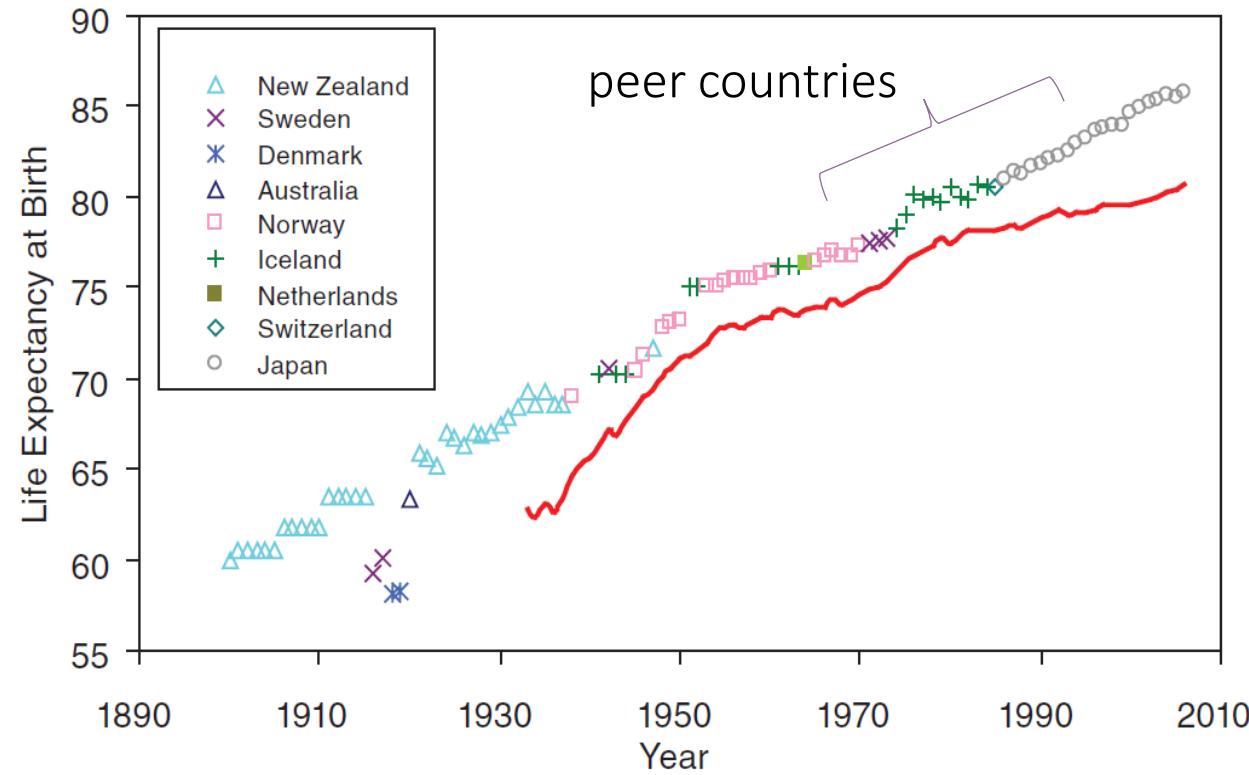
The Big Picture: Women's Health Worldwide

Life expectancy has been increasing worldwide: How does the U.S. compare?

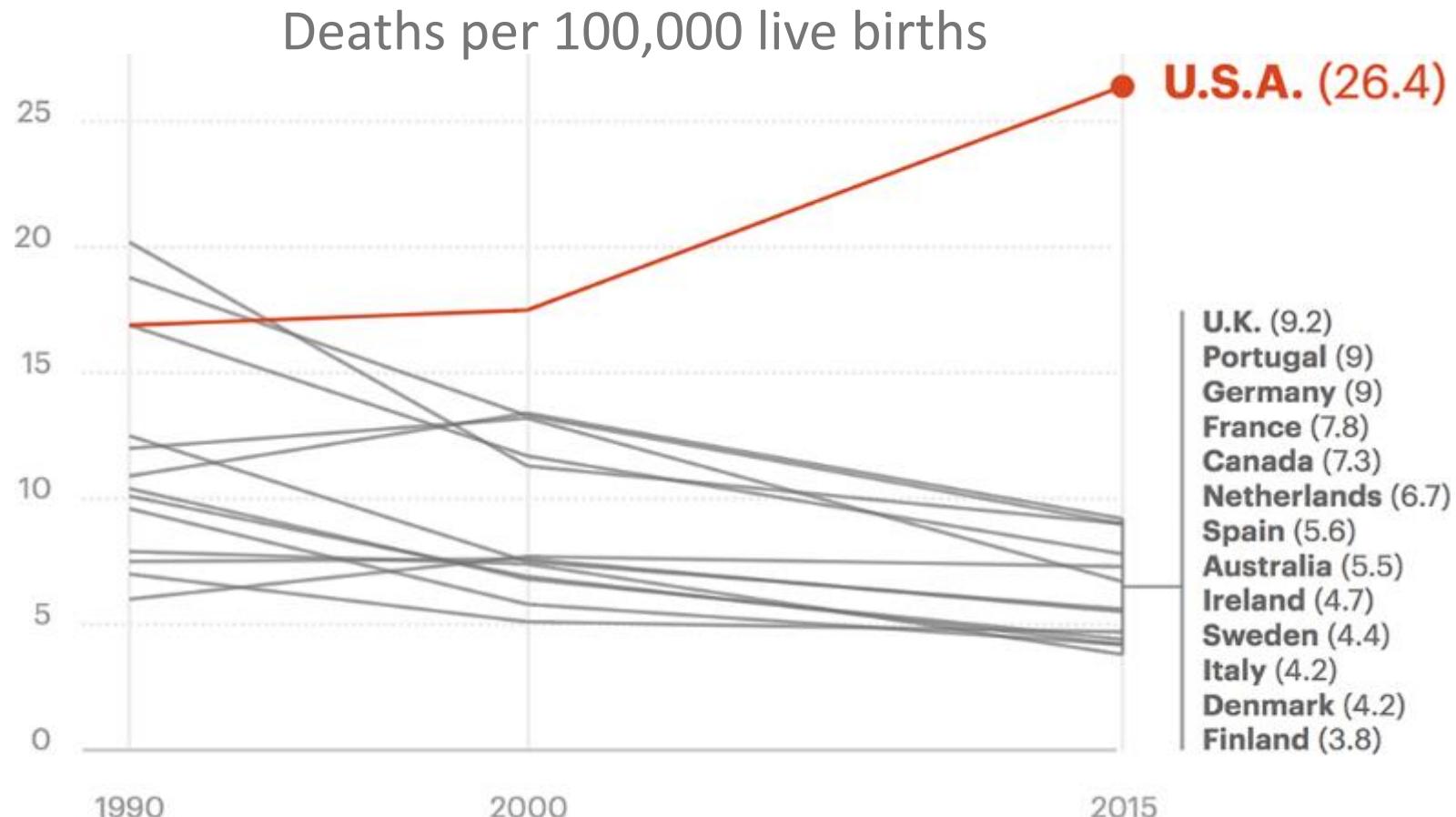
Men



Women



Maternal mortality is rising in the U.S. as it declines elsewhere



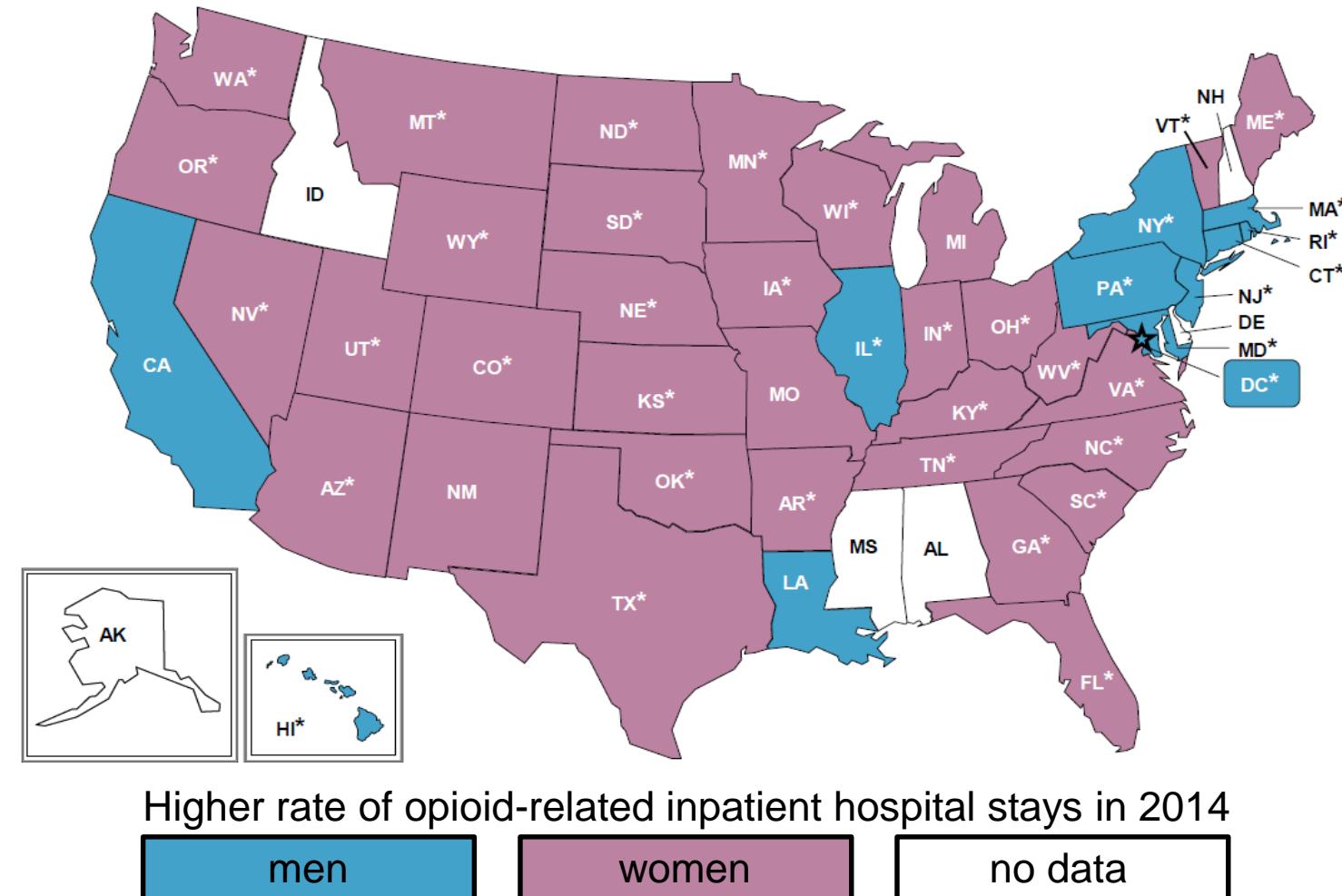
GBD 2015 Maternal Mortality Collaborators. 2016. Global, regional, and national levels of maternal mortality, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet* 388 (10053): 1775-1812.



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The opioid crisis is a women's health issue

- From 2005 to 2015, opioid-related inpatient hospital stays increased 55% in men and 75% in women.
- In 2014, **women** had higher rates of opioid-related inpatient hospital stays in **most states**.
- Between 1999 and 2015, death from Rx opioid overdoses increased 471% in women and 218% in men.



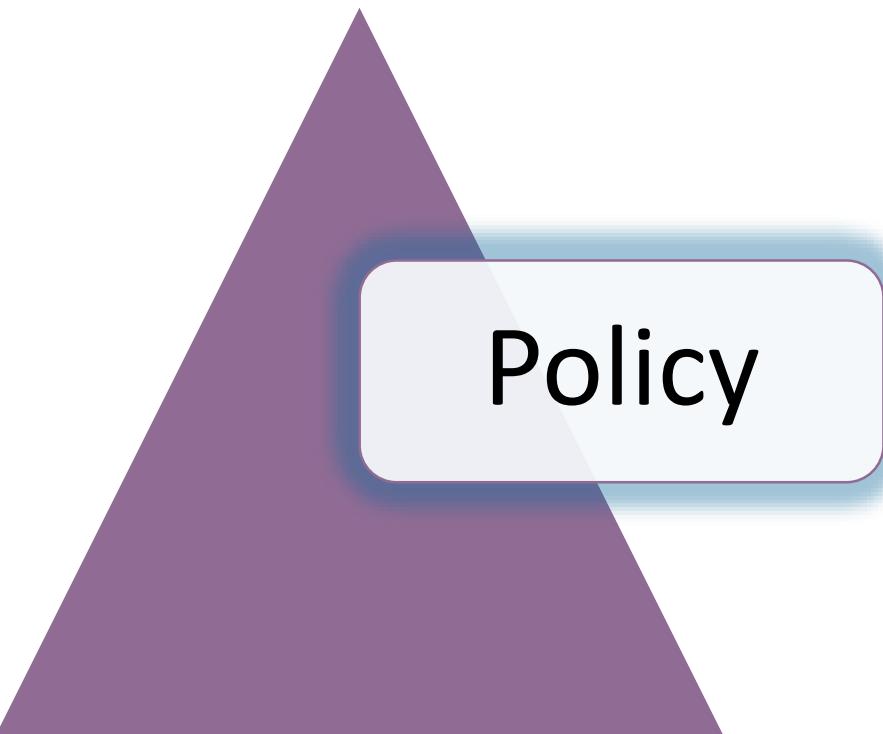
Weiss et al., 2017. Patient Characteristics of Opioid-Related Inpatient Stays and Emergency Department Visits Nationally and by State, 2014. HCUP Statistical Brief #224. Rockville, MD: Agency for Healthcare Research & Quality.



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How Does NIH/ORWH Address Those Trends?



Policy

Rigor &
Reproducibility

NOT-OD-15-103: Enhancing
Reproducibility through Rigor and
Transparency-6/2015

Sex as a Biological
Variable

NOT-OD-15-102: Consideration of
Sex as a Biological Variable in NIH-
funded Research-6/2015



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“Science isn’t science if it isn’t reproducible”*

How did we get here?

- Overreliance on male animals and cells
- Inattention to sex effects
- Lack of transparency
- Inconsistent reporting of sex-specific findings in publications



Consequences

- Incomplete knowledge base
- Risk of erroneous conclusions
- Risk of harm & toxicity surprises
- Failure to maximize ROI
- Erosion of public trust

*Roth and Cox. AJP. Jan 2015.



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Enhancing Reproducibility: Rigor and Transparency

NEW GRANT GUIDELINES

what you need to know

WHY UPDATE THE GUIDELINES?

The updates focus on four areas deemed important for enhancing rigor and transparency:

- 1 PREMISE**
The scientific premise forming the basis of the proposed research
- 2 DESIGN**
Rigorous experimental design for robust and unbiased results
- 3 VARIABLES**
Consideration of relevant biological variables
- 4 AUTHENTICATION**
Authentication of key biological and/or chemical resources

Send inquiries to <http://www.nih.gov/science/reproducibility/>

See <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-011.html>

WHAT ARE THE UPDATES?

1 UPDATES TO RESEARCH STRATEGY GUIDANCE



The research strategy is where you discuss the significance, innovation, and approach of your research plan. Let's look at an R01, for example:

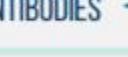
The new **research strategy** guidelines require that you:

- State the strengths and weakness of published research or preliminary data crucial to the support of your application
- Describe how your experimental design and methods will achieve robust and unbiased results
- Explain how biological variables, such as sex, are factored into research design and provide justification if only one sex is used

2 NEW ATTACHMENT FOR AUTHENTICATION OF KEY BIOLOGICAL AND/OR CHEMICAL RESOURCES

From now on, you must briefly describe methods to ensure the identity and validity of key biological and/or chemical resources used in the proposed studies.

These include, but are not limited to:

CELL LINES   SPECIALTY CHEMICALS
ANTIBODIES   OTHER BIOLOGICS

Standard laboratory reagents that are not expected to vary do not need to be included in the plan. Examples are buffers and other common biologicals or chemicals.

DO NOT put experimental methods or preliminary data in this section

DO focus on authentication and validation of key resources

3 NEW REVIEWER GUIDELINES

Here are the additional criteria the reviewers will be asked to use:

→ Is there a **strong scientific premise** for the project?

→ Have the investigators presented adequate plans to address **relevant biological variables**, such as sex, for studies in vertebrate animals or human subjects?

→ Do the investigators present strategies to ensure a **robust and unbiased approach**, as appropriate for the work proposed?

Reviewers will also be asked to comment on that new attachment (see Update 2)!

Sex As a Biological Variable (SABV) Policy

“NIH expects that sex as a biological variable will be factored into research designs, analyses, and reporting in vertebrate animal and human studies.”

NOT-OD-15-102*: Consideration of Sex as a Biological Variable in NIH-funded Research

*Effective date: January 25, 2016

<https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-102>

Videocast of Oct. 26–27, 2017 SABV Workshop available online:
<https://commonfund.nih.gov/sexdifferences/workshop>



SABV Next Steps: Intentional Integration

Sex/Gender Influences on Health and Disease

Accounting for Sex as a Biological Variable in Design, Analysis, Reporting

Preclinical Studies

Phase I, II, III, IV Clinical Trials



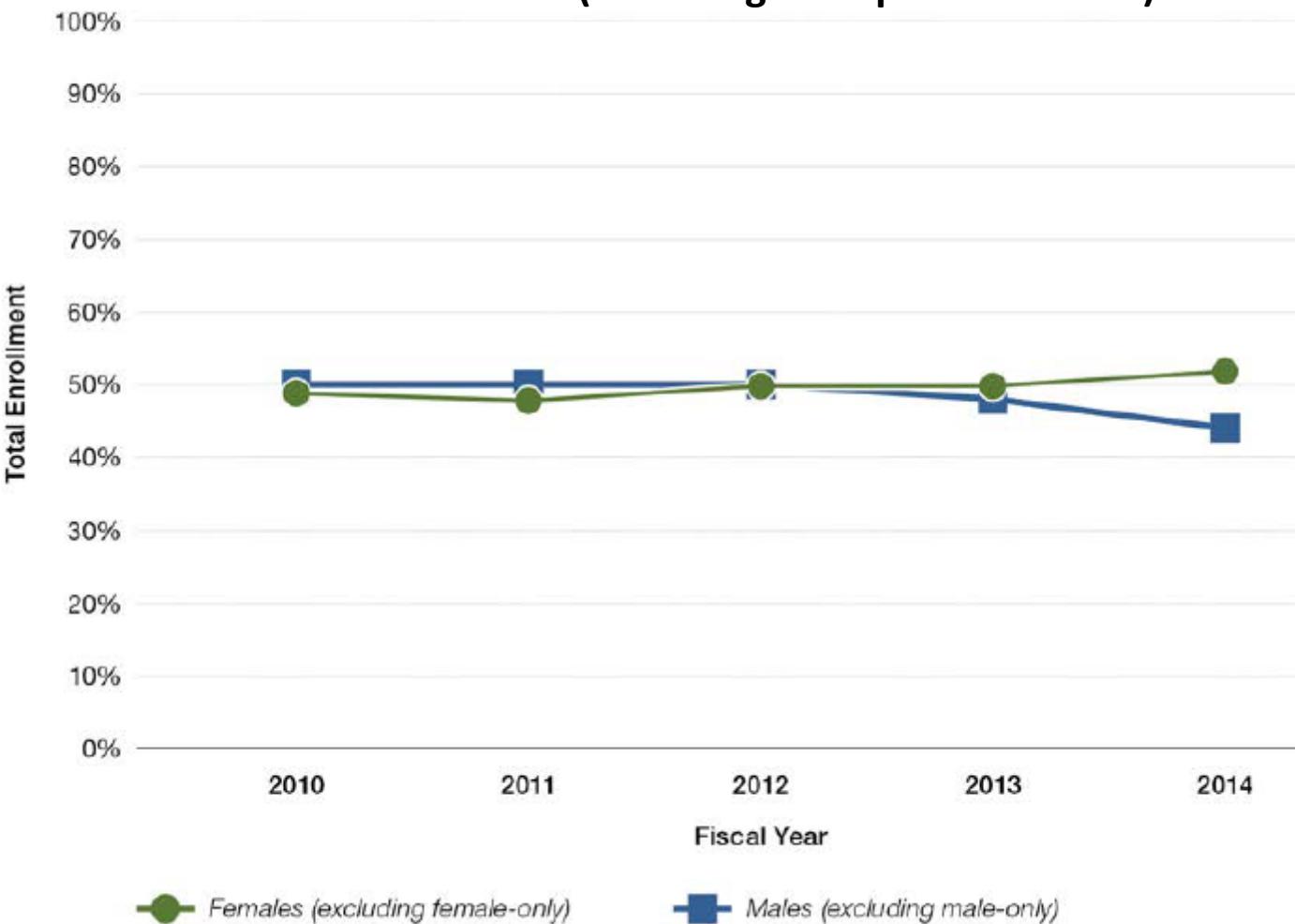
Education

Health Policy

Health Care

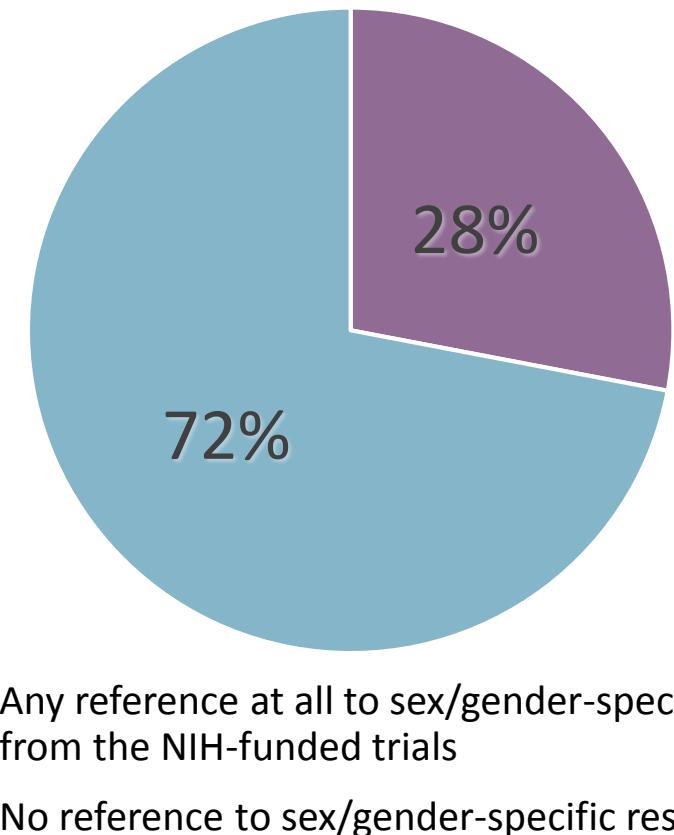
Sex/gender-specific reporting lags behind inclusion

Enrollment Trend for Males and Females in NIH-Defined Clinical Research (Excluding Sex-Specific Studies)



Source: Report of the NIH Advisory Committee on Research on Women's Health for FY13–14. Additional inclusion data available at <https://orwh.od.nih.gov/>.

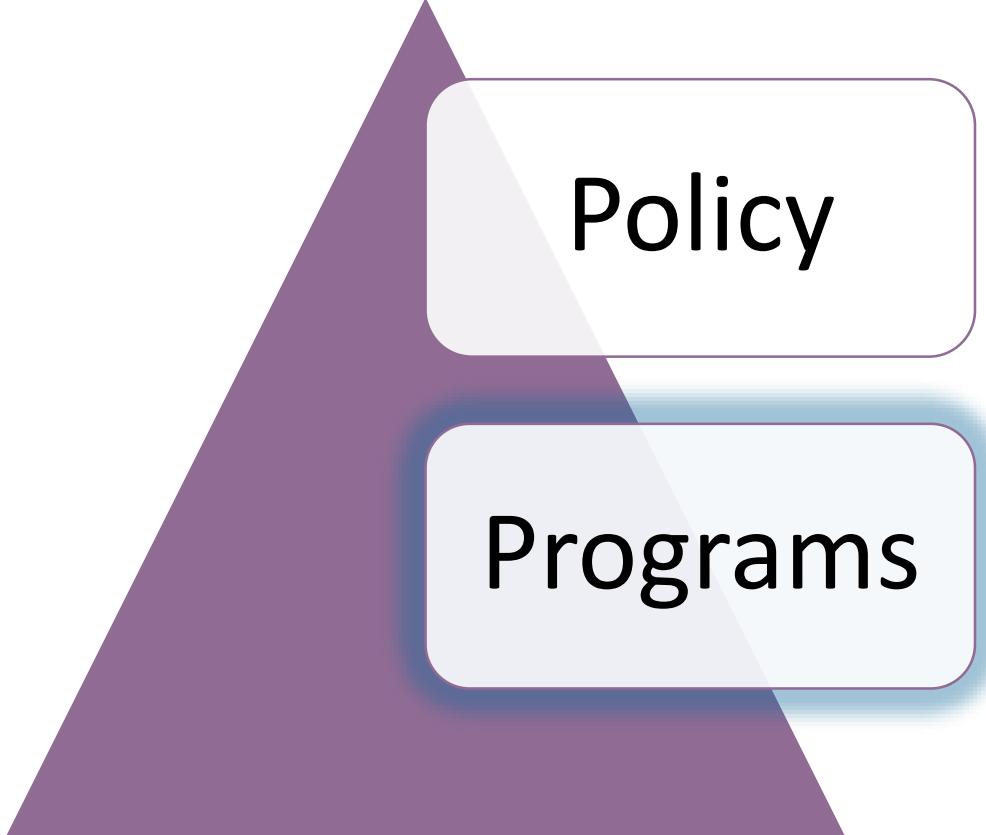
Reporting of Sex/Gender-Specific Results from NIH-Funded Phase III Clinical Trials, 1995–2010



Foulkes MA. 2011. After inclusion, information and inference: reporting on clinical trials results after 15 years of monitoring inclusion of women. *Journal of Women's Health* 20 (6): 829–836.



How ORWH Achieves Results



Policy

Programs

Specialized Centers of Research
(SCOR) on Sex Differences Program

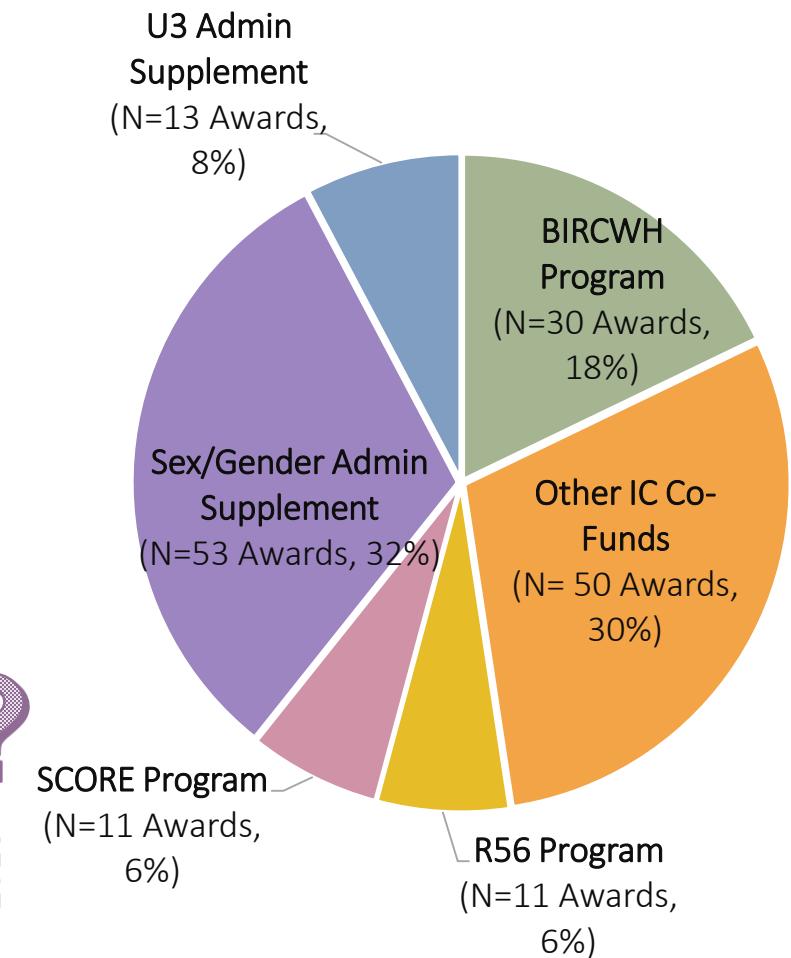
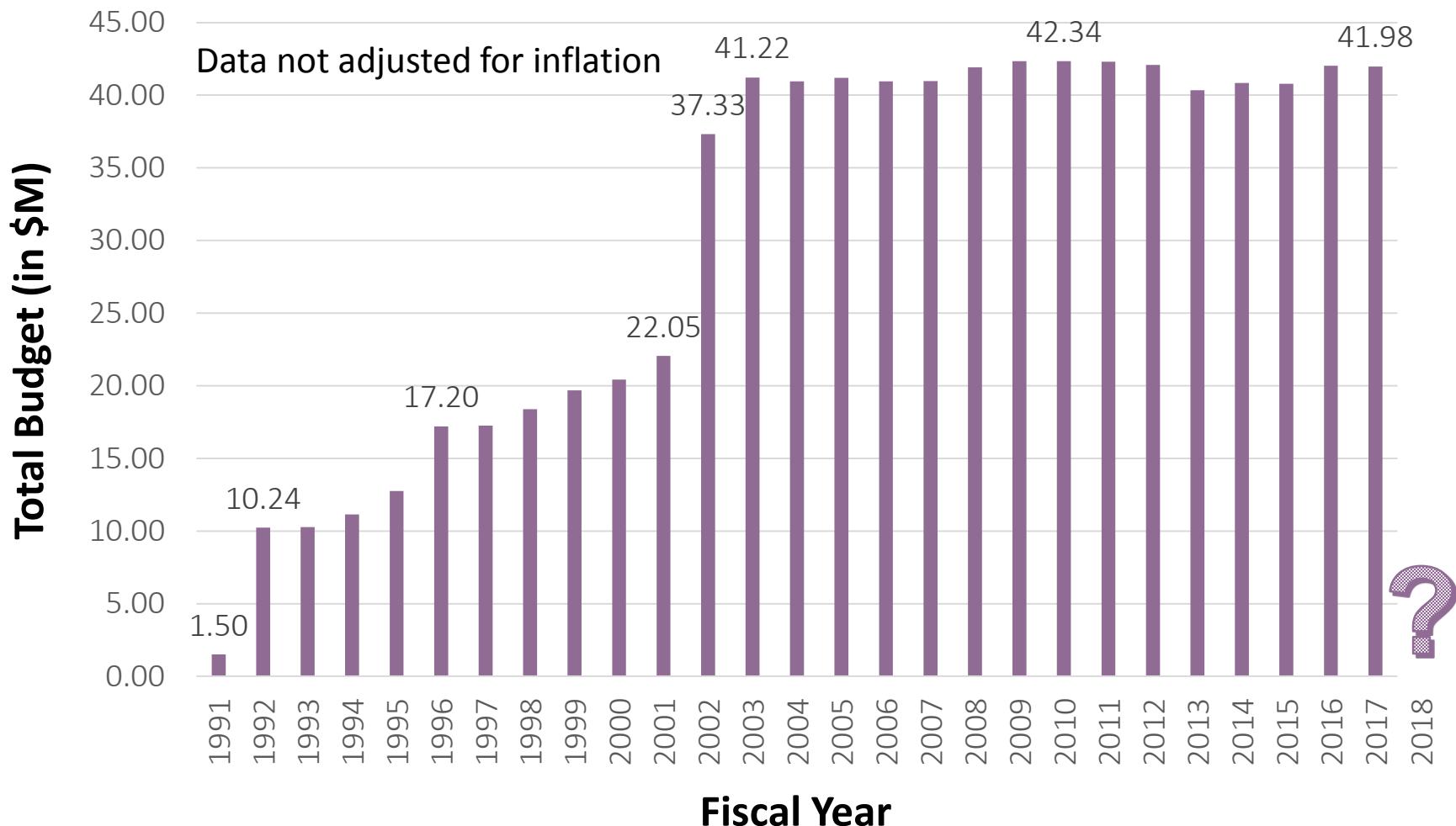
Supplemental Funding

IC Women's Health Research and
Co-Funding



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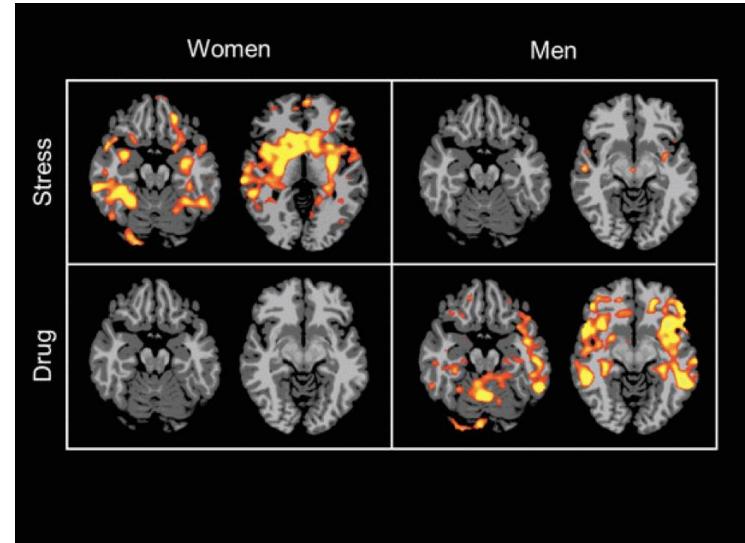
ORWH Funding History & FY17 Extramural Award Profile



FY17 Extramural Awards
(as % of Extramural Budget)

Funding Opportunity: Specialized Centers of Research (SCOR) on Sex Differences

- To foster interdisciplinary research on etiology, treatment & prevention of diseases that affect women
- FY12–FY17: 11 SCOR Awards across 6 ICs
 - NIA, NIAMS, NIDDK, NIMH, NICHD & NIDA
- FY 18: Specialized Centers of Research Excellence (SCORE) on
 - Career Enhancement Core (CEC) now required — to meet career enhancement needs of translational science in the study of sex differences



New Findings from Yale SCOR Investigator

When it comes to addiction, sex matters

Addicts' cravings have different roots in men and women. Read the [new study](#) on brain imaging from Yale School of Medicine. (PDF, 327 KB)

Kober H., Lacadie C.M., Wexler B.E., Malison R.T., Sinha R., Potenza M.N. 2016. Brain activity during cocaine craving and gambling urges: an fMRI study. *Neuropsychopharmacology* 41 (2): 628-637.

New FOA (RFA-OD-18-004) Applications due April 23, 2018

FY17 ORWH Sex & Gender Administrative Supplements

Preclinical



(Modified image from
Wikimedia Commons)

ORIP

Do gut microbiota affect sex differences in Alzheimer's disease?

Clinical



(Photo: Wikimedia Commons)



(Photo: Pixabay, CC0)

NIDA

Gender diffs. in mechanisms of recovery from opioid use disorder & anxiety

Preclinical + Clinical

2x RR of acute MI in W vs. M

Long-term risk of CVD

ART in HIV+ patients

Short-term BMI gain

Long-term risk of diabetes

NIAID

Does obesity in HIV-infected men & women (\uparrow in women) increase risk of CVD / diabetes? A study of markers in adipose tissue.

New FOA (PA-18-658) Applications due March 26, 2018

U3 Administrative Supplement: Research on Understudied Issues Underreported Information Underrepresented Populations of Women



- 1 yr. supplemental funding
- \$1.7 M funded for 15 U3 applications in FY17
- Examples:
 - ✓ MsFLASH Clinical Trials Network: living a healthy menopause
 - ✓ Impact of cocaine and polydrug use on cranial small vessel disease
 - ✓ Ethnic differences in outcomes and treatment barriers after sexual assault



(Images: PublicDomainPictures.net & Pixabay, CC0 Creative Commons)

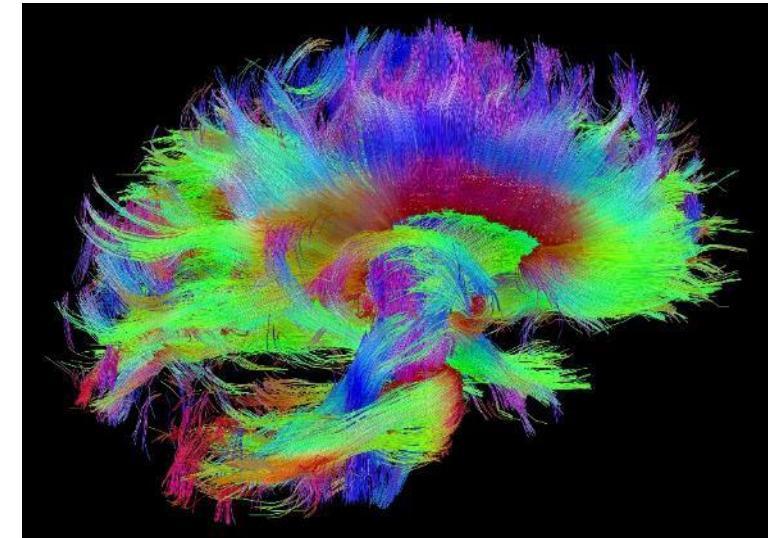
New FOA (PA-18-676) Applications due April 16, 2018



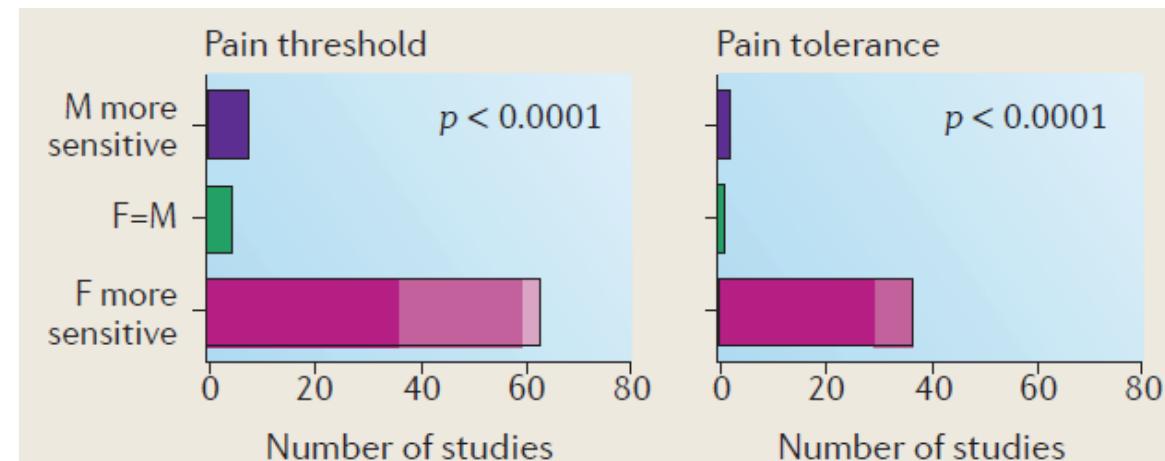
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ORWH Co-funding in Targeted Research Areas

- Brain Research Through Advancing Innovative Neurotechnologies® (BRAIN) Initiative
- NIH Pain Consortium & Centers of Excellence in Pain Research
- Bladder Health, Lower Urinary Tract Symptoms, and Chronic Pelvic Pain Research
- Diabetes Prevention Program & Diabetes Prevention Program Outcomes Study
- Osteoarthritis Initiative



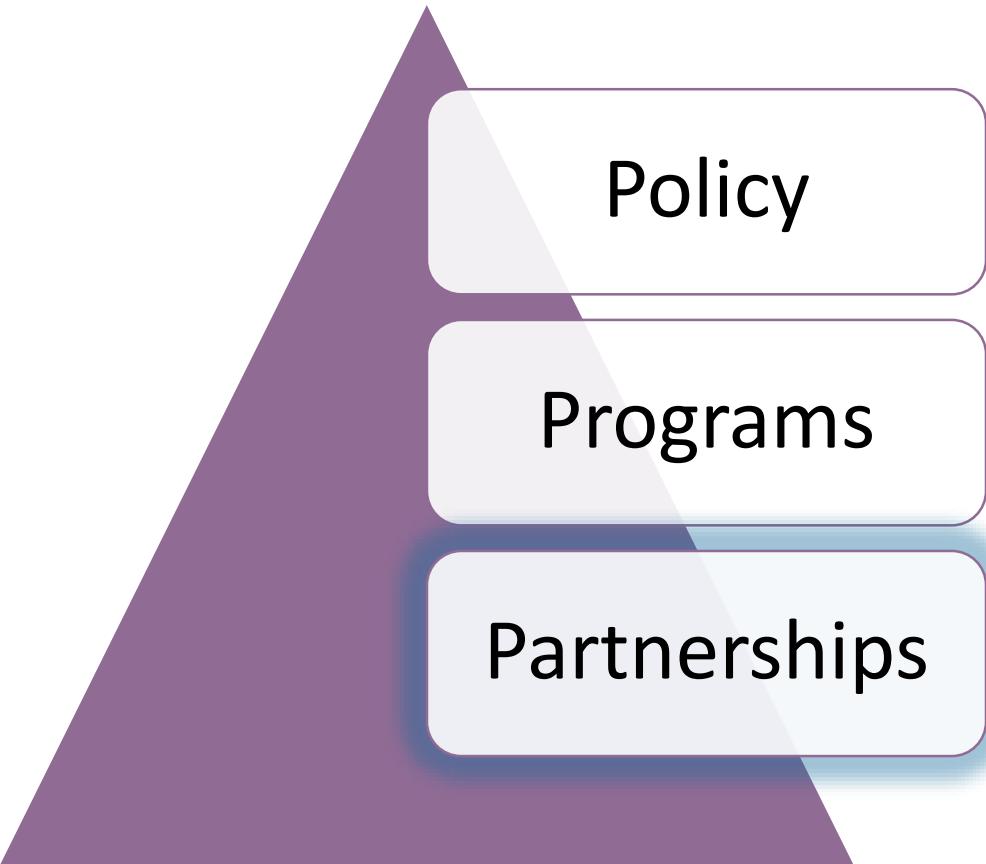
(Lab of Neuro Imaging and Martinos Center for Biomed. Imaging, Human Connectome Project Consortium)



(Mogil. 2012. *Nature Reviews Neuroscience* 13: 859-866.)



It Takes a Village...



Policy

Programs

Partnerships

Publishers

Pharmaceutical
Industry

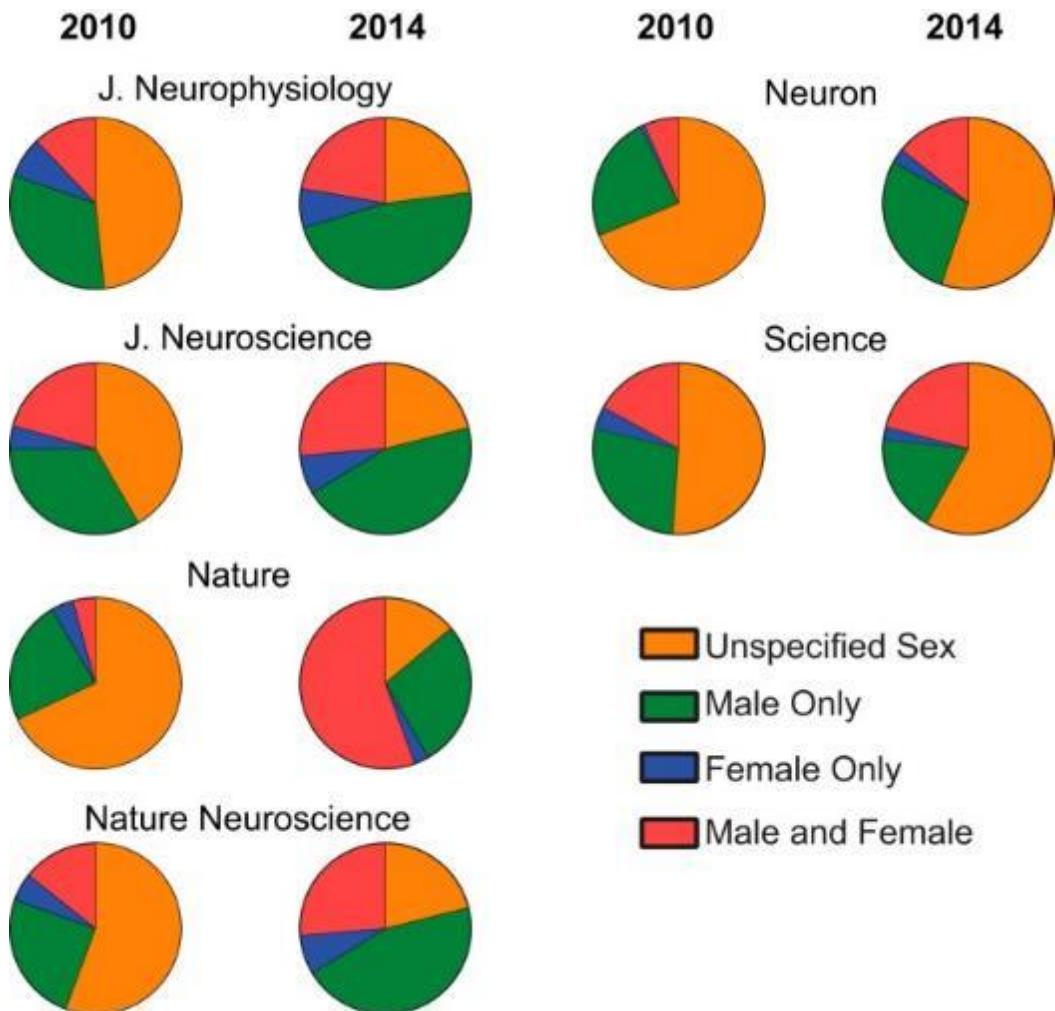
Manufacturers



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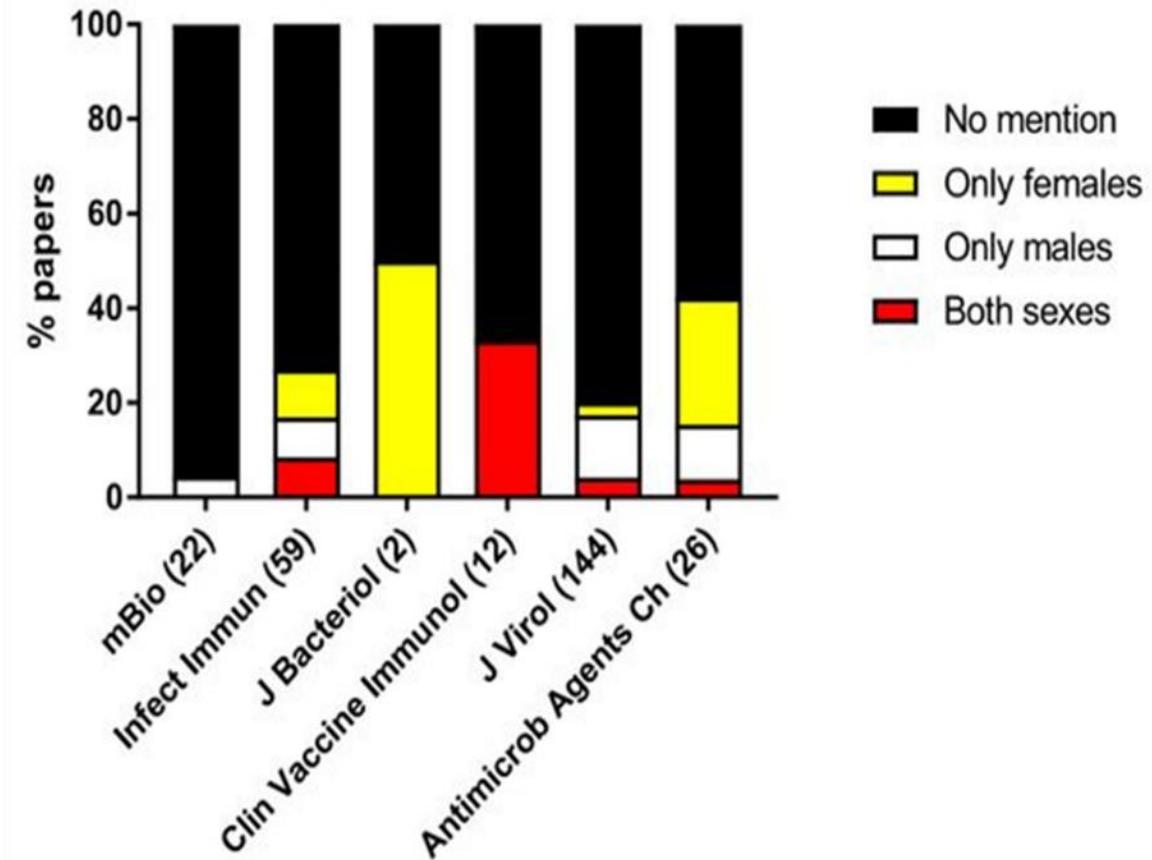
Good News: Decline in Omission of Sex

Bad News: Male Bias Persists



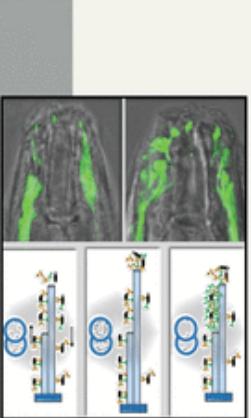
Will et al. 2017. Problems and progress regarding sex bias and omission in neuroscience research. *eNeuro* 4 (6): e0278-17.2017.

Primary Cell Culture Studies in ASM Journals – 2016



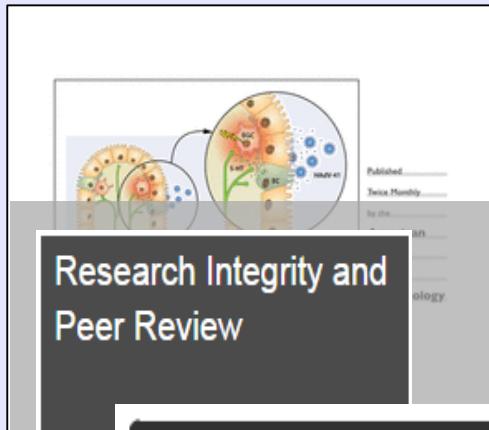
Potluri et al. 2017. Sex reporting in preclinical microbiological and immunological research. *mBio* 8: e01868-17.

Some journals are taking proactive steps to enforce changes in reporting practices



Published Twice Monthly
April 2018, Volume 38, Number 7
**AMERICAN
SOCIETY FOR
MICROBIOLOGY**

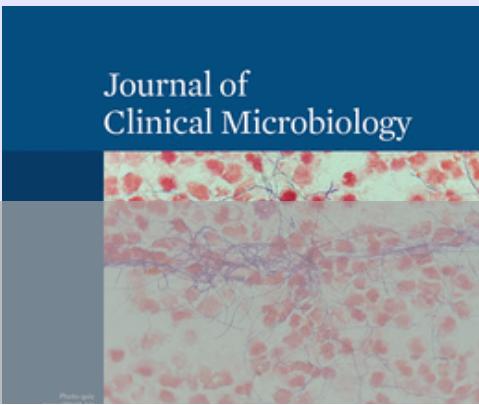
MCB
Molecular and Cellular Biology



REVIEW

Sex and Gender Equity in Research: rationale for the SAGER guidelines and recommended use

Shirin Heidari¹, Thomas F. Babor^{2*}, Paola De Castro³, Sera Tort⁴ and Mirjam Curno⁵



May 3, 2016

SABV Partnerships and Pharma



FDA Office of Women's Health
www.fda.gov/womenshealthresearch



Getting the Dosage Right

The New York Times

THE CONSUMER | JANUARY 28, 2013, 6:02 PM | 30 Comments

Health

The Drug-Dose Gender Gap

By RONI CARYN RABIN



"This is not just about Ambien - that's just the tip of the iceberg," said Dr. Janine Clayton, director for the Office of Research on Women's Health at the National Institutes of Health. "There are a lot of sex differences for a lot of drugs, some of which are well known and some that are not well recognized." ... "For example, Seldane, an antihistamine, and the gastrointestinal drug Propulsid both triggered a potentially fatal heart arrhythmia more often in women than in men. Many drugs still on the market cause this arrhythmia more often in women, including antibiotics, antipsychotics, anti-malarial drugs and cholesterol-lowering drugs, Dr. Clayton said."

Greenblatt DJ, et al. 2000. Comparative kinetics and response to the benzodiazepine agonists triazolam and zolpidem: evaluation of sex-dependent differences. *J Pharmacol Exp Ther.* 293 (2):435-43. 2



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Getting the Dosage Right

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Health

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Drugs With Different Effects in Men and Women

Ambien
(zolpidem)

- Dose 50% less in women

Aspirin

- W: stroke protection
- M: MI protection

Anti-
histamines

- Fatal arrhythmias



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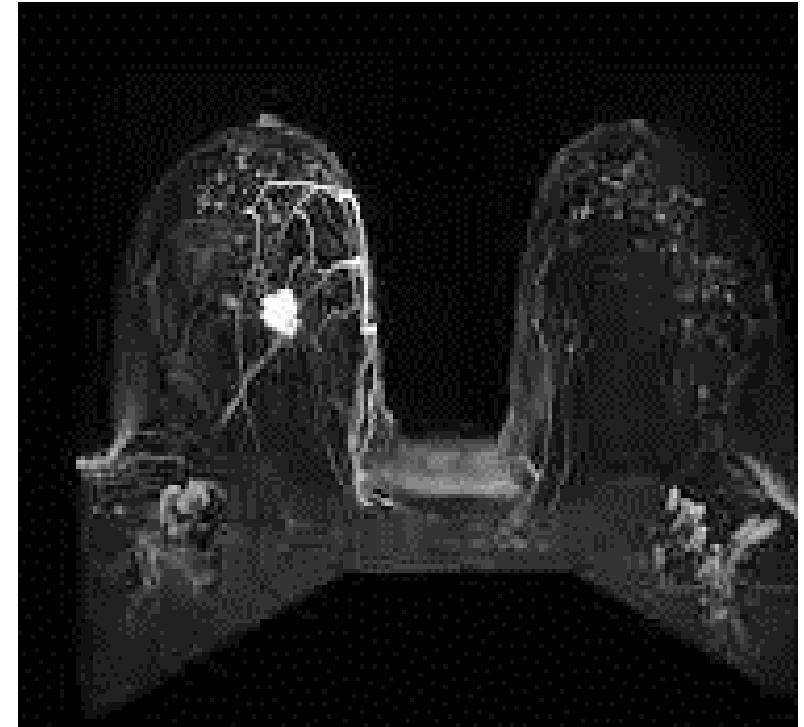
Manufacturing: Turning Discovery into Innovation



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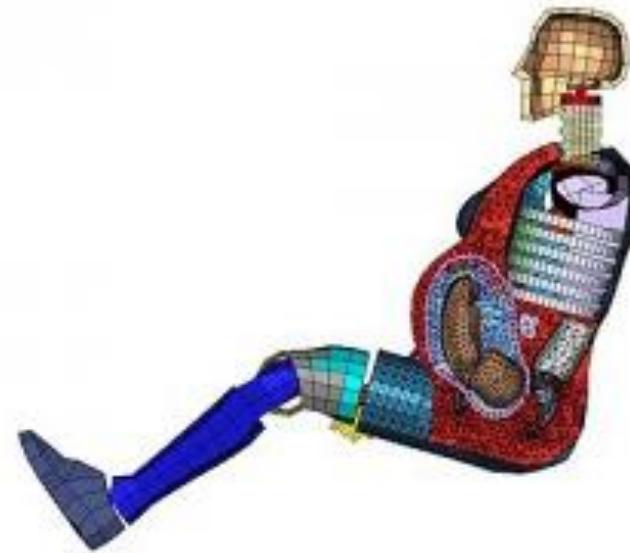
Related to Sex Differences Manufacturing: Turning Discovery ^Λ into Innovation

- MRI: imaging sex differences



Related to Sex Differences Manufacturing: Turning Discovery [^] into Innovation

- MRI: imaging sex differences
- Pregnant crash-test dummies



"Linda" by Volvo, a virtual pregnant crash-test dummy designed in 2002 by engineer Laura Thackray. "Linda" models the effects of high-speed impact on the womb, placenta, and fetus.

Related to Sex Differences Manufacturing: Turning Discovery [^] into Innovation

- MRI: imaging sex differences
- Pregnant crash-test dummies
- mHealth Innovations



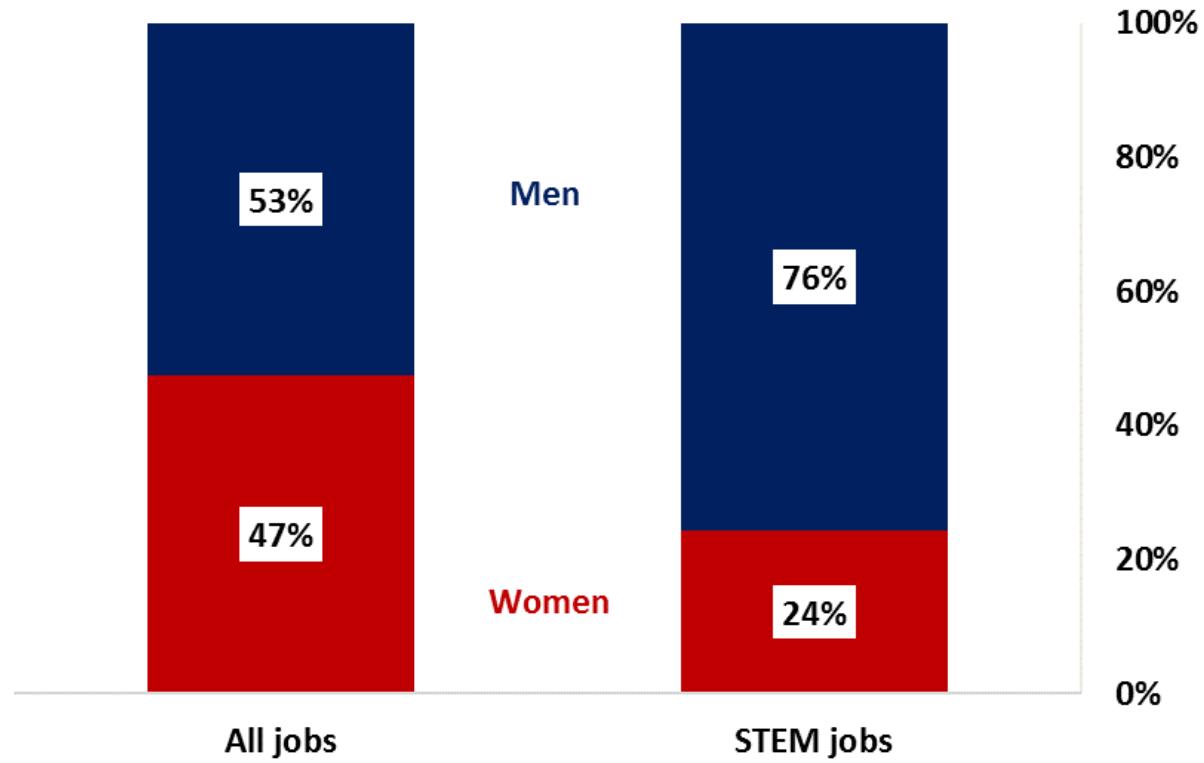
Women in Biomedical Careers



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Women in STEM: Diversity decreases along the biomedical career path

Figure 1. Gender Shares of Total and STEM Jobs, 2015



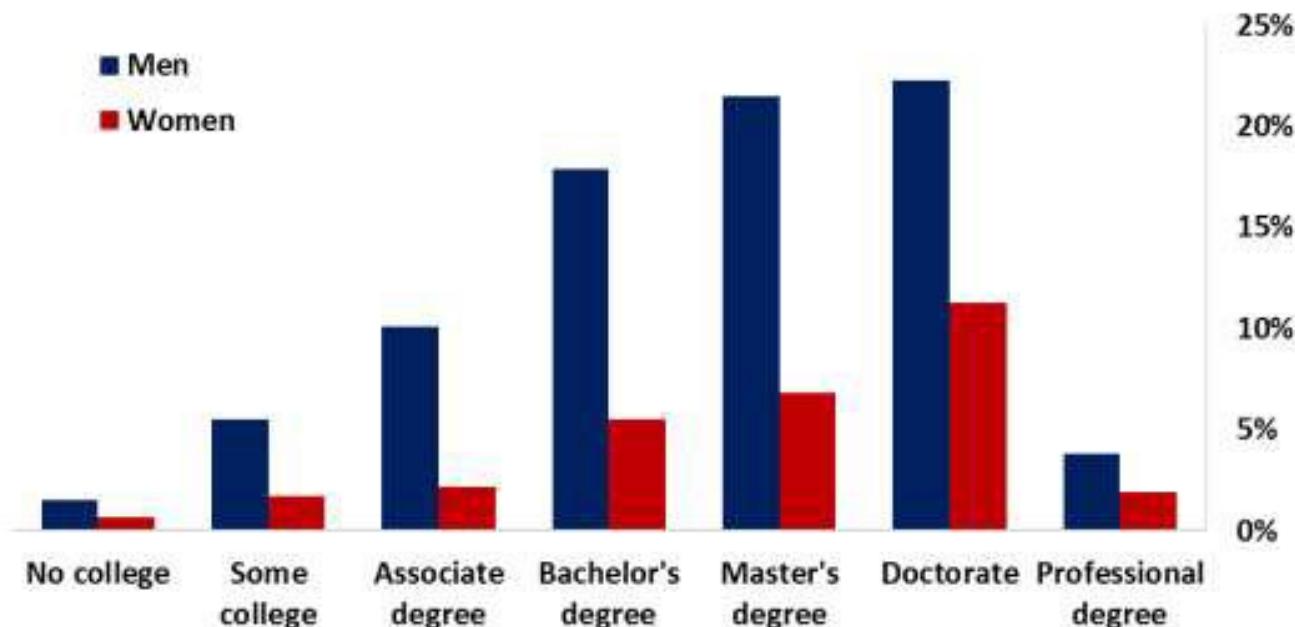
Source: OCE calculations using American Community Survey public-use microdata.
Note: Estimates are for employed persons age 16 and over.



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Women in STEM: Diversity decreases along the biomedical career path

Figure 2. Share of Workers in STEM Jobs by Gender and Educational Attainment, 2015



Source: OCE calculations using American Community Survey public-use microdata.

Note: Professional degrees include medical, dental, veterinary, and law degrees. Estimates are for employed persons age 16 and over.



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BIRCWH (Building Interdisciplinary Research Careers in Women's Health)

- Mentored career-development to promote recruitment, retention & advancement of careers in women's health
- RFA-OD-15-001 and RFA-OD-16-013
- 8 ICs: NICHD, NIAID, NIAAA, NIDA, NIDCR, NCI, NIA, NIAMS
- 20 BIRCWH Programs were funded in FY17
- Selected topics:
 - ✓ reproductive biology
 - ✓ cancer
 - ✓ depression, addiction, adverse childhood experiences
 - ✓ neuro-immune interactions
 - ✓ HIV-related
 - ✓ cardiometabolic risk burden
 - ✓ urinary microbiome in health & disease



NIH Working Group on Women in Biomedical Careers

- Funded the Causal Factors & Interventions RFA
 - 14 research grants investigating a range of obstacles facing women at all stages of the career pipeline
 - \$16.8M over 4 years, with support from 11 ICs & 4 Offices in OD
 - Well over 100 papers published
- Work-life integration policies
- Women of Color Research Network (WoCRN)
 - 4 regional chapters: DC, IN, MD, NC
 - Over 500 members and growing
 - <https://womeninscience.nih.gov/women-of-color/>



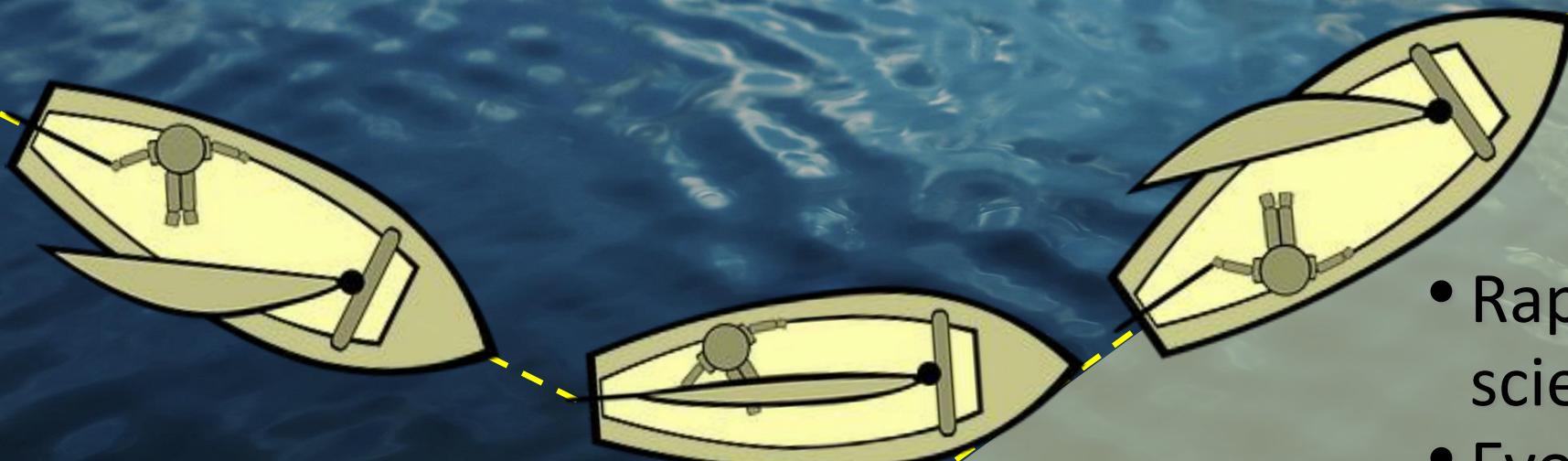
Dr. Lisa Barnes, Rush University, gave the NIH Director's WALS presentation on Feb. 28, 2018.



National Institutes of Health
Women in Biomedical Careers

For more information, visit womeninscience.nih.gov

Adjusting Our Course into the Future



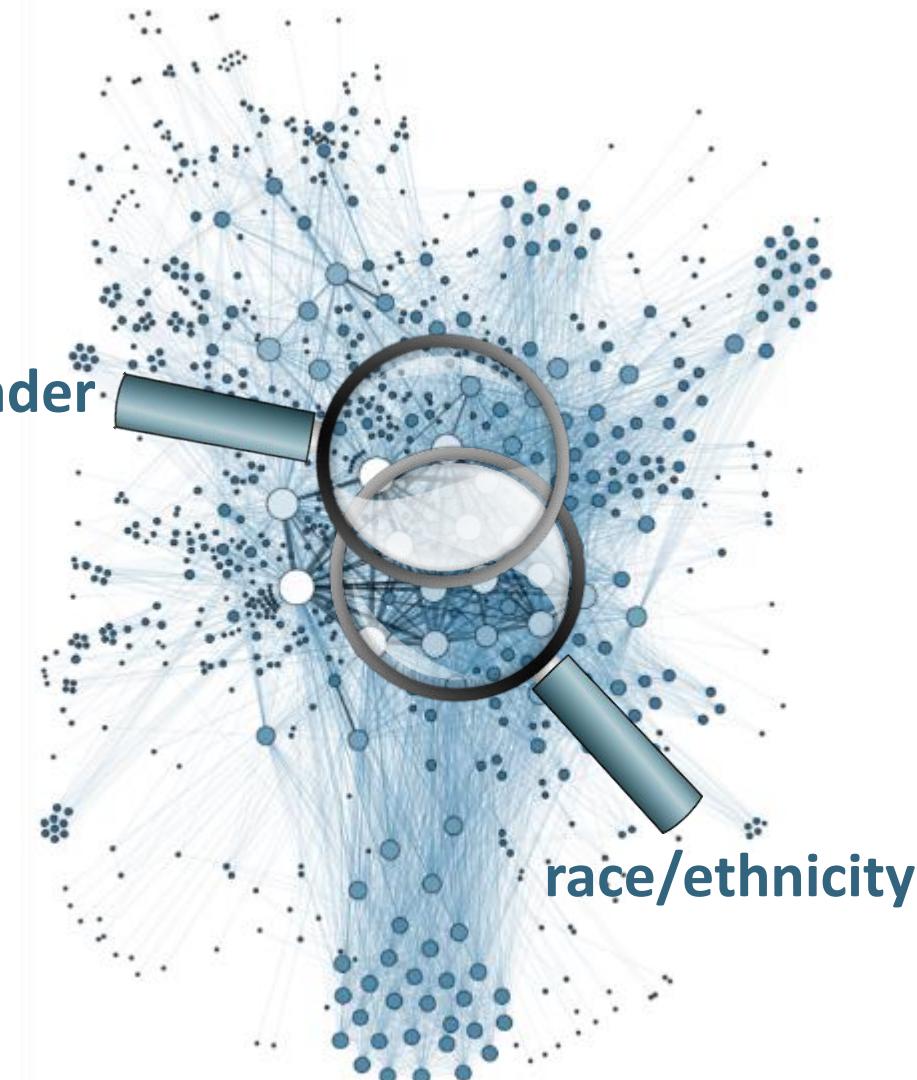
- Rapid advancement of science & technology
- Evolving public health needs
- Mandates of the 21st Century Cures Act

NIH Inclusion Policy for Clinical Research Recently Amended, with backing from the 21st Century Cures Act (Sec. 2053)

- Requires reporting of “valid analyses” on sex/gender & race/ethnicity inclusion data to **ClinicalTrials.gov** after completion of applicable NIH-defined Phase III clinical trials
- **Valid Analyses:** stratified analyses exploring how well intervention works among sex/gender & racial/ethnic groups
- **Applicable Clinical Trials:** in general, trials investigating FDA-regulated therapeutics, biologics & devices
- Applies to all new, competing grants & cooperative agreements **awarded on or after Dec. 13, 2017**

sex/gender

race/ethnicity



(Images: Martin Grandjean, 2014, CC BY-SA 3.0; Max Pixel, CC0)

See: **NOT-OD-18-014**

More information: <https://grants.nih.gov/grants/funding/lifespan/lifespan.htm>

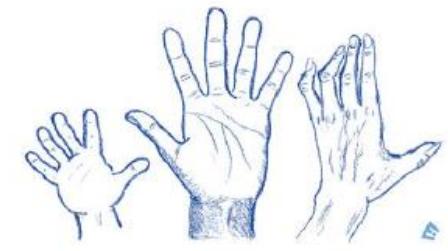
Inclusion Across the Lifespan Policy

- Expands “Inclusion of Children as Participants in Clinical Research” Policy to include all ages
- Clarifies justifications for age-based exclusion
- Requires participant age at enrollment to be provided in progress reports

Inclusion Across the Lifespan Workshop

Natcher Conference Center
National Institutes of Health
Bethesda, MD
June 1-2, 2017

Program Booklet

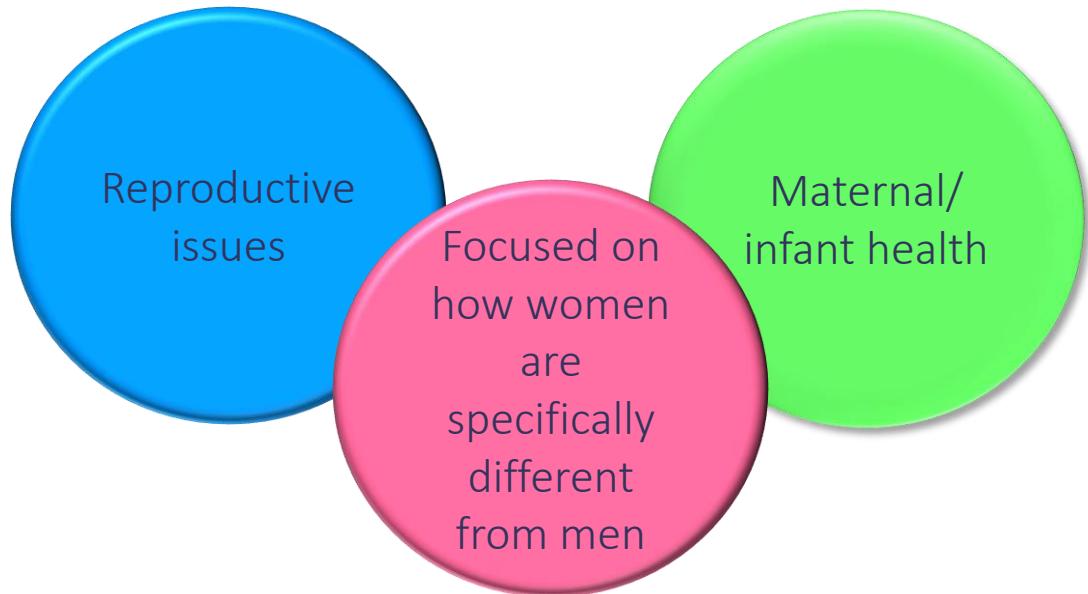


Check out the
Workshop
videos!

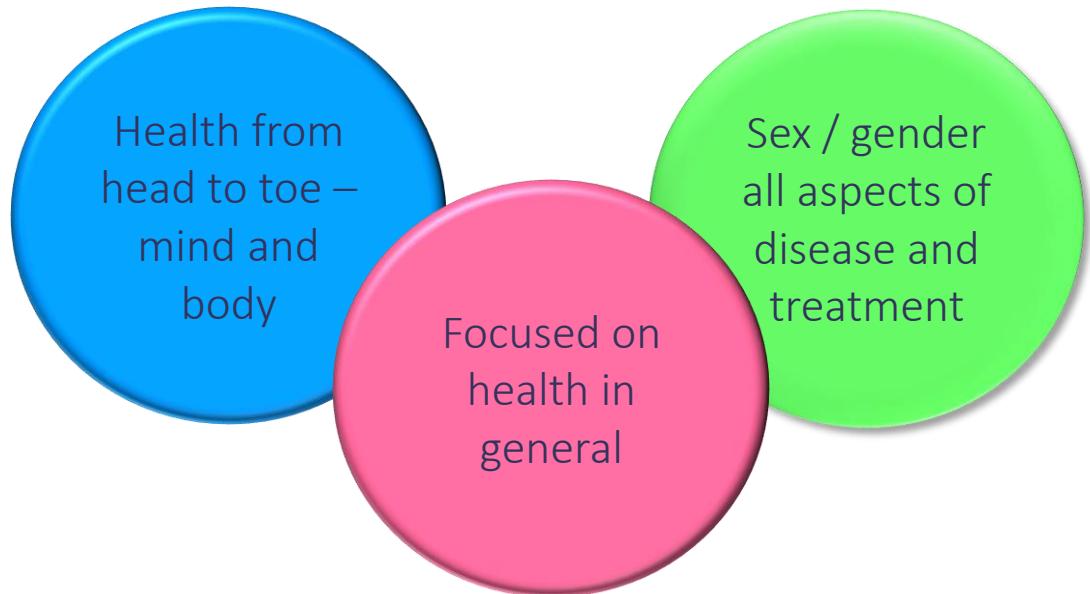
<https://videocast.nih.gov/> (search on “Inclusion Across the Lifespan”)

The Future of Women's Health

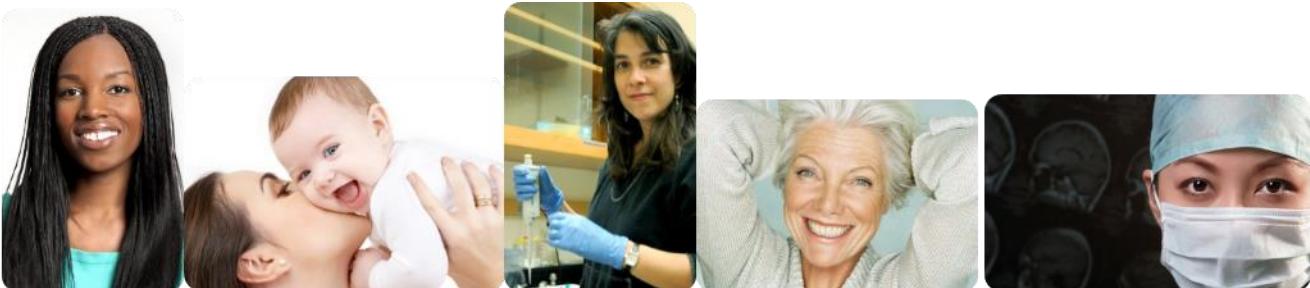
Previous Framework: Women's Health



Current Framework: Health of Women



The US Department of Health and Human Services defines women's health as
“diseases and conditions that affect women...all health concerns experienced by women across
the lifespan and in the social context of their lives”



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NIH Vision and ORWH Mission

Putting Science to Work for the Health of Women

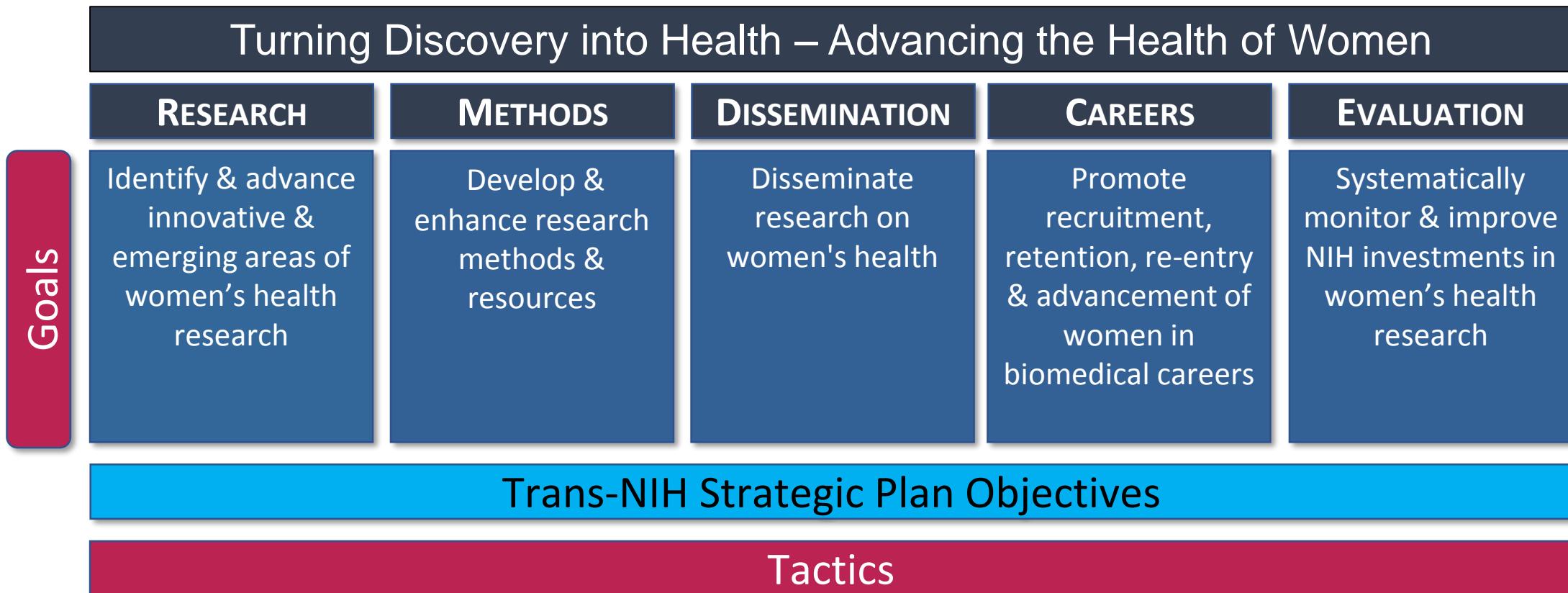
Vision

Sex and gender influences are integrated into the biomedical research enterprise; every woman receives evidence-based disease prevention and treatment tailored to her own needs, circumstances and goals; and women in science reach their full potential.

Mission

To enhance research related to diseases, disorders and conditions affecting women; to help ensure that women are appropriately represented in biomedical research supported by the NIH; and to improve the advancement of women in biomedical careers.

Looking to the Future: Draft Trans-NIH Strategic Priorities for Women's Health Research



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45th Meeting of the ACRWH is April 18

- 9am-1:30pm, Building 31, 6C/Room 10
- Agenda includes:
 - Director's Report
 - Legislative & 21st Century Cures Act Update (Ms. Paris Watson, ORWH)
 - Trans-NIH Strategic Plan for Women's Health Research (Dr. Margaret Bevans, ORWH)
 - Urinary Tract Infection: Complexity Results from Diversity at the Bacterial-Host Interface (Dr. Scott Hultgren, Wash. U.)
 - Inclusion of Pregnant and Lactating Women in Research (Dr. Diana Bianchi, NICHD)
- *Please join us!*



Advisory Committee on Research on Women's Health

Diana W. Bianchi, M.D.
Director, *Eunice Kennedy Shriver*
National Institute of Child Health
and Human Development (NICHD)



3rd Annual NIH Vivian W. Pinn Symposium

LEVERAGING THE NETWORK TO ADVANCE WOMEN IN SCIENCE

Wednesday, May 16, 2018

1:00 - 4:00 pm

NIH Main Campus

Lister Hill Auditorium

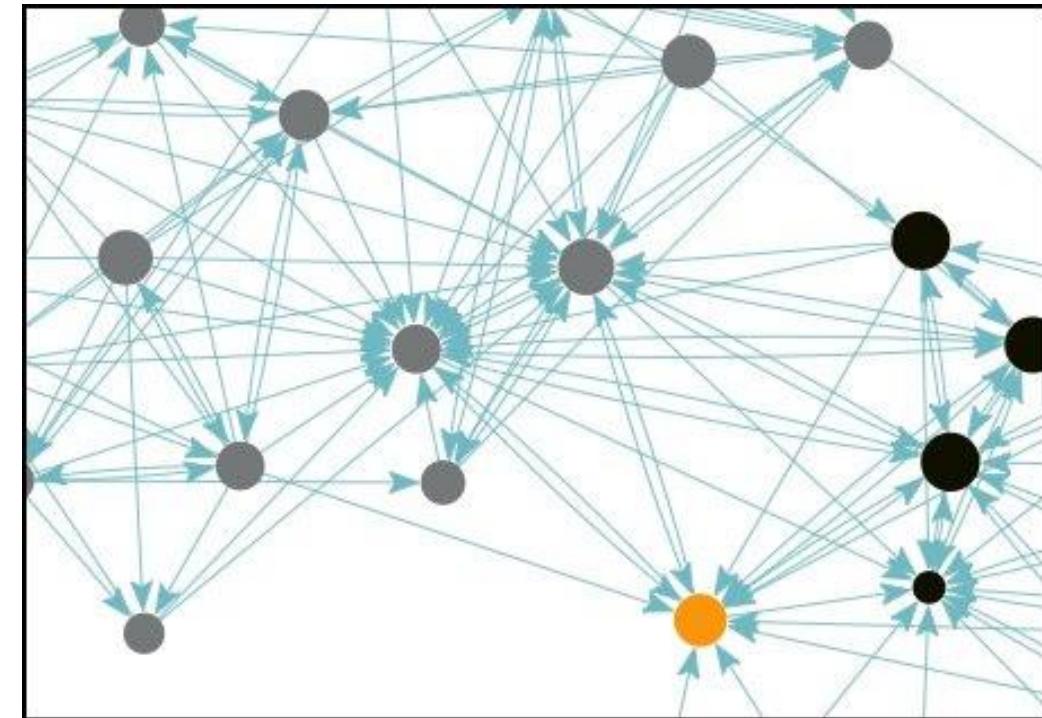
NIH Community Speaker Address: **Kay Lund, Ph.D.**

Academic Community Speaker Address: **Daniel Ford, M.D., M.P.H**, Navigating the Early Years to a Satisfying Career (tentative)

Women in STEM Speaker Address: **Rachelle Heller, Ph.D.**

Catalytic Connections: “Speed” Networking

New!



Warner ET, Carapinha R, Weber GM, Hill EV, Reede JY. 2016. Faculty promotion and attrition: the Importance of coauthor network reach at an academic medical center. *J. Gen. Intern. Med.* 31 (1): 60–67.



National Institutes of Health
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