



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

CONCEPT CLEARANCE:
Reissuance of *The Intersection of Sex and Gender Influences on Health and Disease Research*



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Associate Director,
Basic and Translational Research Programs

ACRWH: April 6, 2022



OUTLINE

- 1 | Rationale and goals for research at the intersection of sex and gender influences on health and disease
- 2 | R01 OD-19-029: The Intersection of Sex and Gender Influences on Health and Disease (R01 Clinical Trial Optional)
Progress report and lessons learned
- 3 | Considerations for concept reissuance

Rationale for a research initiative at the *intersection of sex and gender*

The ORWH program would be the only NIH-wide funding opportunity that focuses broadly on the health of women. It would:

- Encourage new research on the differential effects of **sex and gender and their intersection** on women's health
- Increase **collaborative partnerships** across NIH institutes, Centers and Offices to **support disease - agnostic** topics to advance women's health
- Provide an opportunity to conduct transdisciplinary research that is ordinarily beyond the scope of one NIH IC or Center
- To satisfy **evolving public health needs** and legislative mandates as identified in the 21st Century Cures Act, and the *2019-2023 Trans-NIH Strategic Plan for Women's Health Research*

New initiative builds on current ORWH programs to advance the integration of sex and gender considerations

The 4 Cs of Studying Sex to Strengthen Science

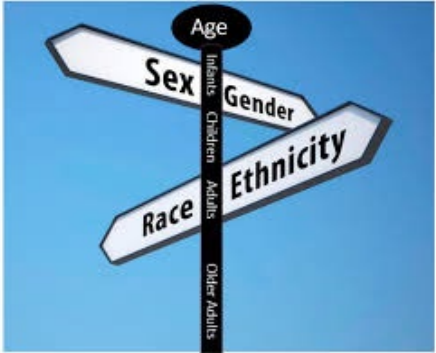
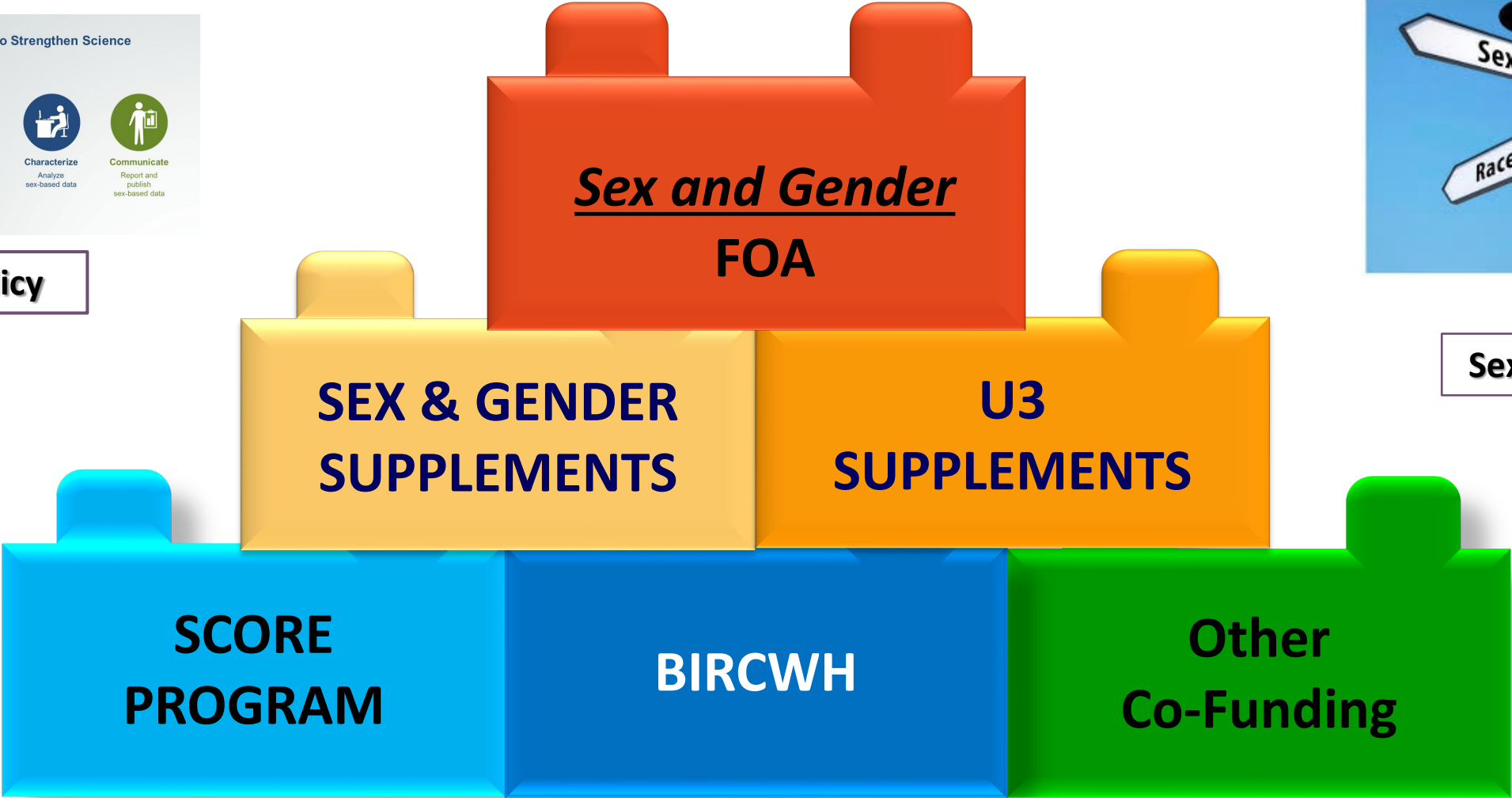
Consider
Design studies that take sex into account, or explain why it isn't incorporated

Collect
Tabulate sex-based data

Characterize
Analyze sex-based data

Communicate
Report and publish sex-based data

SABV Policy



Sex & Gender

FOA applications
must address:



Sex- and gender-
related variables



The intersection
of sex and gender
in health and disease



The 2019-2023
Trans-NIH Strategic Plan
for Women's Health Research
Goal #1

RFA-OD-19-029:

**The Intersection of Sex
and Gender on Health
and Disease**



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

Sex and Gender R01 applications address the Trans-NIH Strategic Plan for Women's Health Research

Goal 1 Objectives:

Additional FOA Considerations:



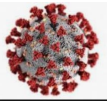
Health Disparities



Life Course/Lifespan



IC-specific Priorities



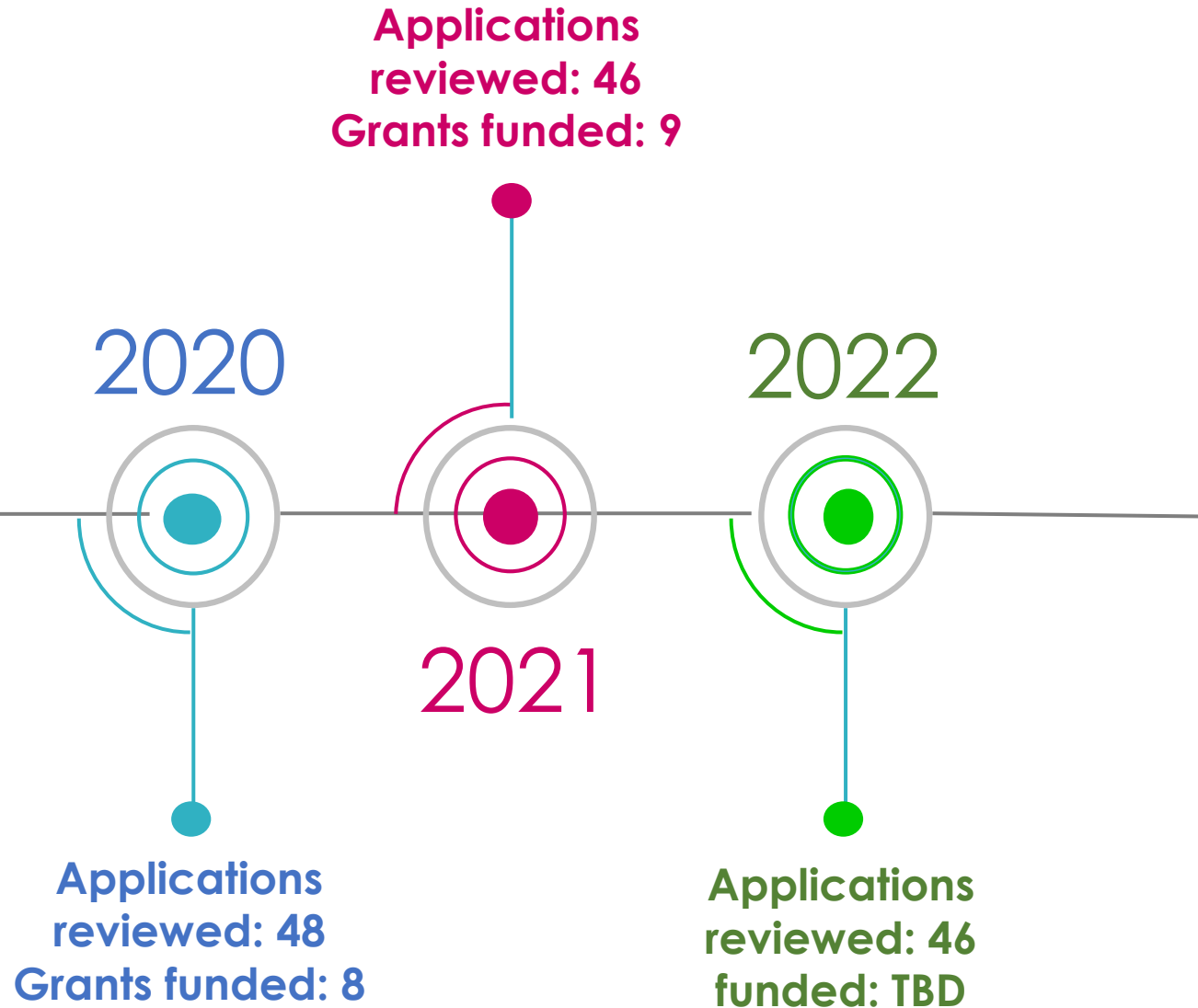
SARS-CoV-2 virus or COVID-19

1. Discover biological differences between females and males.
2. Investigate the influence of sex and gender on disease prevention, presentation, management, and outcomes.
3. Identify the immediate, mid-, and long-term effects of exposures on health and disease outcomes.
4. Promote research that explores the influence of sex and gender on the connection between the mind and body, and its impact on health and disease.
5. Expand research on female-specific conditions and diseases including reproductive stages, and maternal, and gynecologic health.



Sex and Gender R01:

Overview (FY'20-23)



RFA-OD-19-029 Program:
NIH Investment
(2020 + 2021) - \$9 Million
Overall Success rate - 17%



Office of Research
on Women's Health

NIMH

National Institute
of Mental Health



National Institute
on Drug Abuse

Advancing Addiction Science



National Institute of Dental
and Craniofacial Research



National **Heart**
Lung and Blood Institute
People Science Health



NATIONAL INSTITUTE OF
NURSING
RESEARCH



National Institutes of Health
Sexual & Gender Minority Research Office



National Institute
of Allergy and
Infectious Diseases



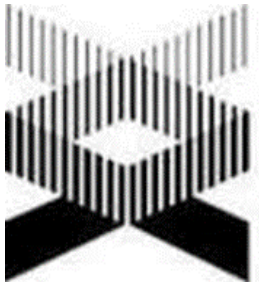
Aging



NIEHS



National Center for
Complementary and
Integrative Health



National
Human Genome
Research Institute

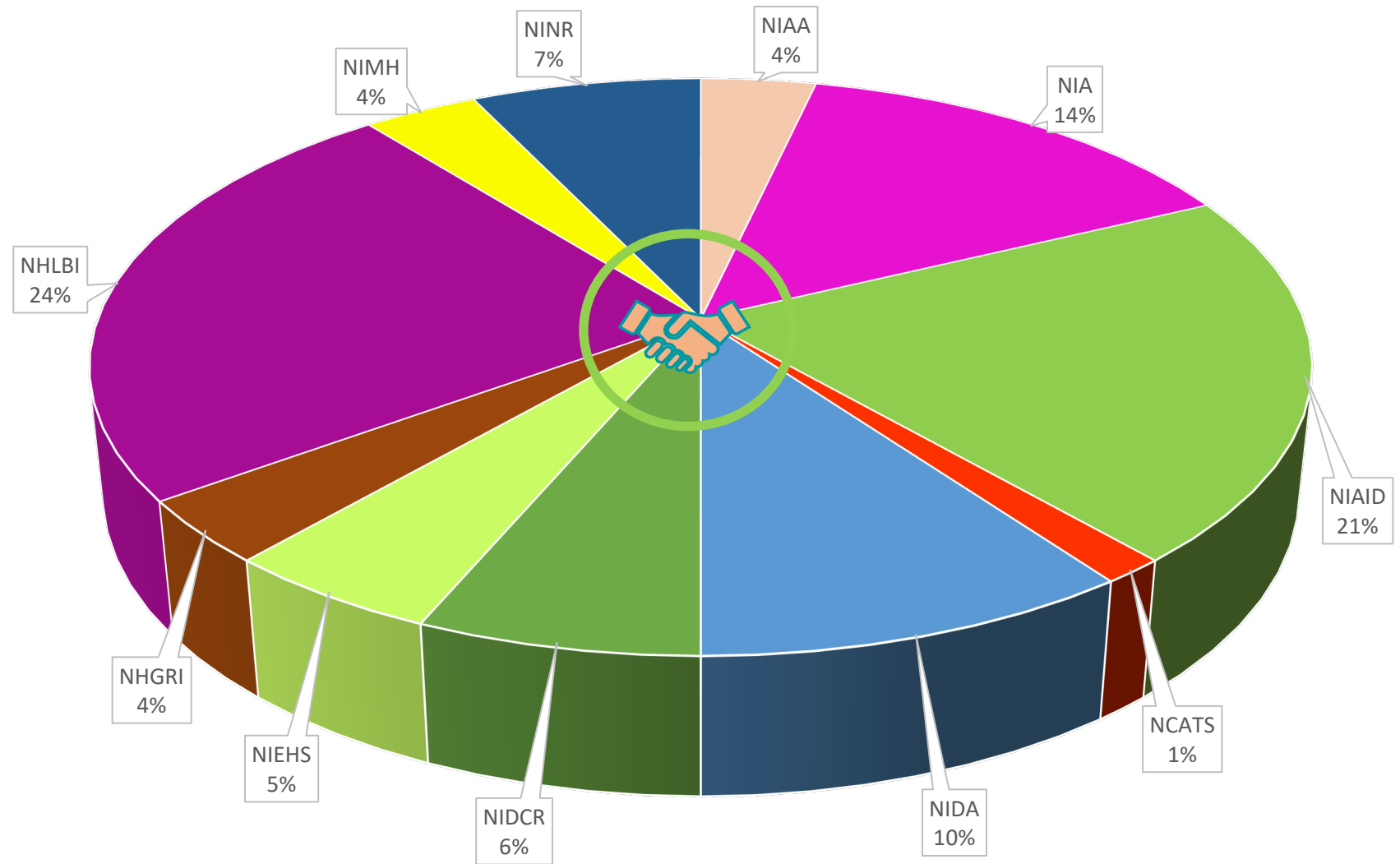
NIAAA

National Institute on Alcohol
Abuse and Alcoholism

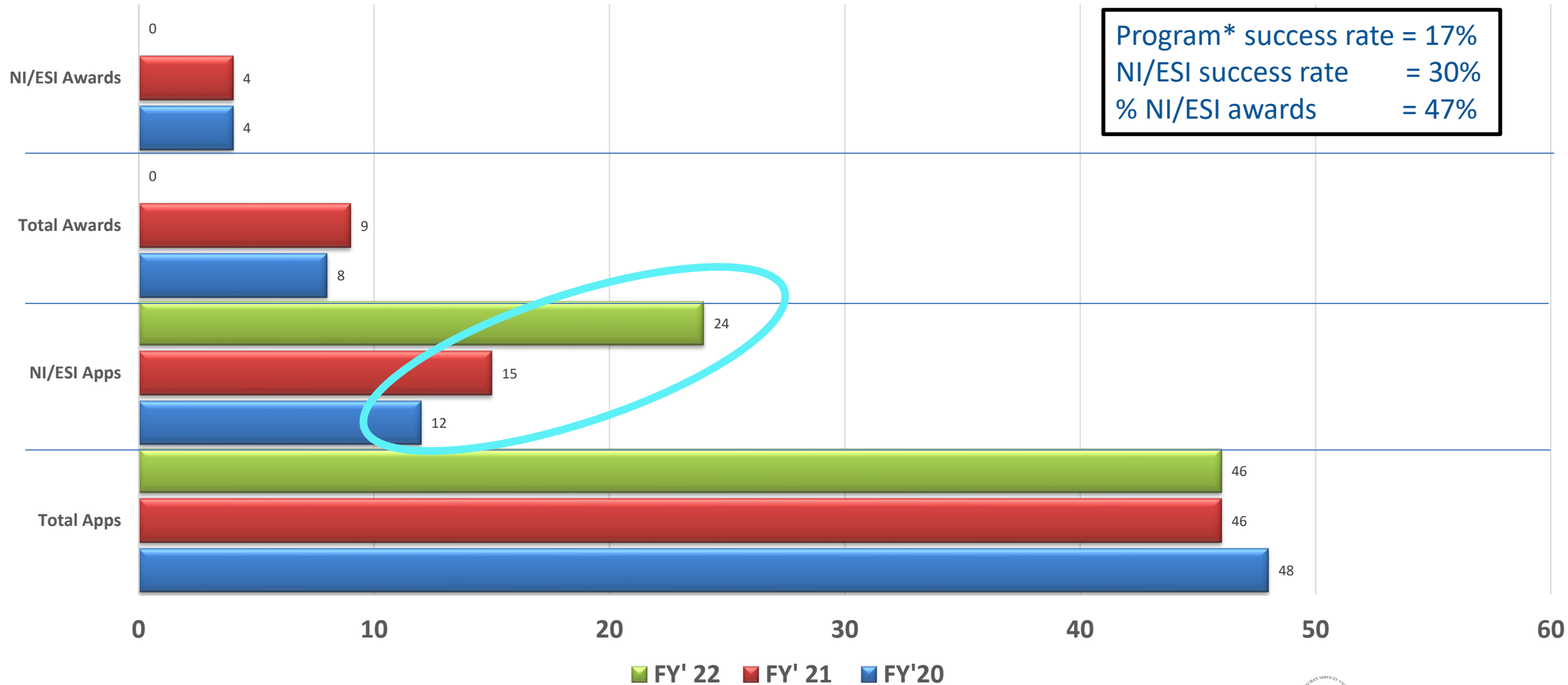
Sex and Gender

R01:

Eleven NIH ICs partnered with ORWH to accept applications focused on the intersection of sex and gender influences in disease



Sex and Gender R01: Applications and Awards by Career Stage of PI



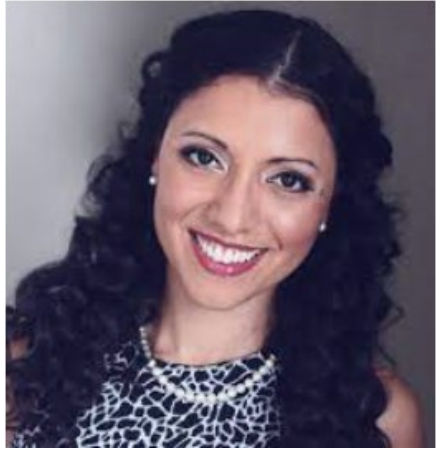
GRANT #	PI	TITLE
1 R01 AI154541	SCULLY, EILEEN P	Sex, Gender and the Immunopathogenesis of HIV
1 R01 AI154533	SIMARD, JULIA F	Implicit Bias in the Evidence: An Evaluation of Female-Predominant Disease
1 R01 AI154539	HOLODICK, NICHOL E	Sex Determines Age-related Changes in the Repertoire and Function of Natural Antibodies Protective against Streptococcus pneumoniae with Increasing Age
1 R01 DA052016	FLENTJE, ANNESA	Substance use and DNA methylation at the intersection of sex and gender
1 R01 AI154518	BOSQUE, ALBERTO	Hormonal control of HIV latency
1 R01 AI154535	PISARSKA, MARGARETA	The impact of sex and gender on disease progression, from developmental origins
1 R01 ES032163	FLAWS, JODI A	Gender and sex differences in phthalate-induced toxicity in the reproductive system
1 R01 ES03225	SHAVIT, JORDAN A	Dissection of the mechanisms underlying sex-influenced cardiovascular disease

Sex and Gender
R01:
Broad scientific diversity of funded grants
FY 2020

GRANT #	PI	TITLE
1 R01 AG074392-01	KIRKLAND CALDWELL JESSICA	Interactions of Sex and Gender Factors in Risk for Alzheimers Disease: Links Between Stress, Neural Activity, Inflammation, and Memory
1 R01 AI164504-01	JEFFERIES CAROLINE	Sex and gender differences in lupus - intersection between immunometabolism, epigenetic remodeling and cardiac involvement
1 R01 DA054617-01	TOMKO RACHEL LYNN	Gender and Sex Hormone Influences on Cannabis Use Disorder Remission
1 R01 DE029963-01A1	RUSSELL STEFANIE L	Pathways to Oral Health Among Low-income Pregnant Urban Women
1 R01 HG011405-01A1	DAVIS LEA K	Elucidating the phenome-wide impact of sex and gender on disease
1 R01 HG011393-01A1	DEMEO DAWN L	Networks Tools to Understand Sex- and Gender-Specific Drivers of Disease
1 R01 HL159760-01	MAJITHIA AMIT	Credentialing novel cardiovascular disease genes in women by sex-specific genomic investigation of insulin resistance
1 R01 HL159764-01	SILVEYRA PATRICIA	Gonadal hormones as mediators of sex and gender influences in asthma
1 R01 NR020309-01	YBARRA MICHELE L	Harnessing the power of technology to develop a population-based HIV prevention program for trans girls

Sex and Gender
R01:
Broad scientific diversity of funded grants
FY 2021

SPOTLIGHT: Sex and Gender RO1 awardee FY 2021



Patricia Silveyra, Ph.D*.
Associate Professor , Indiana
University at Bloomington

Gonadal hormones as mediators of sex and gender influences in asthma 1 R01 HL159764-01

The Study: The first to characterize estrogen-mediated mechanisms of inflammation in asthma phenotypes in the male and female lung, contributing to the characterization of sex- and gender specific factors accounting for inter-individual differences, as well as the effects of feminizing hormone therapy in lung pathobiology

Innovation: The use of the four-core genotype mouse as well as human cells exposed to in an asthma paradigm generating inflammatory responses.

Significance: Potential to provide mechanistic and pre-clinical data that could improve current clinical practices for cisgender and transgender women

* Early Stage Investigator

The *Sex and Gender R01* program has successfully met its objectives to date:

- ✓ To stimulate research that incorporates and/or enhances understanding of the influence of sex and gender **and** its intersectionality in health outcomes across a broad array of scientific disciplines.
- ✓ To include one or more **sex-based variables**, including but not limited to: evaluation of sex as a biological variable; sex-based comparisons on conditions in females and males; biologically based variables such as hormones, physical features, anatomy, or biomarkers.
- ✓ To include one or more **gender-based variables**, including but not limited to: assessment of psychosocial variables relevant to health conditions; measures of socially constructed roles, experiences, identities, or behaviors of girls, women, boys, men, or gender diverse people.

RFA-OD-19-029 *Sex and Gender R01* program provides unexpected dividends to the scientific community to advance women's health:

- ❖ Recruiting new and early-stage investigators into biomedical research investigations on sex and gender
- ❖ Identifying a cadre of reviewers with broad expertise in sex and gender and the intersection of sex and gender research
- ❖ Stimulating cross-cutting research on understudied populations
- ❖ Advancing research on the consideration of sex and gender research and its intersectionality in SARS CoV-2

***Sex and Gender R01* program:**

Future Directions

- ❖ Reissuance of The Intersection of Sex and Gender Influences on Health and Disease Research - R01 mechanism
- ❖ Encourage additional ICs to partner with ORWH
- ❖ Expand scientific areas of interest:
 - COVID-19
 - Leverage and curate large sex and gender datasets
- ❖ New Investigators Forum



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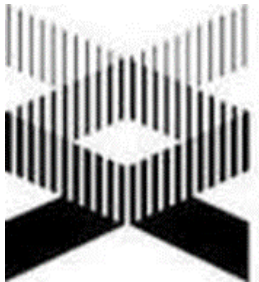
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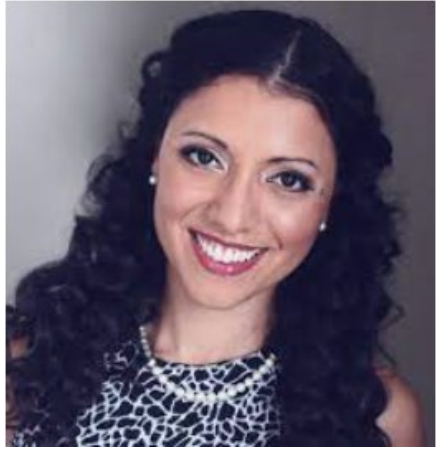
National Institute on Alcohol
Abuse and Alcoholism

Thank you!

Comments and Feedback?

EXTRA SLIDES

SPOTLIGHT: Sex and Gender R01 awardee FY 2021



Patricia Silveyra, Ph.D.
Associate Professor , Indiana
University at Bloomington



Sarah Commodore, PhD
Diversity supplement awardee
Simard Sex and Gender R01

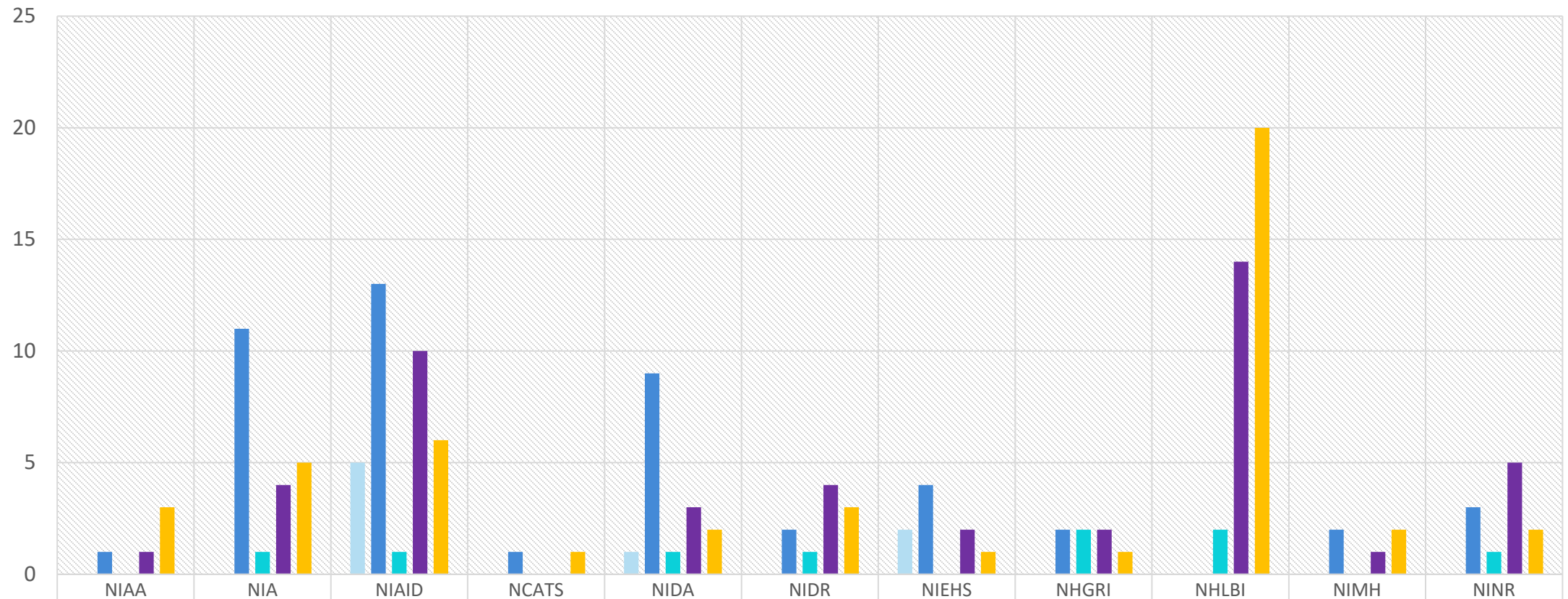
Gonadal hormones as mediators of sex and gender influences in asthma 1 R01 HL159764-01

The Study: The first to characterize estrogen-mediated mechanisms of inflammation in asthma phenotypes in the male and female lung, contributing to the characterization of sex- and gender specific factors accounting for inter-individual differences, as well as the effects of feminizing hormone therapy in lung pathobiology

Innovation: The use of the four-core genotype mouse as well as human cells exposed to in an asthma paradigm generating inflammatory responses.

Significance: Potential to provide mechanistic and pre-clinical data that could improve current clinical practices for cisgender and transgender women

Sex and Gender R01: Applications and Awards by NIH Institute



	NIAA	NIA	NIAID	NCATS	NIDA	NIDR	NIEHS	NHGRI	NHLBI	NIMH	NINR
2020 Awards	0	0	5	0	1	0	2	0	0	0	0
2020 applications	1	11	13	1	9	2	4	2	0	2	3
2021 Awards	0	1	1	0	1	1	0	2	2	0	1
2021 Applications	1	4	10	0	3	4	2	2	14	1	5
2022 Applications	3	5	6	1	2	3	1	1	20	2	2

Sex and Gender RO1 program merits renewal



Julia Fridman Simard, ScD
Stanford University School
of Medicine

Cutting edge research by New Investigator is uncovering sex, gender, and race influences in clinical care

Problem | Over-reliance of the evidence base and potential implicit bias may perpetuate diagnostic delay and poorer management for certain patients

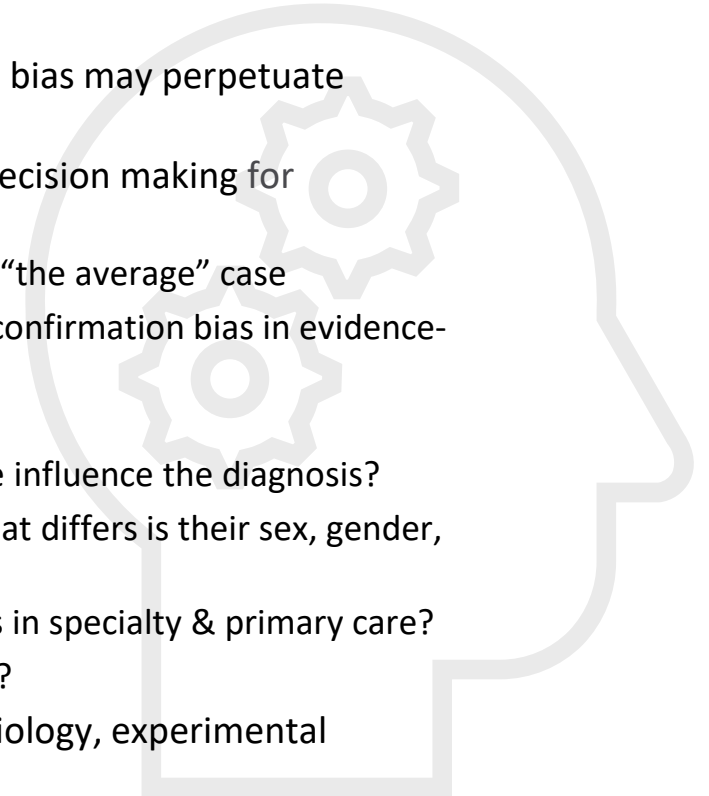
Project Focus | Clinicians' use of mental shortcuts** in diagnostic decision making for conditions that do not have definitive diagnostic tests

- Rules of thumb based on representativeness of given case among “the average” case
- Repeated use introduces errors into evidence base – may lead to confirmation bias in evidence-based medicine

Testing |

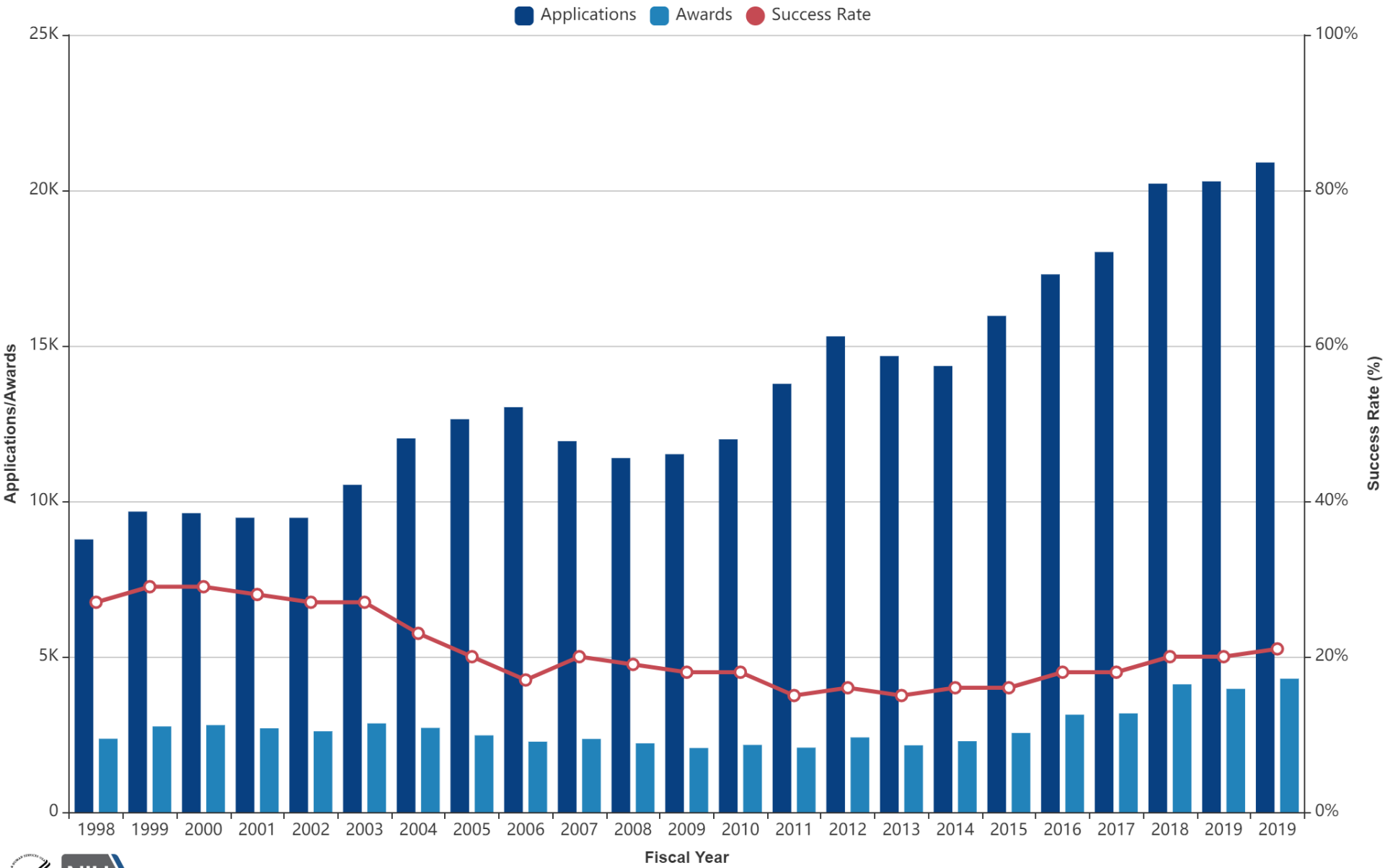
- Does a patient's deviation from the “norm” based on the evidence influence the diagnosis?
- In these circumstances, does a patient's diagnosis vary when all that differs is their sex, gender, and/or race?
- Are there differences in diagnosis of female-predominant diseases in specialty & primary care?
- What's the clinicians' perspective regarding differential diagnoses?

Methods | Adapts a novel method by combining methods from sociology, experimental design, and behavioral science



R01-Equivalent Grants, New (Type 1): Competing Applications, Awards, and Success Rates, by Career Stage of Investigator

Established Contact PI



COVID EXPANSION OF RFA-19-029

- ***ORWH is encouraging application submissions on the influence and intersection of sex and gender factors related to the SARS-CoV-2 virus or COVID-19 disease in alignment with [RFA-OD-19-029](#).***
- ***Within the focus of [RFA-OD-19-029](#), research topics of interest could include investigations of sex- and gender-related risk factors associated with COVID-19 disease prevalence, treatment and prevention, including the influence of co-morbid conditions. Studies examining the influence and intersection of sex and gender on COVID-19 related to health-seeking behaviors, access to health care, and health care systems are also within the scope of this funding opportunity***
- ***Applications submitted in response to this FOA are encouraged to consider populations of women that may be at higher risk for adverse COVID-19 outcomes due to: biological, physiological and genetic factors, cultural and socioeconomic factors such as education, sexual orientation, gender expression or identity, effects of poverty, access to care, quality of care, and access to opportunities for inclusion in clinical trials and studies. Of particular interest are NIH-designated health disparity populations, women living in underserved rural or urban settings, pregnant and lactating women, women who are frontline healthcare workers, or women who are incarcerated or with low socioeconomic status.***
- All other aspects of this FOA remain the same.
-