The Power, Potential and Promise of Considering Sex and Gender to Advance Health

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June 6-7 – RCCN 2019  SEX AND GENDER DIFFERENCES IN AGING
Outline

- History of Sex and Gender
- Promise: Seeing the whole picture
- Power: SABV and disaggregating by sex
- Potential: Programs to advance the health of women (and men)
History of Sex and Gender Studies

The Second Sex published 1949

Sex Is NOT the Same as Gender

**XX XY**
Every cell has a sex.

**XY XX**
Sex affects behavior and perception.

Sex begins in utero.

Gender also affects behavior and perception.

**Female : Male**
Sex: genetic, molecular, cellular, physiological

**Feminine – Masculine**
Gender: behavioral, environmental, social, cultural

*Source: Exploring the Biological Contributions to Human Health: Does Sex Matter?, IOM Report, 2001*
Sex interacts with gender to influence health and disease

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The PROMISE of Studying Sex AND Gender: Seeing the Whole Picture
NIH is clarifying and revising application instructions and existing review criteria, in order to enhance reproducibility of research findings through increased scientific rigor and transparency.

http://www.nih.gov/science/reproducibility/
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
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The **POWER** of disaggregated data
The effects of the selective poly-ADP ribose polymerase (PARP-1) inhibitor PJ-34 in wild-type (WT) mice of both sexes. Treatment with PJ-34 at ischemic onset reduced total infarction in male mice compared with saline-treated controls (* P<0.001). A significant increase in ischemic damage was seen in PJ-34-treated females compared with control (* P<0.001).

What can we do to strengthen science?

SABV Checklist

1. Consider the influence of sex when formulating research questions
2. Review available literature for the influence of sex
3. Account for the influence of sex in study design
4. Incorporate both males and females
5. Alternatively, articulate a strong justification for a single-sex study
6. Collect, analyze data and report data disaggregated by sex
7. Characterize the influence of sex in the interpretation of results
8. Communicate appropriately generalized research findings
What can we do to strengthen science?
The 4 Cs of Studying Sex

Consider
Design studies that take sex into account, or explain why it isn’t incorporated

Collect
Tabulate sex-based data

Characterize
Analyze sex-based data

Communicate
Report and publish sex-based data
Connecting the Dots: The Research Continuum

SABV

Basic Preclinical Clinical Research & Trials Regulatory Review Clinical Practice

Cell studies, samples of human or animal tissues, computer-assisted models, animal models

Optimal health for everyone at every age and every stage
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Multi-level Model of Women’s Health across the Life Course

**External Factors**
socio-demographic characteristics, SES, and health policies
(women’s health in context)

**Internal Factors**
sex influences at molecular, cellular, tissue, and organ levels
(women’s health in biological perspective)

Pre-conception | Childhood | Adolescence | Adulthood

Check out the Workshop videos!

Multiple triggers – Exact Etiology Unclear

Occurs more often in women than men, over 90% of the women are postmenopausal.
Bio-Social Interactions with Sex Influences on Heart Disease


(Image: Pixabay, released under Creative Commons CC0)
A Diversity of Perspectives increases the POTENTIAL for finding Answers
The leading causes of death in U.S. women vary by race and ethnicity

- Black women
  - heart disease > cancer > stroke > diabetes
- White women
  - heart disease > cancer > CLRD > stroke


Cervical cancer rates vary among communities of women

- Virtually all cervical cancer is caused by 15 HPV types
- New approaches for cervical cancer prevention:
  - HPV vaccination
  - Carcinogenic HPV DNA testing
- Women at high risk do not have access to preventive services, or choose not to use them

Saslow et al. 2007. American Cancer Society Guideline for human papillomavirus (HPV) vaccine use to prevent cervical cancer and its precursors. CA Cancer J.

- An ORWH Administrative Supplement Program, first FOA issued in FY’17
- Research on influences of sex/gender at intersection of race/ethnicity and other social determinants of health & disease
- Focus on health disparities in populations of women who are understudied, underreported, or underrepresented (U3) in biomedical research
Examples of FY 18 U3 Projects by Research Category

• Clinical Research
  • A Novel Wireless Ingestible Sensor System - Measurement of Medication Adherence

• Prevention
  • Risk-based Breast Cancer Screening and Surveillance in Community Practice

• Behavioral and Social Sciences
  • Development of Co-Morbid PTSD and Chronic Pain Among Inner-City Women

• Mental Health
  • The role of cultural risk and resiliency factors and the built neighborhood on maternal depressive symptoms in pregnant Mexican American women

• Clinical Trials
  • A Cluster-Randomized Trial of Pharmacist-Coordinated Implementation of the DPP

• Pediatric
  • Building Evidence for Effective Palliative/End of Life Care for Teens with Cancer

• Minority Health/Health Disparities
  • Demographic and Health Disparities in Recovery from Hurricane Katrina: KATRINA@10

• Infectious Disease
  • Primary Infection Resource Consortium (PIRC) – Barriers to HIV testing for Native American women in Urban Settings
Administrative Supplements for Research on Sex/Gender Influences (Admin Supp)

- In FY 2013, ORWH initiated a trans-NIH program to catalyze exploratory research on sex/gender differences by providing “Administrative Supplements (Admin. Supp.)” to ongoing peer-reviewed NIH-funded grants.

- The initiative provided one year supplements of ~ $100,000 total cost.

- The new proposal and approaches were required to fall within the scope of parent award: preclinical, preclinical and clinical, or clinical research.

- The Admin. Supp. program supported following types of Research Approaches:
  - Add the Opposite Sex/Gender
  - Increase Sample Size (N)
  - Analyze Existing Data

- The proposed research must address at least one of the objectives from Goals 1 through 3 of the [NIH Strategic Plan for Women's Health Research](#).
ORWH has supported 341 S/G Admin Supps since FY13 and renewed the program for FY19

**Spotlight on Sex/Gender Admin. Supp.**

<table>
<thead>
<tr>
<th>PI &amp; Institution</th>
<th>Parent Grant</th>
<th>Admin Supp</th>
<th>Study Type</th>
<th>Main Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Esther Dupont-Versteegden, Ph.D.</strong></td>
<td><strong>NIH</strong> National Center for Complementary and Integrative Health</td>
<td><strong>R01</strong> AT009268-01</td>
<td>Preclinical</td>
<td>Addition of subjects to existing study to increase power for testing sex diffs.</td>
</tr>
<tr>
<td><strong>Forest White, Ph.D.</strong></td>
<td><strong>NIH</strong> National Cancer Institute</td>
<td><strong>U54</strong> CA210180-02</td>
<td>Preclinical + Clinical</td>
<td>Addition of new sex/gender to single sex/gender research</td>
</tr>
<tr>
<td><strong>Monica Uddin, Ph.D.</strong></td>
<td><strong>NIH</strong> National Institute on Minority Health and Health Disparities</td>
<td><strong>R01</strong> MD011728-01</td>
<td>Clinical</td>
<td>Sex/gender-based comparative analysis of existing samples/data sets</td>
</tr>
</tbody>
</table>

- **Mechanisms underlying anabolic effects of cyclic compressive loading in muscle**
- **Glioblastoma cell invasion profiles & implications for therapeutic response**
- **Epigenomic predictors of PTSD & traumatic stress in an African American cohort**
SABV expertise and knowhow in sex & gender analysis considered for peer review: ODP efforts

ODP enhanced their database of peer reviewers, which is populated via the Prevention Research Expertise Survey (PRES). They added:

- A methodological field of expertise related to sex & gender analysis
- A content topic area of expertise in assessing SABV
Integrating all these perspectives through a sex and gender lens

- **Power:** Rigor and Reproducibility considering sex and gender
- **Potential:** Seeing analytically, differentially, integrating diverse perspectives
- **Promise:** Seeing the whole picture Medical and technological innovation

Medical and technological innovation
Connect With Us

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