Sex as A Biological Variable: Program Update

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

48th Meeting of the NIH Advisory Committee on Research on Women's Health
April 10, 2019
SABV Policy in a Nutshell

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

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

*January 25, 2016 (effective date)
There has been slow progress on results reporting for preclinical research.

Sex of rodents in 6,636 neuroscience papers from 6 top journals

2010

2014

Unspecified Sex
Male Only
Female Only
Male and Female

Implementation of the NIH Sex-Inclusion Policy: Attitudes and Opinions of Study Section Members

Nicole C. Woitowich, PhD1 and Teresa K. Woodruff, PhD1,2

Volume 28, Number 1, 2019
From 2016 to 2017, surveyed NIH study section members perceived an increase in the consideration of SABV by applicants.

Q: Did applicants adequately address the incorporation of SABV into their experimental design, analysis, and reporting?

- 2016: 51% vs 2017: 66%
- p < 0.0001
- A: The majority of them did so.

Q: Did applications account for the consideration of SABV within the research strategy?

- 2016: 61% vs 2017: 71%
- p < 0.0001
- A: Half or fewer of them did so.

Outline

• SABV policy uptake and adoption is not complete
• **New impetus for assessment of SABV policy uptake**
  • New partnerships for SABV resource development
  • Other SABV resources
  • SABV application to the science
Trans- NIH SABV Working Group

Established: September 11, 2014
Mandate: To inform SABV Policy development
Chair: ORWH Director
Members: Senior IC staff nominated by IC Director
Meetings: Quarterly
ORWH Staff contacts:
  ▪ Rebecca DelCarmen-Wiggins, Ph.D.
  ▪ Elena Gorodetsky MD., Ph.D.
  ▪ Chyren Hunter, Ph.D.
## Trans-NIH SABV Working Group Members

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21st Century Cures Act – Enhancing the Rigor and Reproducibility of Scientific Research – ACD Recommendations

1) Resources on rigor
2) Clarify scientific premise
3) Examples of authentication plans
4) Training in rigor scored
5) Outcomes evaluation
Public Law 115-135

One Hundred Fifteenth Congress of the United States of America

AT THE SECOND SESSION

Begun and held at the City of Washington on Wednesday, the third day of January, two thousand and eighteen

An Act

To amend titles 5 and 44, United States Code, to require Federal evaluation activities, improve Federal data management, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE—This Act may be cited as the “Foundations for Evidence-Based Policymaking Act of 2018”.

(b) TABLE OF CONTENTS—The table of contents for this Act is as follows:

On Monday, January 14, 2019, the President signed into law:

H.R. 672, the “Combating European Anti-Semitism Act of 2017,” which expresses the sense of the Congress that it is in the United States national interest to combat anti-Semitism at home and abroad;

H.R. 4174, the “Foundations for Evidence-Based Policymaking Act of 2018.”

Efforts, and improving access to data for statistical purposes while protecting confidential information;

H.R. 7279, the “Water Infrastructure Improvement Act,” which amends the Federal Water Pollution Control Act to provide for the use of green infrastructure to reduce stormwater flows;

H.R. 7318, which eliminates the deadline for the appointment of members to

signed into law
January 14, 2019
New OD Office of Evaluation boosts NIH goal for evidenced-based evaluation of SABV policy implementation

Office of Evaluation, Performance, and Reporting, DPCPSI

Mission: To better capture, communicate, and enhance the value of NIH research through strategic planning, performance monitoring, evaluation, and reporting.
• SABV policy uptake and adoption is not complete
• New impetus for assessment of SABV policy uptake
• **New partnerships for SABV resource development**
• Other SABV resources
• SABV application to the science
ORWH and NIGMS establish a new partnership to develop a primer for SABV

- An interactive, e-learning course to enhance and improve the consideration of SABV in research design, analyses, and reporting
- A resource for designing research studies, preparing NIH grant applications, and training the next generation of investigators
- Audience: researchers of any level, from predoctoral trainees to senior faculty
- Developed by an ORWH-designated contractor with the input of NIH and NIH-designated subject matter experts
- Designed as independent, interrelated modules, with an instructor guide, glossary and references
SABV Primer – Goal:

To enhance the consideration of SABV in the context of conducting rigorous research to improve the reproducibility of data.

- Clarify the SABV policy
  - What is required and what is not?
- Create better buy-in and compliance
  - Myth-busting
  - Address perceived challenges
- Help investigators better apply the policy to their research
  - Research design / analysis / reporting
  - Basic / pre-clinical / clinical / population health
Expert Panel on SABV Curriculum Development

Major questions posed to the BIRCWH PI Panel:

✓ Do scientists understand how to incorporate SABV principles into scientific thinking?

✓ How do we teach incorporation of these principles in order to change existing paradigms?

✓ How do researchers incorporate both sexes and/or genders into their research within cost and time constraints?

Speakers: BIRCWH PIs & Program Directors from Mayo Clinic, U of CO, U of PENN, & ORWH
• SABV policy uptake and adoption is not complete
• New impetus for assessment of SABV policy uptake
• New partnerships for SABV resource development

• **Other SABV resources**
• SABV application to the science
ORWH co-funds field-specific training on SABV

RFA GM-18-002 : Training Modules to Enhance the Rigor and Reproducibility of Biomedical Research (R25 Clinical Trial Not Allowed)

GOALS:
To develop exportable training modules in areas with the potential to enhance data reproducibility and to provide for communication and coordination of the development and deployment of such modules.

It is expected that the proposed training modules will identify deficiencies and teach best practices in the following general areas:

- Scientific culture and principles
- Good laboratory practices and record keeping
- Experimental design and analysis
The ORWH Sex and Gender infographic is now available in Spanish.

Available on the ORWH website under Downloadable Resources or in the NIH Salud Spanish Health Information portal.

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Cómo el SEXO y el GÉNERO influyen sobre la salud y la enfermedad

El sexo y el género pueden influir en la salud de formas importantes. Si bien el sexo y el género son conceptos distintos, su influencia generalmente está inextricablemente relacionada. Las evidencias científicas que generan los dos más complejos asocian las influencias de sexo y género en el diseño de soluciones, intervenciones y análisis de datos, e incremento de resultados.

**Sexo** es una clasificación biológica, calificada en nuestro ADN. Los hombres tienen cromosomas XY y las mujeres tienen cromosomas XX. El sexo varía para hombres y mujeres. Cada célula de nuestro cuerpo tiene un sexo —conteniendo ovocitos y esperma, como el del corazón, cansancio y estrés—. Cada célula es masculina o femenina según el ADN del sexo masculino o femenino, aunque existe una diversidad considerando en cómo las personas se perciben y se sienten, y cómo actúan e interactúan. El género usualmente reemplaza o complementa el sexo biológico (género y sexualidad), aunque no es una dualidad considerando en cómo los papeles y las expectativas son restringidos y experimentados.

Visite NIH.gov/women para conocer cómo el estudio del sexo y género fortalece a la ciencia.

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**Salud mental**

Las mujeres tienen dos veces más probabilidad de que los hombres sufran depresión, con algunas razones que afectan más a los hombres y la mujer de un estado de la función relacionada con las cambios hormonales durante la pubertad, el embarazo, y la menopausia.

Las mujeres que tienen propensión a ayudar se involucran más en la búsqueda de tratamiento para problemas de salud mental en diferentes hombres.

**Dejar de fumar**

A las mujeres les resulta más difícil dejar de fumar. Las mujeres pueden experimentar la excitación, el apetito adictivo del tabaco, el mayor riesgo de los hombres. Las diferencias en el metabolismo pueden ayudar a explicar por qué las mujeres mayores consumen más que los hombres, como posibles y difíciles, funcionan mejor en las mujeres que en los hombres. Las mujeres también son más sensibles a los efectos terapéuticos de las drogas más relaxantes con la adicción.

Si bien los hombres son más sensibles que las mujeres a los efectos terapéuticos con la adicción, los hombres pueden ser más propensos que las mujeres cuando se están relacionando con sustancias o bien de manera o social, y así acceden a los problemas de salud mental.

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**Riesgo cardiovascular**

Las mujeres son más propensas al desarrollo de una enfermedad más temprana y vital que se refiere más directamente relacionada con las dos en hombres. Frecuentemente, en el caso como explicación del por qué las mujeres son más propensas que los hombres a la enfermedad o la enfermedad de las mujeres, y los hombres tienen un menor en el desarrollo cardíaco, pero parten de ellas al final de la evolución en una enfermedad cardíaca cardiovascular.

**Osteoporosis**

Los hombres con osteoporosis son más en mujeres porque tienen menos huesos en los huesos y la mujer de un contenido de potasio de ecología biológica los cambios hormonales de la menopausia.

Los hombres con osteoporosis en las mujeres mayores de 50 años solo que son afectadas y gravemente en un estado de forma, recomendándose que los patrones y prevención puesta en la osteoporosis como una enfermedad de la mujer.

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**Artros de rodilla**

Las mujeres tienen más probabilidad de que los hombres con osteoartritis de las rodillas al practicar deportes, en parte debido a la estabilidad de sus rodillas y cambios, la hueso machi articulaciones de las mujeres, y las rodillas y artritis más doloridas. La osteoartritis de los tejidos y enfermedad dentro de la articulación de las rodillas, y las mujeres con osteoartritis.

Correr con zapatos de tacón alto aumenta la presión en la articulación de las rodillas, a la rodilla y a las mujeres con mayor riesgo de desarrollar osteoartritis.

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NATIONAL INSTITUTES OF HEALTH

Office of Research on Women’s Health

NIH.gov/women | @ORWH_ORTHE | @SexSci
SABV Application to the Science

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Emerging Research on Alcohol and Women’s Health: What Do We Know and Where Do We Go from Here?

George F. Koob, PhD
Director,
National Institute on Alcohol Abuse and Alcoholism

NIH Coordinating Committee on Women’s Health March 13, 2019
The Brain Undergoes Widespread Sexual Differentiation During Adolescence – Implications?

Females and males develop different densities of gray matter in cortical areas.

Areas with more gray matter in female (RED) or in male (BLUE) adult brains.

Females have more functional brain connectivity.

Alcohol Induces More Dopamine Release in Male than Female Nucleus Accumbens

PET imaging using the D2/3 radiotracer [11C]raclopride.

Delta BP release and subjective effects are related in men but not women.

Decreased D2/3 binding reflects displacement by endogenously released dopamine.

NIH Coordinating Committee on Women’s Health March 13, 2019
Using the Adolescent Brain and Cognitive Development (ABCD) data set, study finds relationship between sex, sports activity and mental health in preadolescents

Findings

• Greater sports involvement, but not non sport activity involvement, was associated with less depression in boys

• Involvement in all types of sports except for individual sports and non-sport activities was related to hippocampal volume in both boys and girls.

• Hippocampal volume was associated with depression in boys only

ABCD data set = 4191 children ages 9-11

Involvement in Sports, Hippocampal Volume, and Depressive Symptoms in Children
Lisa S. Gorham, Terry Jernigan, Jim Hudziak, and Deanna M. Barch: Biological Psychiatry: Cognitive Neuroscience and Neuroimaging - 2019 In Press
ORWH hosted a GWAS, Sex & Chromosomes Think Tank on Feb. 27, 2019, which was attended by 15 NIH ICOS.

- What factors explain underrepresentation of sex chromosomes in GWAS results?
- How much info is lost when sex is controlled for statistically, but the influence of sex is not reported?
- Are there emerging solutions to these issues?
- To what extent can historical GWAS datasets be re-examined to achieve a more thorough consideration of sex?  
- How should additional information (pubertal/menopausal, hormonal, reproductive) be incorporated?

Coming Soon! A Think Tank summary will be posted on the ORWH website.

Gender and the Genome Core
Co-Chairs
Jamie White    Matt Arnegard
Members
Rajeev Agarwal   Elena Gorodetsky
Advisor
Chyren Hunter

ORWH ‘SCORES’ at OSSD / IGM 2019:

**Current SCORE U54 Principal Investigators**

Session 5: Sex differences in immune function and disease
*Sex differences in vaccine-induced immunity against influenza*
*Sabra Klein, PhD, Johns Hopkins Bloomberg School of Public Health*

Session 8: Sex differences in prescription, efficacy, and adverse drug reactions of commonly prescribed drugs
*Sex hormones and adverse drug reactions*
*Virginia Miller, PhD, Mayo Clinic*

**Prior SCOR P50 Principal Investigator**

Session 4: Sex differences in nicotine and smoking: From brain and behavior to smoking cessation
*Chairs: Cora Lee Wetherington, PhD, National Institute on Drug Abuse, Sherry McKee, PhD, Yale School of Medicine*
Thank You