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DIRECTOR'S CORNER



SCIENTIST SPOTLIGHT



SEX AS A BIOLOGICAL VARIABLE POLICY

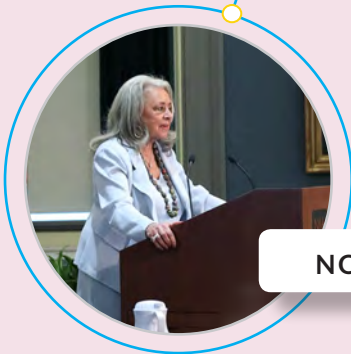


FEATURE STORY

How Sex-Specific Characteristics Can Influence Pain and Opioid Use



NOTEWORTHY



WOMEN IN SCIENCE



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How Sex-Specific Characteristics Can Influence Pain and Opioid Use

Beginning in the mid-1990s, a massive increase in the prescription of opioid pain medications in the United States and other nations inadvertently helped to initiate an opioid crisis years later. An estimated 2.5 million Americans now suffer from opioid use disorder (OUD; see *Terminology* on page 6), and 47,600 fatalities from opioid overdoses occurred in 2017.¹ Although the prescription of opioid medications and their nonmedical use have declined since 2007, heroin use has increased dramatically.² The severity of the opioid crisis warrants a concerted and rigorous response from clinicians, researchers, and policymakers.

Opioids affect men and women differently. Men and women have unshared risk factors for opioid misuse (see *Terminology* on page 6); distinct trajectories of OUD development and progression; and variable responses to available medications for OUD and behavioral treatments. Gender differences also affect how LGBTQ+ individuals react to opioids, develop OUD, and respond to treatment. Despite these sex and gender differences, to date, much of the research and clinical practice aimed at mitigating the opioid problem has adopted a one-size-fits-all strategy. This suboptimal approach has failed to address fully the needs of individuals in pain and those requiring OUD treatment. Research into sex and gender differences as they relate to pain and opioid use will inform more effective prevention efforts and clinical practices. Below, we describe some of the salient features of the opioid public health crisis, review the current understanding of sex and gender differences as they relate to pain and opioids, and explore some of the current and forthcoming avenues of research in this area.

Patterns of Drug Use Among Men and Women Have Changed

The increase of prescriptions for opioid medication has resulted in new patterns of opioid use for medical and nonmedical purposes, and in the United States, women have experienced the most dramatic changes. Fatal opioid overdoses in women increased fivefold between 1999 and 2010.³ From 1999 to 2017, opioid overdoses increased 492% among women ages 30 to 64.⁴ Estimates of increases in women's mortality related to synthetic opioids, such as fentanyl (a prescription opioid similar to morphine but 50–100 times more potent), over this period range from 850% to 1,643%.^{4–6} Women now account for a third of opioid-related deaths.⁶ Although nonmedical prescription opioid use decreased overall between 2007 and 2014, use among women decreased at a slower rate than that of men.² Among adolescents, more girls misuse opioids than boys.⁷

The opioid crisis has also resulted in increases in heroin use. David Thomas, Ph.D., an opioid specialist and Special Advisor to the Director of the NIH Office of Research on Women's Health (ORWH), says, "Most people who initiate heroin use began by misusing or abusing prescription opioids. Heroin is generally cheaper and easier to obtain through illegitimate channels than prescription opioids." Between 2007 and 2014, heroin use increased in both men and women, though use among women increased at a faster rate.² Another study shows that heroin use increased 100% in women and 50% in men between



David Thomas, Ph.D.

2002 and 2013.⁵ Over the past 40 years, heroin use among women has climbed to such an extent that women and men now use heroin at comparable rates.⁸ In 2017, the number of heroin overdose deaths in the United States (15,482) was comparable to the number of prescription opioid overdose deaths (17,029).¹

The current opioid crisis in the United States has widespread public health implications for all Americans. Yet there are distinct risks and medical concerns specific to women. For instance, women have experienced disproportionate increases in the nonmedical use of prescription opioids, heroin use, and overdose fatalities. Sex-specific biological and social factors have influenced these trends, and researchers and clinicians who take these differences into account will deepen their understanding of the opioid problem and better position themselves to develop more effective, individualized treatments for pain and opioid use disorders.

Through the [Specialized Centers of Research Excellence \(SCORE\) on Sex Differences program](#), the NIH Office of Research on Women's Health (ORWH) supports research on sex and gender differences, including how they pertain to illicit drug use and substance use disorders. SCORE researcher Kathleen Brady, M.D., Ph.D., of the Medical University of South Carolina studies sex and gender influences on the relationship between stress and addiction. SCORE-supported studies on cocaine use and cigarette smoking by Marilyn Carroll, Ph.D.,

Continued on page 3

Trajectories Toward OUD Vary by Sex and Gender

"We don't know how many people transition from using opioids legitimately for pain, as prescribed, to misuse, full-blown addiction, and OUD," says Dr. Thomas. "Reports vary widely in the literature, but the percentage is very low. The opioid crisis was caused less by pain patients developing OUD and more by the glut of opioid medications that were prescribed in the early years of the opioid crisis that found their way to illegitimate channels."



Cora Lee Wetherington,
Ph.D.

Cora Lee Wetherington, Ph.D., the Women and Sex/Gender Differences Research Coordinator at the [National Institute on Drug Abuse \(NIDA\)](#), says, "[National Survey on Drug Use and Health \(NSDUH\)](#) data have shown that, historically, men have been more likely than women to use heroin. However, among users of heroin, men and women were equally likely to become dependent. While the likelihood is the same, causal factors and trajectories may be very different." Although gaps in the current understanding exist, sex and gender influence the risk factors for OUD and the patterns of nonmedical drug use among individuals with OUD. Risk factors for women include psychological and emotional stress; psychiatric comorbidities such as anxiety, depression, emotional fluctuations, and posttraumatic stress disorder; a history of intimate partner violence, other gender-based violence, or sexual abuse; a history of problem drinking or inhalant use; and previous overdose.^{3,9} The fact that women seek medical intervention for pain more often than men also increases their risk.⁹ Sex-specific stress response mechanisms may also contribute to the development of OUD in women.¹⁰ Other contributors to risk may include sex-specific prescribing patterns and pharmaceutical marketing. LGBTQ+ individuals also have a greater risk for OUD because of a greater incidence of trauma, stress, and other psychiatric problems.³

Continued on page 4



of the University of Minnesota characterize the interactions among sex differences, hormonal status, impulsivity, and drug-motivated behavior. Similar studies that account for sex and gender differences in opioid use, misuse, and addiction will help us to stem the tragic and costly opioid crisis.

I trust you will find this issue of Women's Health in Focus at NIH to be informative and helpful in your areas of focus. Please share this resource with your colleagues, family, and friends and encourage them to subscribe.



Janine Austin Clayton, M.D.
Director, NIH Office of Research on Women's Health
NIH Associate Director for Research on Women's Health

Symptoms and drug use patterns vary between men and women with OUD. Numerous studies identify a “telescoping effect,” whereby women with OUD tend to have a more rapid disease progression than men and to transition more quickly from initiation to addiction.⁷ “Women are also more likely to misuse prescription opioids to counter negative affect or to cope with pain than men,” says Dr. Wetherington. She adds, “Women with OUD are more likely to obtain their drugs through legitimate prescriptions than men and are more likely to take the drugs by the intended route of administration—orally or sublingually—than men, who are more likely to inject or snort them.” One study showed that women who misuse prescription opioids are more likely to take opioids in the morning to prepare for the anticipated stresses of the day, whereas men are more likely to take them in the evening, recreationally.¹¹ Women with OUD have more functional impairment, a greater number of psychiatric conditions, and more dysregulation of stress responses.^{5,6} “Whether these conditions and impairments cause or result from OUD is an open question that needs to be addressed by researchers to identify prevention targets and by care providers to determine a course of treatment for individual patients,” says Dr. Wetherington.

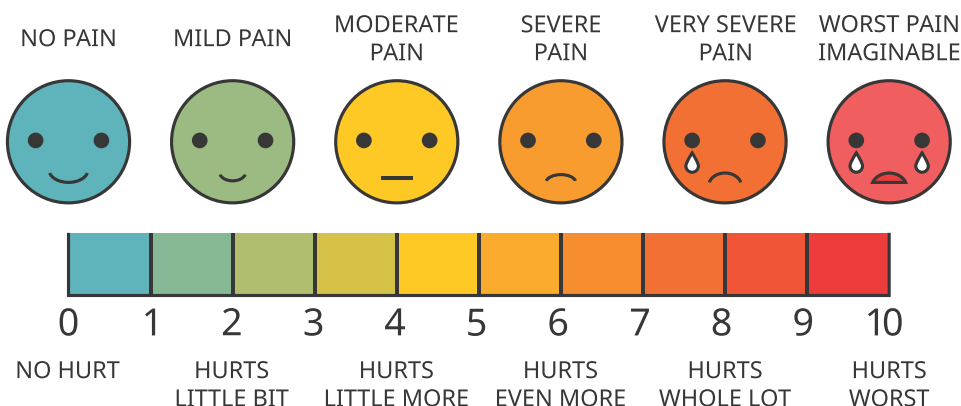
Pain Perception, Severity, Frequency, and Mechanisms Vary Profoundly by Sex and Gender

The need for effective medications for treating acute and chronic pain underlies the opioid crisis. A large body of scientific literature demonstrates that women are more sensitive to pain, have more chronic pain conditions, and experience more severe, more frequent, and lengthier episodes of pain than men.^{1,3,12} Physiologically, men and women process pain signals through different biological pathways,¹³ and estrogens, androgens, and gonadal hormones play roles in the experience of pain, the analgesic effects of drugs, and the effect of stress on both pain and analgesia.³ Societal gender conventions also influence how men, women, and transgender/gender-nonconforming individuals perceive, process, and cope with pain.¹⁴ These fundamental sex and gender differences related to pain intersect with patterns of opioid treatment, use, misuse, and addiction.

“Women experience more pain,” says Dr. Thomas. “Pain can be a healthy, functional response to harmful stimuli, but it can also result from improper nerve signaling or from our brains becoming overly sensitive to stimulation. This can result in chronic pain conditions, and almost every chronic pain condition occurs more frequently and more severely in women.” Such conditions include fibromyalgia, temporomandibular disorder, migraine, and interstitial cystitis. Why chronic pain conditions occur more frequently

Continued on page 5

PAIN MEASUREMENT SCALE



A pain measurement scale typical of the ones used in clinical practice.

- 2 Director’s Corner**
- 2 Feature Story**
How Sex-Specific Characteristics Can Influence Pain and Opioid Use
- 11 Sex as a Biological Variable Policy**
ORWH-Supported Mechanism and Biomarkers Research Aims to Advance Prevention and Treatment Strategies
- 13 In the Journals**
Pilot Study Suggests Gender Differences in Stress Responses Among Opioid-Dependent Individuals
Investigators Review Scientific Literature on Pain, Gender, and Opioid Use
Study of Conditioned Pain Hypersensitivity Identifies a Sex-Specific Mechanism for Pain Memory
- 15 Women in Science**
Study Investigates Whether Bias or Research Quality Drives Gender Disparities in Grant Funding
Survey Identifies Factors Correlated with Success of Women and Minorities in STEM Graduate Programs
Women Speak at Medical Conferences in Greater Proportions but Remain Underrepresented
- 16 Scientist Spotlight**
Munira Z. Gunja, M.P.H.
- 17 Initiative Spotlight**
If/Then
- 18 Current News and Reports**
- 21 Noteworthy**
- 27 Teaming Up for Women’s Health**
- 27 Staff Updates**
- 28 Upcoming Events**
- 28 Funding Opportunities**

in women remains unclear, and Dr. Wetherington and many other experts have identified this discrepancy as an important research question. She notes that the NIH Common Fund initiative [Acute to Chronic Pain Signatures](#) has the potential to address this discrepancy.

Numerous laboratory studies demonstrate that women are more sensitive to pain.^{3,12} Inna Belfer, M.D., Ph.D., a pain specialist and Program Director at the [National Center for Complementary and Integrative Health \(NCCIH\)](#), explains, “Women have a lower



Inna Belfer, M.D., Ph.D.

threshold for pain, the point at which a sensation becomes painful, and a lower tolerance for pain, how long they can stand it. A lower pain threshold and a higher willingness to acknowledge pain are female characteristics, probably evolutionary protective mechanisms by which greater self-recognition of pain leads to earlier seeking for care.”

Researchers have also identified a phenomenon called “pain catastrophizing,” which is more common in women than in men, by which the patient experiences fear and anxiety in anticipating painful sensations, which can make the pain worse.¹⁵ Dr. Wetherington states, “Catastrophizing contributes to women’s tendency to take opioids to cope

with pain, is a major predictor of misusing prescribed opioids in women, and may result in higher dosages being required to obtain the same pain relief.”

Physiologically, men and women process pain through different biological mechanisms of the immune system and neurocircuitry.¹³ “Very different types of cells respond to pain in men and women, as well as in male and female animals,” says Dr. Belfer. “Microglia are involved in pain in males, but T cells fulfill a similar function in females, a fact that indicates that treating men and women with the same pain medications may not be the best strategy.” Animal studies have revealed robust sex differences in the central nervous system, and research into these differences could inform new analgesic strategies.¹²

Sex hormones also play a role in pain perception. A 2007 study showed increased sensitivity to pain in response to hormone therapy in transgender women, whereas transgender men had decreased pain sensitivity.¹⁴ Further, some transgender men stopped suffering from pain conditions they experienced before hormone therapy, and some transgender women acquired new functional pain conditions, such as migraine, temporomandibular disorder, and fibromyalgia. Dr. Belfer says, “These outcomes were, in part, a physiological response to the hormones but also demonstrate the impact of gender on pain.”

These sex and gender differences in pain influence opioid prescription practices and use patterns. Dr. Wetherington asks, “Are prescribers taking sex and gender into account appropriately when treating patients with pain? Are they gender-blind? Are they gender-biased?” Despite women’s greater sensitivity to pain, as well as their greater likelihood of seeking treatment for it, many people dismiss women’s pain complaints as exaggerations. “It’s a bias in society that extends to the medical field,” says Dr. Thomas. “Studies show that men and boys in pain are believed more than women and girls.” Their increased sensitivity to pain, combined with the reluctance of some clinical personnel to believe their complaints, may increase women’s likelihood of taking prescription opioids without a prescription to manage pain.¹ Studies show that women are more likely to be prescribed opioids, to receive higher doses, and to use them for longer periods of time than men.^{1,3} One study showed that nurses tended to treat the same symptoms with pain medication for men but with sedatives for women, according to Dr. Belfer. “One of the reasons we do pain research and focus on sex and gender differences is to fight stigma and care-provider bias,” she says.

Continued on page 6

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Future research will identify and address sex and gender differences in pain and pain management. Dr. Thomas identifies one possible avenue of investigation: “Prospective studies could follow men and women in pain receiving opioid medications for the first or second time. By comparing their outcomes with those of control groups that did not get opioids, we could better identify effective treatments and what causes some pain patients to develop addictions.” Another area of research, one prioritized by Dr. Belfer and NCCIH, involves nonopioid treatments for pain, including mind–body therapies and natural, nonopioid medications. (See *Nonopioid Therapies for Pain* on page 7.)

Prescription Opioid Medications Affect Men and Women Differently

Dr. Thomas states, “Simply put, men and women are different in how they react to drugs.” Studies of pharmacokinetics and pharmacodynamics reveal that sex differences affect drug metabolism, absorption, and elimination. Compared with men, women generally have lower body weight, slower metabolism, and slower digestion, all of which influence pharmacokinetics. These differences, in part, result in women generally having greater sensitivity to opioids.

Opioids also have different analgesic effects in men and women. Dr. Belfer explains, “Several controlled trials of patient-controlled analgesia found greater opioid consumption by men than women. Morphine had greater potency in women but a slower onset of action. In women, morphine was associated with more numerous and more severe side effects.” Recent studies have resulted in complex and sometimes contradictory findings

Terminology

Although definitions and usage differ, here, *misuse of prescription drugs* refers to use in a manner inconsistent with prescription instructions, often for psychotropic or other effects. *Addiction* refers to compulsive drug use despite negative consequences and personal harm. *Opioid use disorder* (OUD) is a “problematic pattern of opioid use leading to clinically significant impairment or distress.”²³ Misuse and addiction as well as prescribed medical use may be accompanied by *dependence*, a physiological state wherein withdrawal symptoms follow cessation of drug use. *Addiction* and *OUD* are often used synonymously, but the *Diagnostic and Statistical Manual of Mental Disorders* distinguishes between mild, moderate, and severe OUD based on the number of symptoms each patient exhibits, such as craving, tolerance, withdrawal, personal risk, and lifestyle disturbances.²³ For more information see reference 24.

regarding sex differences in opioid analgesia. Some studies show that women vary more in their response to opioid pain medication and may need higher doses to receive the same level of analgesia.³ Other studies find that opioids more consistently produce stronger pain relief in women than in men. Some clinical and animal studies have found that morphine is a stronger analgesic in males than in females.¹⁶

Many women with OUD may have been prescribed opioid medications initially—and perhaps inappropriately—to treat psychiatric conditions. Sandra Springer, M.D., of the Yale School of Medicine is a researcher and clinician whose areas of interest include OUD treatment and medications for OUD, particularly for people with HIV/AIDS and individuals involved in the justice system. She explains, “It is unclear why psychosocial trauma manifests as physical pain, is described as pain, or is perceived as pain by prescribers who believe they need to treat these patients with opioids.” She adds, “Women are more likely than men to be prescribed benzodiazepines for anxiety. When coprescribed with opioids, benzodiazepines increase the likelihood of fatal overdose.”



Sandra Springer, M.D.

Sex differences can also affect cessation of prescription opioid use. “Most people who take opioids for pain long term will become dependent—not necessarily addicted—but dependent,” says Dr. Thomas. “Clinicians must take care when tapering dependent patients off drugs, because there will be withdrawal, and withdrawal needs to be managed.” He explains that prescribers tend to take women and African-American patients off opioid medications more quickly than they do White men. Dr. Thomas adds, “There’s some research suggesting that quickly tapering patients off opioid medications can do more harm than good by leading to suicidal thoughts and increasing the likelihood of turning to street drugs.” Animal studies have shown that female rats are more sensitive to opioid withdrawal than male rats,⁷ suggesting that clinicians should remain vigilant when tapering women off these medications.

Sex and Gender Differences Create Obstacles and Opportunities in OUD Treatment

Researchers have developed effective treatments for OUD. Medications such as buprenorphine, methadone, and extended-release naltrexone can treat OUD, and naloxone, usually delivered in a fast-acting nasal spray, can quickly reverse the effects of an opioid overdose. Experts at NIDA and throughout the medical community recommend combining medications for OUD with behavioral interventions to address both the addiction and any psychiatric comorbidities and

Continued on page 7

Nonopioid Therapies for Pain

The opioid crisis has underscored the need for nonopioid pain treatments without the liabilities of addiction and overdose. At NIH, research and funding opportunities aim to foster the development of new medications and nonpharmacological strategies for treating pain in men and women, including mind–body techniques and treatment with natural products.

Mind–body approaches involve several well-known techniques, such as yoga, tai chi, meditation, mindfulness strategies, various forms of acupuncture, “affective touch” treatments (including massage and chiropractic manipulation), and therapies involving exposure to various stimuli—e.g., music, lights, and aromas. Historically, research into these therapies has stalled, in part because of their nonserious reputations. However, rigorous scientific inquiry involving genetics, imaging technologies, and other advanced methods has demonstrated the efficacy of these techniques. Upcoming studies will pair medical conditions with appropriate therapies, refine treatment protocols, and match patient factors (e.g., sex differences, genetic profiles, and medical history) to appropriate treatments. “With the opioid crisis, there is now a public interest in self-managing pain—not self-medicating for it, but self-managing it—with mindfulness techniques and nonopioid therapies,” says Dr. Belfer.

NIH also supports research into natural products for treating pain, including compounds derived from the cannabis plant. Tetrahydrocannabinol (THC) is the primary psychoactive compound in cannabis. Other compounds derived from cannabis can yield analgesia without psychoactive effects. Researchers are investigating whether some cannabis-derived medications could be effective treatments for some patients with cancer or HIV/AIDS, as these medications may provide beneficial effects on appetite and weight control, as well as pain relief.

with social services to assist with child care, employment, and financial difficulty.

Although effective pharmaceutical and behavioral interventions are available, only about 1 in 10 individuals with OUD receive treatment, and women are less likely than men to be treated for OUD.¹ Sex differences influence the risk of craving and relapse, the likelihood of seeking treatment, and the outcomes associated with different types of treatment. According to Dr. Springer, men with OUD in early abstinence will tend to experience drug cravings in response to drug-related cues, environmental or situational reminders of past drug use; cravings in women with OUD more often result from negative moods, stress, and interpersonal conflict. Women beginning OUD treatment tend to experience more intense cravings in early abstinence.⁶ Drug craving and withdrawal symptoms increase the likelihood of relapse, and some studies show that women with OUD are more prone to relapse.¹

Sex- and gender-related barriers to treatment further decrease women’s likelihood of receiving OUD care. Such obstacles may include lack of child care, financial vulnerability, comorbid psychiatric disorders, intimate partner violence, pregnancy (see *Pregnancy and Opioids* on page 8), potential loss of dependent children, physical or sexual trauma, inadequate testing of medications for OUD on women, chronic pain, and involvement in the justice system.^{1,6} Dr. Wetherington points out that these obstacles may be compounded in racial, ethnic, sexual, or gender minorities; people with HIV/AIDS; adolescents; and people who are incarcerated or otherwise involved in the justice system.

Although the biomedical community recognizes addiction as a disease, the social stigma attached to drug use constitutes another treatment barrier. Numerous studies indicate that women with addictions bear a disproportionate burden of the associated stigma. Dr. Springer says, “Culturally embedded power imbalances between men and women leave women exposed to increased stigma.” Dr. Thomas adds, “Stigma is not our friend when it comes to OUD treatment. Stigma keeps people away from treatment and away from the community that could support them.”

Historically, many care providers have adopted the one-size-fits-all approach to OUD treatment, even though studies show that men and women respond differently to behavioral and pharmaceutical interventions.³ Given the sex-specific needs and treatment barriers of women, many experts now recommend gender-sensitive or women-specific treatment services for OUD.¹⁷ “We need to treat women with addictions differently from men and understand the family and social issues that are unique to them,” says Dr. Thomas. “We need to address these issues, as well as the addiction.”

Dr. Wetherington adds, “For long-term positive treatment outcomes for women, pharmacotherapeutics need to be combined with wraparound services as needed, including treatment of psychiatric comorbidities, instruction on coping skills for negative affect and stress, addressing intimate partner violence, and social services to help with stable housing, employment, and parenting skills.” She points to the [Horizons Program](#) at the University of North Carolina (UNC) at Chapel Hill as an example of a successful treatment

Continued on page 9

Pregnancy and Opioids

One of the most lamented consequences of the opioid crisis has been its effect on pregnant women, mothers, and their babies. Although clinicians do not routinely screen pregnant women for opioids, survey data show that 0.8% of pregnant women have used opioids for nonmedical purposes in the past 30 days and that 0.4% of pregnant women met criteria for opioid misuse or dependence at the time of delivery.²¹

The opioid crisis led to a fivefold increase in the incidence of neonatal opioid withdrawal syndrome (NOWS). In 2012, almost 22,000 babies with NOWS were born in the United States.⁶ Infants with NOWS may experience seizures, tremors, irritability, sleep problems, poor ability to feed, dehydration, and other symptoms, which can last up to 6 months postpartum. *In utero* exposure to opioids is associated with poor intrauterine growth, premature birth, and birth defects. Long-term effects include developmental delays and problems with learning and socialization. Treating infants with NOWS requires enormous hospital resources (up to \$1.5 billion in hospital charges⁶) and a corresponding commitment from social services.

Aside from established protocols for treating heroin and methadone withdrawal in pregnant women, clinical approaches to treating pregnant women with OUD remain inconsistent. In 2010, the MOTHER study demonstrated that babies of opioid-dependent women who received buprenorphine required less morphine to treat their neonatal abstinence syndrome (NAS), spent less time in the hospital, and spent less time being medicated for NAS than babies of women treated with methadone.²² The American College of Obstetricians and Gynecologists (ACOG) has made several [practical clinical recommendations](#) for pregnancy and OUD involving screening, pain treatment, opioid agonist pharmacotherapy, treating neonates, and breastfeeding. However, more research is required in these areas to establish clinical best practices.

More information on NOWS and associated NIH research is available from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD; <https://www.nichd.nih.gov/research/supported/opioids>).

NIH

Helping to End
Addiction Long-term

NIH HEAL
INITIATIVE

A trans-NIH effort to address the
opioid crisis through science

PAIN
MANAGEMENT

OVERDOSE
REVERSAL

OPIOID
ADDICTION
TREATMENT

The HEAL Initiative

In early 2018, NIH launched a precision medicine program called the [HEAL \(Helping to End Addiction Long-termSM\) Initiative](#). NIH, along with other public and private organizations, has dedicated considerable resources toward scientific solutions to stem the opioid crisis. Basic research elucidates the current understanding of neurological pathways involved in pain and addiction. Implementation research tests new behavioral and pharmaceutical treatments. Pain studies will design new, objective measures for pain to minimize bias in diagnoses and develop treatments preventing the transition from transient acute pain to chronic pain.

Continued on page 9



program that responds to the needs of women and their families. The UNC Horizons Program treats only women with addiction problems who are mothers or pregnant, many of whom have experienced abuse or violence. The UNC Horizons Program is funded, in part, by the U.S. Department of Health and Human Services (HHS) Substance Abuse and Mental Health Services Administration (SAMHSA) and treats only women with addiction problems who are mothers or pregnant, many of whom have experienced abuse or violence. The comprehensive UNC Horizons Program offers a recovery and relapse-prevention program, medications for OUD, psychiatric and social services, obstetrical and gynecological care, and numerous other services. Similar programs could meet the care needs of women with OUD throughout the United States and help curb the opioid crisis.

Sex and gender differences also play a role in the response to medications for OUD and behavioral treatments. Different studies show methadone programs to be equally effective in men and women, differently effective in men and women depending on dosage, or more effective in women.^{3,18} Naltrexone treatment may result in more adverse

effects in women.³ Mortality rates differ between men and women with OUD involved in behavioral treatment programs, depending on the focus of the intervention.³ As men and women respond differently to stress, sex-specific stress responses may also affect the likelihood of stress-induced relapse and treatment cessation, as well as the response to treatment with buprenorphine and adrenergic agents, such as clonidine, guanfacine, and lofexidine.^{6,19} The dysregulation of hormonal stress responses is a potential pharmaceutical target for women with substance use disorders.¹⁰ “We don’t know definitively if there are sex or gender differences in the responses to different medications for OUD, because no research has prospectively evaluated these differences,” says Dr. Springer. “Most studies have looked at these sex differences only retrospectively and were never powered to detect sex and gender differences.”

Future Research into Precision Medicine May Enhance Treatment of Pain and OUD

In 2015, NIH Director Francis Collins, M.D., Ph.D., and then-National Cancer Institute (NCI) Director Harold

Varmus, M.D., published an article in *The New England Journal of Medicine* in response to President Barack Obama’s announcement of the [Precision Medicine Initiative](#).²⁰ Rejecting the one-size-fits-all approach, precision medicine accounts for each patient’s genes, sex, gender, medical history, environment, and lifestyle in a more holistic, individualized approach to treatment. Precision medicine strategies drive NIH’s HEAL Initiative (see sidebar on page 8), which aims to enhance pain management and improve prevention and treatment of opioid misuse and addiction.

Precision medicine strategies might prevent acute pain from transitioning to chronic pain and might more accurately predict pain outcomes. “Genetics, genomics, proteomics, and other fields can help us predict outcomes for various interventions,” says Dr. Belfer. “For example, knee replacement surgery is a common but painful procedure. The postsurgical pain can be worse than the pain from the original poor knee. With accurate pain predictions based on individualized genetic, psychological, and other factors, we can make better recommendations for or against such procedures.”

Continued on page 10



Precision medicine strategies also strive to stem the opioid crisis by reducing reliance on opioid pain medications. Dr. Belfer explains, “Research is being done on analgesics that work only in small populations, such as men of a certain genotype who are not under stress or women under 35 of a certain genotype. Precision medicine will help us identify interactions between genetic, demographic, sex, and environmental factors that can affect drug efficacy.” Ideally, with individualized predictions, precision medicine techniques for OUD will optimize behavioral interventions and medications for OUD for each patient while addressing his or her pain and risk of relapse.

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ORWH-Supported Mechanism and Biomarkers Research Aims to Advance Prevention and Treatment Strategies



Chyren Hunter, Ph.D.,
Associate Director, Basic
and Translational Research
Program, ORWH

This spring, ORWH welcomed David Thomas, Ph.D., one of NIH's foremost authorities on pain and opioid research, to serve as Special Advisor to ORWH Director Janine A. Clayton, M.D. His arrival from the [National Institute on Drug Abuse \(NIDA\)](#), where he served as Deputy

Director of the Division of Clinical Neuroscience and Behavioral Research, is timely, given the nation's worsening opioid crisis. It's also a tragic

recognition of the opioid crisis's disproportionate impact on women and the little we know about its underlying mechanisms.

"This may be a once-in-a-lifetime opportunity," Dr. Thomas says. "With the resources Congress has provided, it's critical that we take this opportunity to advance our understanding of the pathways, the mechanisms, and the metrics of pain." Dr. Thomas points to a handful of funding opportunities in which ORWH has significant research interest, including studies associated with the Helping to End Addiction Long-term (HEAL) Initiative. Launched in April 2018, the HEAL Initiative is an aggressive, trans-agency effort to expedite scientific solutions to stem the national opioid public health crisis. The HEAL Initiative will build on extensive, well-established NIH research, including basic science of the complex neurological pathways involved in pain and addiction, implementation science to develop and test treatment models, and research to integrate behavioral interventions with medications for opioid use disorder.

BACPAC

The Back Pain Research Consortium (BACPAC), part of the HEAL Initiative, focuses on lower back pain, one of the most common forms of chronic pain among adults, especially women. BACPAC studies seek to deepen our understanding of the mechanisms of chronic low back pain (CLBP), improve patient phenotyping, and develop improved diagnostic and treatment tools. More ambitiously, they aim to identify, prioritize, and test mechanistically based, nonaddictive therapies targeted to individual patients. Thousands of lives could be saved, and many more addictions prevented with the fruits of this research.

The BACPAC research program consists of the following four components, which will work collaboratively:

- [RFA-AR-19-026](#) invited applications to establish interdisciplinary mechanistic research centers (MRCs) to conduct translational and clinical research addressing critical gaps and opportunities in CLBP treatment. The MRCs will generate data for deep patient phenotyping and for the development of patient-based algorithms, with the goal of improving and expanding targeted therapies. *[The deadline for this and the other three requests for applications (RFAs) was March 2019.]*
- [RFA-AR-19-027](#) will fund a Data Integration, Algorithm Development, and Operations Management Center to guide and coordinate BACPAC's activities, including a consortium-wide registry of patient-reported outcomes and preferences. The center will develop patient-centered algorithms for prediction of optimized therapeutic interventions.
- [RFA-AR-19-028](#) is funding technology research sites that will conduct technology development and deployment.
- [RFA-AR-19-029](#) will fund phase 2 clinical trials to test the safety and efficacy of nonaddictive therapies for CLBP.

Biomarkers and Endpoints for Pain

Another potentially fertile area of research involves biomarkers and endpoints for pain. The development of nonopioid pain medications faces numerous challenges, including lack of reliable measures of pain biology and perception, paucity of validated targets, and heterogeneous patient populations. One potential solution is the use of objective biomarkers and endpoints.

Here are two ORWH-supported HEAL Initiative research opportunities in this area:

- [RFA-NS-18-041](#) seeks the discovery of strong candidate biomarkers and endpoints for pain that can be used to facilitate the development of nonopioid pain therapeutics, from discovery through phase 2 clinical trials.
- [RFA-NS-18-046](#) focuses on advanced analytical and clinical validation of pain biomarkers, biomarker signatures, and/or endpoints using retrospective and/or prospective methods.

ORWH's involvement with these two opportunities, as well as others mentioned here, is noteworthy in another regard. The language in the funding opportunity announcements expresses the importance of sex and gender differences, sex as a biological variable, and the inclusion of women in clinical research. (See *Excerpt from RFA-NS-18-041 and RFA-NS-18-046* below.)

Continued on page 12

Enhancing Pain Management and Improving Treatment for Opioid Misuse

Also noteworthy are promising ORWH-supported HEAL Initiative funding opportunities in two other categories of research: enhancing pain management and improving treatment for opioid misuse and addiction. (See list below.)

Moving forward, look to ORWH to focus more closely on understanding why women suffer disproportionately from pain and the opioid crisis. The ongoing and planned research will aim to offer a carefully strategized approach for translating science and knowledge into improved clinical practice and outcomes. Stay tuned.

Enhancing Pain Management

- [RFA-NS-19-016](#) – Translational Devices to Treat Pain. Upcoming deadlines: Oct. 2020 and Feb. 2021.
- [RFA-NS-19-017](#) – Translational Devices to Treat Pain. Upcoming deadlines: Oct. 2020 and Feb. 2021.
- [RFA-NS-19-018](#) – Clinical Devices to Treat Pain. Upcoming deadlines: Oct. 2020 and Feb. 2021.

- [RFA-NS-19-020](#) – Optimization of Nonaddictive Therapies [Small Molecules and Biologics] to Treat Pain.
- [RFA-NS-19-021](#) – Pain Management Effectiveness Research Network: Clinical Trial Planning and Implementation Cooperative Agreement.

Other, non-HEAL Initiative opportunities include:

- [RFA-NS-19-010](#) – Optimization of Nonaddictive Therapies [Small Molecules and Biologics] to Treat Pain.
- [PA-19-200](#) – Mechanisms Underlying the Contribution of Sleep Disturbances to Pain.
- [PA-19-201](#) – Mechanisms Underlying the Contribution of Sleep Disturbances to Pain.

Improving Treatment for Opioid Misuse and Addiction

- [RFA-MH-19-525](#) – HEAL Initiative: Effectiveness Trials to Optimize, Implement, Scale, and Sustain the Collaborative Care Model for Individuals with Opioid Use Disorders and Mental Health Conditions.

To access these and other funding opportunities cosponsored by ORWH, visit the ORWH [website](https://orwh.od.nih.gov/research/funded-research-and-programs/funding-opportunities-announcements) (<https://orwh.od.nih.gov/research/funded-research-and-programs/funding-opportunities-announcements>).



Excerpt from RFA-NS-18-041 and RFA-NS-18-046

“Given the higher prevalence of pain disorders in females and their greater sensitivity to pain, there is a crucial need to recruit women into pain and opioid-related clinical research in sufficient numbers to determine sex-specific responses as well as sex differences in opioid use, misuse, and overdose. It is critical to address sex influences in basic science research on pain neurobiology and pathology, and in translational, interdisciplinary, behavioral, clinical, and/or health services research relevant to women’s health, and, where appropriate, the use of both sexes to better understand the influence of sex as a variable on health and disease.

“Integrating the purposeful accounting for sex as a biological variable (SABV) in biomedical research on pain, from the most basic to the clinical and applied efforts, will fill gaps in our knowledge, will inform more effective, personalized approaches to control pain acquisition, tolerance and effect pain resolution for women and men.”

Pilot Study Suggests Gender Differences in Stress Responses Among Opioid-Dependent Individuals

(Original article by [Gilmore et al. 2019. *Addict. Behav.* 92: 143-154.](#))

Despite greater numbers of opioid-dependent men in the United States, the prevalence of opioid dependence and the rate of opioid-related deaths are increasing faster in women than in men. To understand the mechanisms driving this disparity, Amanda Gilmore, Ph.D., and colleagues conducted a pilot study of the psychosocial and biological differences between men and women that may influence substance use patterns, disease course, treatment, and risk of relapse. The researchers randomly assigned opioid-dependent participants into different experimental groups.

One group began with a standardized social stress task followed by a drug cue. The other group experienced the same drug cue without the preceding stress task. To measure perceived stress, researchers asked participants to complete a validated questionnaire immediately after the stress task and again after 15-minute intervals following the drug cue. After each interval, heart rate and stress hormone levels were measured to assess individual physiological responses. Results from this study show that although the women in the stress + drug cue group experienced increased subjective levels of stress, their stress hormone levels were not elevated compared with those of men. Additionally, while men's heart rates returned to baseline 30 minutes after the drug cue, women's heart rates remained elevated. These data suggest that biological stress responses vary by gender and may explain gender-based differences in vulnerability to opioid dependence and relapse. As new treatments are developed, targeting the dysregulation of hormonal stress responses may be particularly effective for women with substance use disorders.

Investigators Review Scientific Literature on Pain, Gender, and Opioid Use

(Original article by [Koons et al. 2018. *Clin. Ther.* 40: 190-196.](#))

The opioid crisis affects women disproportionately for several reasons, and instances of fatal opioid overdose in women increased fivefold between 1999 and 2010. However, research on pain and opioids has largely relied on male animal models and overlooked sex differences in the pain experience and the response to opioids, including their analgesic effectiveness, the risk of misuse, and the development of opioid use disorder (OUD). In a review of the literature, Andrew Koons, D.O., Gillian Beauchamp, M.D., and colleagues characterized common findings from studies on women, pain, and opioids.

Compared with men, women have greater pain sensitivity; experience more severe, more frequent, and lengthier episodes of pain; and have more chronic pain-related diseases, such as fibromyalgia and interstitial cystitis. Because of anatomic, hormonal, social, and other factors, women vary more than men in their response to opioid pain medication and may require higher doses to receive the same degree of relief.

Because of the confluence of several factors, women are more likely to misuse opioids and develop OUD. Many sex- and gender-related factors contribute to this increased risk, including prescribing patterns, subjective pain experience, cultural norms, withdrawal symptoms, the tendency to seek out health professionals, psychiatric comorbidities, pharmaceutical marketing, gender-based violence, and sexual abuse. LGBTQ+ individuals also have a greater risk for opioid misuse, in part because of higher instances of trauma, psychosocial stress, posttraumatic stress disorder, and other psychiatric causes.

Men and women respond differently to OUD treatment, although sex and

gender seldom inform the treatment of OUD. Data from several studies have identified sex differences in response to naltrexone and buprenorphine, mortality rates as they relate to treatment plan focus, and patient satisfaction with methadone programs.

The reviewers conclude by calling for more sex- and gender-specific research and approaches to treatment to help curb the opioid crisis.

Study of Conditioned Pain Hypersensitivity Identifies a Sex-Specific Mechanism for Pain Memory

(Original article by [Martin et al. 2019. *Curr. Biol.* 29: 192-201.](#))

Chronic pain, with its associated economic costs and heavy disease burden, is a leading human health concern. Research suggests that initial pain sensitivity becomes chronic pain in part because of the memory of prior painful stimuli. Loren Martin, Ph.D., Jeffrey Mogil, Ph.D., and colleagues investigated sex differences in pain memory by examining conditioned hypersensitivity to pain, spatial memory, and hormonal influences in male and female mice and human research participants. On day 1, subjects were exposed to painful stimuli and conditioned to associate the stimuli with a specific location. On day 2, subjects were randomized either to the same place (and, with the human volunteers, the same experimenter) or to an unfamiliar place (and, with humans, a different experimenter) and again exposed to painful stimuli. In both mice and humans, males, but not females, exhibited hypersensitivity to pain in the familiar context. Neither sex demonstrated hypersensitivity in the new context. To test the role of sex-specific factors in context-dependent pain hypersensitivity, the investigators repeated the experiments with gonadectomized mice treated

Continued on page 14

with testosterone, gonadectomized mice with no injections, mice injected with metyrapone to block the stress response, and mice injected with zeta inhibitory peptide, which suppresses the established ability of male mice to retain spatial information longer than female mice. The results of these experiments suggest that pain hypersensitivity is linked to testosterone, stress, and sex-specific place conditioning.

With this study, the investigators have established a novel, translatable model for studying the relationship between memory and pain and have identified a male-specific pain memory mechanism. Importantly, this study also serves as an object lesson of the importance

of incorporating [sex as a biological variable](#) into biomedical research. Had the researchers conducted a single-sex investigation, they might not have observed the sex-specific nature of conditioned pain hypersensitivity.

Sex-Based Differences in Chronic Pain and Withdrawal Symptoms May Drive Opioid Misuse

(Original article by [Huhn et al. 2019. Pain Med. doi: 10.1093/pm/pny295.](#))

The Centers for Disease Control and Prevention (CDC) reported that since 2006, the number of individuals receiving

opioid prescriptions for pain management has decreased. However, prescription duration, opioid use disorder (OUD), and overdose-related deaths are still on the rise. With the strong relationship between self-reported pain and opioid misuse driving much of the crisis and with women reporting more chronic pain and potentially experiencing elevated levels of opioid withdrawal, understanding the connections among sex, gender, pain, and withdrawal is critical in identifying people who are at elevated risk for OUD. Using three standard assessments, Andrew Huhn, Ph.D., and colleagues asked individuals self-reporting both chronic pain and opioid misuse in the previous 30 days (101 men and 80 women) to rate their chronic, current, and 24-hour pain; the degree to which pain interfered in daily activities; their emotional response to pain; and the severity of their symptoms associated with opioid withdrawal. The researchers found that women experienced more pain-related interference in their daily activities, greater average current pain, and higher levels of worst pain in the last 24 hours than men. Additionally, women scored higher on various aspects of pain “catastrophizing,” i.e., the tendency to magnify or exaggerate pain. Dr. Huhn and colleagues made the novel observation that opioid withdrawal severity affected the relationship between pain catastrophizing and past-24-hour worst pain in women, with more intense withdrawal resulting in more perceived pain. This finding suggests that women may be more vulnerable to ongoing opioid misuse, as withdrawal contributes to their overall perception of pain. Clinicians who understand this aspect of opioid withdrawal in women can make safer, more informed treatment decisions for patients with chronic pain when prescribing pharmacological interventions—particularly because women who misuse opioids often obtain them from physicians through legitimate channels.



Featured Research and Perspectives

Study Investigates Whether Bias or Research Quality Drives Gender Disparities in Grant Funding

(Original article by [Witteman et al. 2019. Lancet 393: 531-540](#), commentary by [Raymond et al. 2019. Lancet 393: 494-495](#).)

Over the past few decades, evidence of a gender-based imbalance in grant funding has mounted. To investigate this disparity, researchers evaluated a systemic change in the funding strategy of the Canadian Institutes of Health Research (the Canadian equivalent of NIH). In 2014, changes to the traditional investigator-initiated funding programs were implemented, resulting in two new programs: one that focuses on the research proposed and one that focuses on the scientist. Leveraging these changes, Holly O. Witteman, Ph.D., and colleagues asked the provocative question, “Are gender gaps due to evaluations of the applicant or the science?” Reviewers in one grant program assessed program proposals primarily on research quality. Reviewers in another, less traditional grant program based 75% of each proposal’s score on the investigator’s leadership, productivity, and contributions to the field. Dr. Witteman



and colleagues analyzed reviews of 7,093 unique applicants and 23,918 grant applications submitted from 2011 to 2016. Adjusting for confounding factors, the researchers observed significant gender-based differences in funding success only when greater importance was placed on the evaluation of the scientist rather than on the science itself. This finding suggests that conscious, unconscious, or systemic bias most likely contributes to disparities. In a follow-up commentary, Jennifer L. Raymond, Ph.D., and Miriam B. Goodman, Ph.D., highlighted the importance of these findings, as an increasing number of organizations have adopted review practices bestowing more weight to individual scientists than to the quality and significance of proposed research.

Survey Identifies Factors Correlated with Success of Women and Minorities in STEM Graduate Programs

(Original article by [Fisher et al. 2019. PLOS One 14: e0209279](#).)

Women and minority students in Ph.D. programs in science, technology, engineering, and mathematics (STEM) fields who perceive themselves to be well-prepared for graduate coursework and feel accepted by faculty and their fellow students tend to have more robust publishing portfolios. Their portfolios are comparable to those of their White male peers. This finding, reported recently by Aaron Fisher, Ph.D., and colleagues, emerged from analysis of data from a recent National Science Foundation (NSF) survey of approximately 500 students from four leading California STEM graduate programs. The researchers analyzed the survey data via path analysis, a methodology that identifies direct and indirect connections between predictors and outcomes of interest. They examined the effects of gender, race, academic preparedness, students’ understanding of their program’s structure and expectations, and their sense of belonging on publication rates—which were taken as a measure of professional success—as well as on the students’ perceptions of their well-being. A stated purpose of the study was to identify potential methods of improving the success of women and minority Ph.D. students and thereby, in time, increase diversity in STEM fields, particularly professorships and other leadership positions, where women and minorities remain underrepresented. The researchers also found that the women surveyed experienced significantly more distress than both White and minority male peers. However, the investigators found that academic preparedness, collegial acceptance, and well-articulated scholarly expectations mitigated distress among both women and minority students. The researchers concluded that a few low-cost cultural and structural changes, such as clarifying expectations and standards in STEM graduate programs, could improve the success of women and minority students.

Women Speak at Medical Conferences in Greater Proportions but Remain Underrepresented

(Original article by [Ruzycki et al. 2019. JAMA Netw. Open. 2: e192103.](#))

From 2007 to 2017, the proportion of female speakers at medical conferences increased from 24.6% to 34.1%. Though this increase parallels similar increases in the percentages of women physicians practicing during this time frame, women remain underrepresented as speakers at academic medical conferences. Shannon M. Ruzycki, M.D., and colleagues reached this conclusion after conducting a cross-sectional analysis of the 181 English-language medical conferences that met the inclusion criteria of being held in the United States or Canada and having 100 or more physician attendees.

These conferences convened a total of 701 times during the years sampled. The researchers also identified similar increases in the proportion of women speaking at specialized medical conferences, and these increases were analogous to trends in the specialized physician workforce over the study period. The investigators concluded that gender-based disparities at medical conferences most likely result from overall disparities in the field of academic medicine rather than from a bias unique to conferences. Nonetheless, Dr. Ruzycki and her coauthors called for conference organizers to invite and select more women to speak at medical meetings, as research shows that doing so can decrease gender bias in the field, improve career satisfaction and career retention among female physicians, and provide strong role models for students and young medical professionals.

SCIENTIST SPOTLIGHT

Munira Z. Gunja serves as a senior researcher in the Commonwealth Fund's Health Care Coverage and Access program. Prior to joining the Commonwealth Fund, she worked at the U.S. Department of Health and Human Services in the Office of the Assistant Secretary for Planning and Evaluation, where she was the lead analyst and author of a widely cited [fact sheet](#) about the decline in uninsured Americans that followed enactment of the Affordable Care Act (ACA). She contributed to further analysis of ACA data that appeared in [The New England Journal of Medicine](#). For this work and other contributions, Ms. Gunja won the Secretary's Award for Distinguished Service. Earlier in her career, Ms. Gunja conducted data analysis at the National Cancer Institute (NCI), and much of her work was published in scientific journals. She studied at Tulane University, where she earned a Bachelor of Science in public health and international development and a Master of Public Health in epidemiology.

How did your Federal work experience prepare you for your current role?

I worked for the Federal Government during the rollout of the ACA marketplaces. I learned that politics can affect health policy and that no matter the data that support a decision, policy can be successful only after winning hearts and minds. I regularly apply this lesson to my current work. Effective communication with the American public is essential to improving and changing health policy.

Why is it important to disaggregate data by sex?

We cannot make health recommendations applicable to both men and women without research on how those recommendations will affect men and women. Women have greater health care needs, especially during their reproductive years. On the policy side, we need to work actively to



Munira Z. Gunja, M.P.H.

understand how problems such as underinsurance and access to care affect women. The only way to make informed health and policy decisions is to disaggregate the data.

How has mentorship shaped your career?

I grew up in a house of all women, with my three older sisters and my mom. While other women in my career have certainly mentored me and helped shape my career path, my sisters and mother were the ones who taught me from a young age about the importance of hard work, compassion, and appreciating opportunities. My mother, a Muslim immigrant and physician, fought to come to America and to secure a spot in a residency program. She encouraged all four of her daughters to be independent thinkers and do work that will help make the world a better place. The values my mother and sisters instilled in me led me to choose a career about which I am proud and passionate.

What are the barriers to women in science?

When I started at NIH, I was fortunate to be surrounded by a team of accomplished and brilliant women who showed me that

Continued on page 17

women can be effective players and leaders within the scientific community. Although many messages can lead us to believe that scientific fields are dominated by men, I'm hopeful and optimistic the tide is turning. Of course, there are still significant challenges and barriers to entry. We know that young girls are discouraged from engaging in the sciences and that the media perpetuate notions that science is just for boys. Women professionals in the field face deterrents to advancement. Men continue to dominate leadership positions in many health and policy organizations. Parental leave policies in the field lag behind the recommendations of health policy advocates, which makes it harder for women to advance in their careers.

Do you have advice for young female scientists?

Seek help when you need it. Never be afraid to take initiative. Scientific and health policy organizations tend to be top-down structures, where entry-level employees receive little authority and only a vague path to growth and advancement. Get your foot in the door. Speak up when you can contribute to the organization's work. Find causes that you can champion. I will give the same advice to my three young nieces and 5-month-old daughter.

What have been the most rewarding aspects of your career?

I love the work I've done to expand health care coverage to uninsured Americans and promote more equity within health care. I'm also proud of the publications on women's health I've written, which have garnered attention from the media, policymakers, health professionals, and stakeholders. There is a growing interest in women's health in this country, and that is truly exciting. It is critical that researchers continue to monitor, analyze, and evaluate the challenges women face when it comes to their health and access to care.

What other female scientists do you admire and why?

Elizabeth Blackwell, M.D., was a woman who faced many barriers and challenges in college but nevertheless became the first woman to graduate from medical school in the United States. She became a champion of women's health. I also admire Melinda Gates. Although, strictly speaking, she's not a scientist, she has become a powerful advocate for promoting women in science and technology. She is someone who fights, takes action, and motivates me to work harder.

INITIATIVE SPOTLIGHT

IF/THEN

In March, [Lyda Hill Philanthropies](#) announced that it would dedicate \$25 million to [If/Then](#), a new initiative for encouraging girls to pursue careers in science, technology, engineering, and mathematics (STEM). In the United States, only 25% of STEM professionals are women, most of whom are White. To redress this disparity, If/Then will provide funding for women in STEM careers, publicize women in STEM careers as role models for girls of middle school age, and create positive, realistic media portrayals of women in STEM and advocate for other content providers to follow suit.

If/Then has partnered with over [two dozen organizations](#), including the American Association for the Advancement of Science (AAAS), National Geographic, The Nature Conservancy, Girl Scouts of the USA, Teach for America, the Howard Hughes Medical Institute, U.S. Soccer, and the World Wildlife Fund. An inaugural project initiated in partnership with AAAS, the [If/Then Ambassadors program](#), will convene 100 women in STEM careers to contribute to outreach efforts to middle school girls. If/Then Ambassadors will demonstrate how STEM education and related skills can apply, not only to research, but also to sports, fashion, gaming, manufacturing, entertainment, retail, music, and other endeavors. These role

models will share their experiences and stories in classrooms, at AAAS Family Science Days, and at Girl Scouts events. To complement these efforts, Girl Scouts of the USA will soon offer a STEM career badge and associated programming.

"If we support a woman in STEM, THEN she can change the world."

If/Then will also advocate for more equitable and accurate representations of STEM professionals in the media. If/Then will create original entertainment and informative content with media partners such as Magical Elves, the production company behind Bravo's *Project Runway*; the [National Girls Collaborative Project](#); the popular YouTube channel GoldieBlox; and the [Geena Davis Institute on Gender in Media](#) (GDI). A recent GDI study found that girls and women who know someone or have a role model in STEM are more likely to pursue a career in a STEM field. This study also found that a majority of girls and women endorse the importance of portraying women in STEM in films and on television but that almost 63% of STEM characters in popular media are men. By propagating positive portrayals of women like Katherine Bouman, Ph.D., whose algorithm helped to capture the first image of a black hole, and fictional characters like Dana Scully, M.D., from *The X-Files*, whom numerous young women currently in STEM careers cite as an inspiration, If/Then hopes to inspire a new generation of women in STEM.

Survey Research Identifies Career Goal, Salary, and Gender Differences Among Postdocs

(Original article by [McConnell et al. 2018. eLife 7: e40189.](#))

Sean C. McConnell, Ph.D., and colleagues recently surveyed over 7,600 current postdoctoral researchers involved in 351 formal, structured mentorship programs in U.S. academic and nonacademic institutions (e.g., hospitals, government labs, industry research facilities) that represented all 50 states. Survey questions investigated postdocs' career preferences, professional development, mentee experiences, lifestyle, and demographics. Most respondents (55%) identified life sciences as their primary field. Others indicated that they were working in engineering, physical sciences, environmental sciences, social sciences, medicine, psychology, or the humanities. Survey data showed that gender significantly influenced the experiences of postdocs. Men reported higher salaries (\$47,678 on average, versus \$46,477 for women). This disparity in earnings was observed even in men and women who were of similar age, postdoc status, institutional status, race, marital status, and parental status. Men were more likely to report having a same-gender mentor, having a same-gender role model, being a citizen of a nation other than the United States, having a spouse or partner, and having children. Most postdocs

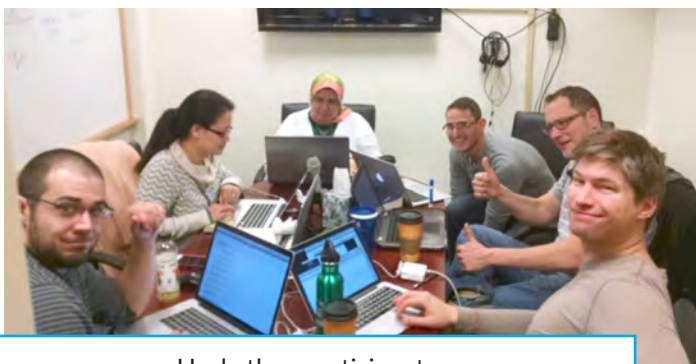
(57.7%) responded that an academic research position was their first career choice, although estimates approximate that only 15% of postdocs secure tenure-track research positions after their training. Satisfaction with the postdoctoral mentee experience also affected the likelihood of wanting to pursue an academic research career. Overall, 60% of respondents indicated that they were "satisfied" or "very satisfied" with their mentorship, with men and women responding similarly. However, male respondents indicated greater interest in future academic research positions than women, a result that may stem from gender differences in other aspects of the postdoctoral experience.

National Library of Medicine "Hackathon" Promotes Diversity in Data Science

On May 8-10, the National Library of Medicine hosted the Hackathon, a collaborative bioscience data event on the NIH main campus. Female data scientists at NIH organized the Hackathon to attract a broad set of researchers as part of the overall effort by NIH to enhance the diversity of the scientific workforce and address the underrepresentation of women in the sciences. Hackathon participants included students and postdocs with a working knowledge of computer

Continued on page 19





Hackathon participants

scripting, those engaged in the use of large datasets, and those developing informatics software tools. Over the course of the event, small teams of participants wrote code to analyze large datasets and discussed bioinformatics best practices, coding styles, and related topics. Products generated by Hackathon participants are available at a public [GitHub repository](https://github.com/NCBI-Hackathons) (<https://github.com/NCBI-Hackathons>).

Four Ways Sex Bias Hinders Women's Success in Medicine and Research

(Original article by [Garrett. 2018. BMJ 363: k5232.](#))

In an essay describing both historical and current sex biases in the sciences, Pulitzer Prize-winning journalist Laurie Garrett detailed four areas where female medical researchers and practitioners have faced and continue to face professional disadvantages: education, funding, publication, and presenting at elite conferences. The essay gave examples of obstacles to women's advancement in education and academic science, including unfair admissions practices, sex disparities in appointments to junior and senior tenure-track faculty positions, wage gaps, gender harassment, and unwanted sexual attention. Research funding institutions select men to be principal investigators more often than they do women, and female scientists receive smaller grants than their male peers. However, when review committees are blinded to the sex of applicants, they award more and larger grants to women. Scientific journals continue to underrepresent women. Although the number of articles with a female first author increased by 37% from 1994 to 2014 in leading medical journals, these numbers have plateaued or, in the case of some journals, declined. Conference organizers invite women to be speakers and panelists less often than they do men, a fact that prompted the *Oxford English Dictionary* to add the recently coined term "manel," which mockingly identifies an all-male academic panel. Ms. Garrett concluded by describing the "childbirth bias" and the steps that NIH and other institutions are taking to mitigate the effects of childbirth and family rearing on women's professional advancement.

Anthropologists Promote Diversity to Achieve Equity and Better Science

(Original article by [Bolnick et al. 2019. Am. Anthropol. 121: 464.](#))

The May issue of *American Anthropologist* featured a forum titled "How Academic Diversity Is Transforming Scientific Knowledge in Biological Anthropology." Edited by anthropologist Deborah Bolnick, Ph.D., this Vital Topics Forum collected a series of essays by scientists from different racial, ethnic, class, sex, gender, educational, and religious backgrounds; from fields spanning anthropology, genetics, and biology; and from career stages from graduate student to full professor. Articles included "But You're Not a *Real* Minority': The Marginalization of Asian Voices in Paleoanthropology," by biological anthropologist Sheela Athreya, Ph.D.; "Feminist, Queer, and Indigenous Thinking as an Antidote to Masculinist Objectivity and Binary Thinking in Biological Anthropology," by interdisciplinary scientist Kim TallBear, Ph.D.; and "Identities, Experiences, and Beliefs: On Challenging Normativities in Biological Anthropology," by zoologist and anthropologist Agustín Fuentes, Ph.D. Collectively, the forum essays argued that diverse research teams can pose new types of research questions, alter traditional scientific methodologies, adopt new and different approaches to data collection and interpretation, and overall improve the robustness of scientific findings. In short, as Dr. Bolnick concisely stated, "[O]ur collective efforts to change *who we are* entails expanding and reconstituting *what we know*." A complete list of forum essays is available [here](https://anthrosource.onlinelibrary.wiley.com/toc/15481433/2019/121/2) (<https://anthrosource.onlinelibrary.wiley.com/toc/15481433/2019/121/2>).

Forbes Articles Address Obstacles to Women in Science

(Original articles by [Michelson. Mar. 31, 2019, Forbes](#) and [Dickerson. April 3, 2019, Forbes.](#))

Two recent articles in *Forbes* magazine featured themes and events related to ORWH's mission. An article by author, commentator, and podcaster Joan Michelson covered the March 11 "Symposium Highlighting Evidence-Based Interventions for Addressing the Underrepresentation of Women in Science, Engineering, and Medicine" of the National Academies of Sciences, Engineering, and Medicine, which was cosponsored by NIH, the National Science Foundation, and the L'Oréal Foundation. Ms. Michelson's article highlighted one of the conference's major concerns: the institutional and cultural barriers that hinder women from pursuing successful careers in the fields of science, technology, engineering, mathematics, and medicine (STEMM). The article synthesized recommendations from the symposium into "9 unusual tips" for how to advance women in STEMM to guide scientific organizations in removing

Continued on page 20

these obstacles. The unusual tips included redefining terms such as “talented” and “accomplished” to avoid traditional, male-oriented models of professional and scholarly excellence and considering candidates’ professional involvement with diversity and inclusion in assessments and evaluations.

In the other *Forbes* article, Elyse Stoltz Dickerson, M.B.A.—Cofounder, President, and CEO of Eosera, Inc., a biotechnology company that makes consumer products—discussed three things women should do to overcome obstacles in science, technology, engineering, and mathematics (STEM). The first suggestion was to cultivate curiosity and a learning mindset. Cultural biases and stereotypes divert many young women from careers in STEM. By adopting an inquisitive mentality, particularly when it comes to scientific topics, young women can train themselves to ask questions of experts and build knowledge over a lifetime. Second, Ms. Dickerson recommended considering “every obstacle as a challenge and opportunity.” She suggested that rather than turn obstacles into problems or causes for self-doubt, young women in STEM should reframe them as learning opportunities and chances to grow intellectually and professionally. Third, she encouraged young women to identify their fears, ask themselves “what’s the worst that could happen” in any given situation, and take calculated risks on their way to success.



Faustine Williams,
Ph.D., M.P.H., M.S.

A Personal Journey Faustine Williams

Born and raised in Ghana, Faustine Williams, Ph.D., M.P.H., M.S., began her career as a scientist at a young age. Her father, a mathematician, taught her at home until she was 6 years old. At 13, she was the youngest participant in a training program organized by the World Health Organization and the International Task Force for Disease Eradication to involve citizens in preventing transmission of dracunculiasis, a disease caused by a water-borne parasite called the Guinea worm. Providing education on water filtration and other preventive techniques to villages throughout Ghana sparked Dr. Williams’ interest in a career in public health. After her undergraduate work in Ghana, she earned her graduate degrees in health informatics, public health, and social sciences at the University of Missouri, after which she completed a postdoctoral fellowship at Washington University’s Public Health Sciences Division. A [2018 NIH Distinguished Scholar](#), Dr. Williams is now a Stadtman tenure-track investigator in the [Division of Intramural Research at the National Institute on Minority Health and Health Disparities \(NIMHD\)](#). She conducts transdisciplinary multilevel research to examine health disparities and develop interventions to improve the health and well-being of minority and underserved populations. She is also passionate about mentoring the next generation to enhance and promote scientific workforce diversity at NIH.

ORWH Hosts 4th Annual NIH Vivian W. Pinn Symposium During National Women’s Health Week



On May 15, ORWH hosted the 4th Annual NIH Vivian W. Pinn Symposium as part of the observation of the 20th anniversary of National Women’s Health Week (May 12–18). This year’s topic, “Improving Maternal Health: Behind the Numbers,” addressed the lasting medical complications that can result from pregnancy, as well as the U.S. maternal morbidity and mortality rate, which is the highest among high-income nations. Leading clinicians and researchers discussed relevant statistics, research, and Federal programs and described approaches to improving women’s health before, during, and after pregnancy and throughout a woman’s life course.

Vivian Pinn, M.D., the first full-time Director of ORWH, delivered introductory remarks, and Lisa Hollier, M.D., President of [The American College of Obstetricians and Gynecologists \(ACOG\)](#), delivered the keynote address.

Lamenting the increasing problem of maternal mortality in the United States, Dr. Hollier said, “We have the most exceptional

infrastructure. We have a strong commitment to research. We have some of the most brilliant minds in the world, and yet we fail our mothers.” After the keynote, ORWH Associate Director for Science Policy, Planning, and Analysis Samia Noursi, Ph.D., characterized further some of the troubling statistics surrounding U.S. maternal morbidity and mortality.

In a panel discussion titled “Framing a Research Agenda to Advance Maternal Health Equity: From Bench to Bedside to Curbside,” Jacquelyn Campbell, Ph.D., RN, FAAN, of The Johns Hopkins University School of Nursing; Joia Adele Crear-Perry, M.D., FACOG, President of the National Birth Equity Collaborative; Michael Lu, M.D., M.P.H., M.S., of [The George Washington University Milken Institute School of Public Health](#); and Dr. Hollier shared their insights.

Continued on page 22



Former ORWH Director Vivian Pinn, M.D., addresses symposium attendees.



(From left) Elizabeth Spencer, BSN; Vivian Pinn, M.D.; Lisa Hollier, M.D.; Janine Clayton, M.D.; and Samia Noursi, Ph.D.



ORWH Associate Director Samia Noursi, Ph.D., discusses maternal morbidity and mortality.

A series of Federal health professionals then shared updates on maternal health activities from throughout the U.S. Department of Health and Human Services (HHS), including Sarah Foster, M.P.H., of the Centers for Disease Control and Prevention (CDC); Lynne P. Yao, M.D., of the U.S. Food and Drug Administration (FDA); Michael D. Warren, M.D., M.P.H., FAAP, of the Health Resources and Services Administration (HRSA); Sung Sug (Sarah) Yoon, Ph.D., RN, of the National

Institute of Nursing Research (NINR); and Megan Mitchell, M.P.H., of the National Heart, Lung, and Blood Institute (NHLBI). Closing remarks were provided by Janine A. Clayton, M.D., the current Director of ORWH, and Stacey D. Stewart, M.B.A., President of the March of Dimes. A videocast of the symposium is available [here](https://videocast.nih.gov/summary.asp?live=31479&bhcp=1) (https://videocast.nih.gov/summary.asp?live=31479&bhcp=1).



Panelists discuss “Framing a Research Agenda to Advance Maternal Health Equity” (from left, Lisa Hollier, M.D.; Jacquelyn Campbell, Ph.D., RN, FAAN; Joia Adele Crear-Perry, M.D., FACOG; and Michael Lu, M.D., M.P.H., M.S.).

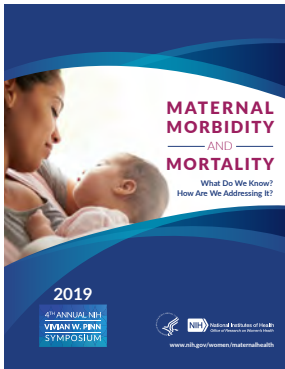


From left, Janine Clayton, M.D.; Michael Lu, M.D., M.P.H., M.S.; and Elizabeth Spencer, BSN



From left, Vivian Pinn Symposium participants Samia Noursi, Ph.D.; Jacquelyn Campbell, Ph.D., RN, FAAN; Joia Adele Crear-Perry, M.D., FACOG; Lisa Hollier, M.D.; Sarah Foster, M.P.H.; Michael Lu, M.D., M.P.H., M.S.; Sabrina Matoff-Stepp, Ph.D.; Janine Clayton, M.D.; Sung Sug (Sarah) Yoon, Ph.D., RN; Elizabeth Spencer, BSN; Lynne P. Yao, M.D.; and Megan Mitchell, M.P.H.

ORWH Launches New Maternal Morbidity and Mortality Web Portal and Booklet



Pregnancy entails far more than giving birth to a baby and can have long-lasting effects on the health of both mother and child. ORWH recently produced an informative web portal and booklet to help identify and mitigate the risks of childbirth, as well as associated health effects later in a mother's life. The [web portal](http://www.nih.gov/women/maternalhealth) (www.nih.gov/women/maternalhealth) presents information on maternal health;

pregnancy-related complications; pregnancy-associated chronic conditions, such as diabetes and depression; pregnancy loss; and data resources related to maternal health, such as the Pregnancy Risk Assessment Monitoring System (PRAMS). The booklet, published for this year's NIH Vivian W. Pinn Symposium, details the current troubling trends in maternal morbidity and mortality, risk factors, preventive steps, how pregnancy-related conditions can affect a woman's health throughout her life course, and how Federal health agencies are addressing the problem. A [downloadable copy](https://bit.ly/2NFQ2GI) is available from the ORWH website (<https://bit.ly/2NFQ2GI>).

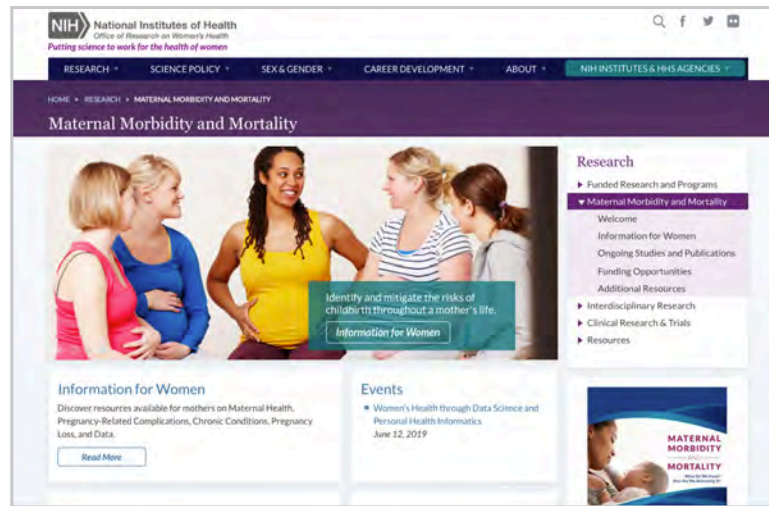
ORWH Congratulates and Thanks Francis S. Collins for 10 Years of Service as NIH Director

On August 17, NIH Director Francis S. Collins, M.D., Ph.D., will celebrate his 10th anniversary as the 16th Director of NIH. In 2009, after his appointment by President Barack Obama and confirmation by the U.S. Senate, Dr. Collins assumed leadership of the largest supporter of biomedical research in the world. Dr. Collins is a physician-geneticist noted for his pivotal discoveries of disease genes and his leadership of the international Human Genome Project, which was completed in April 2003. He served as Director of the National Human



Francis S. Collins, M.D., Ph.D.

Genome Research Institute at NIH from 1993 to 2008. He is an elected member of the National Academy of Medicine and the National Academy of Sciences and a recipient of the Presidential Medal of Freedom and the National Medal of Science. ORWH is grateful for his enduring support of women's health research and, recently, for his guidance with and contributions to [Advancing Science for the Health of Women: The Trans-NIH Strategic Plan for Women's Health Research](#). This



plan—developed in collaboration with leaders from across NIH, external stakeholders, and the public—will guide women's health research at NIH and throughout the biomedical community for the next 5 years. ORWH congratulates Dr. Collins and thanks him for his leadership.

NIH and the American Journal of Public Health (AJPH) Address Health Disparities

The [National Institute on Minority Health and Health Disparities \(NIMHD\)](#) led an NIH-wide 2-year initiative to plot a new research course for improving minority health and reducing health disparities. Throughout this process, participants identified 30 research strategies pertaining to methods/measurement, etiology, and intervention.

A [special issue of the American Journal of Public Health](#), titled "New Perspectives to Advance Minority Health and Health Disparities Research," articulated these strategies in detail. Essays and editorials described leveraging data sources, addressing social determinants of health, building evidence bases and designing



NIMHD Director
Eliseo J. Pérez-Stable, M.D.



ORWH Associate Director
Victoria Cargill, M.D.,
M.S.C.E.

interventions for minority populations, and related topics. NIMHD Director Eliseo J. Pérez-Stable, M.D., and NIH Director Francis S. Collins, M.D., Ph.D., wrote the [introductory editorial](#) for this special issue, and then—ORWH Associate Director for Interdisciplinary Research Victoria Cargill, M.D., M.S.C.E., cowrote the [article](#) "Building the

Continued on page 24

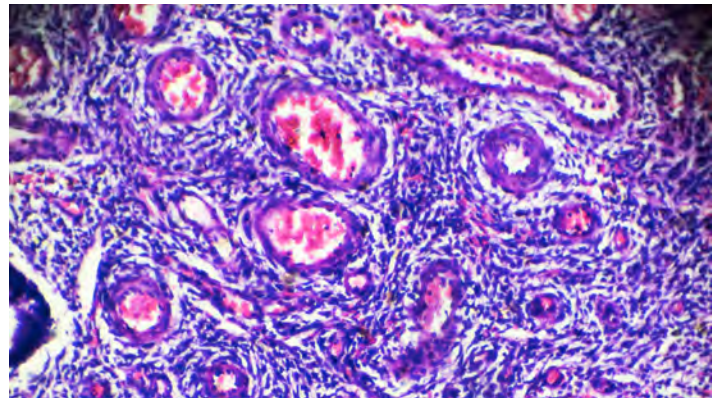
Evidence Base to Inform Planned Intervention Adaptations by Practitioners Serving Health Disparity Populations.”

The Lancet Publishes Profiles of Women Leaders in Medicine

Earlier this year, *The Lancet* published a special double-length issue on “Advancing Women in Science, Medicine, and Global Health” ([Volume 393, Issue 10171](#)) that explored the institutional and systemic barriers faced by women in science and presented evidence of bias within scientific systems and institutions. (See [Volume 2, Issue 1 of In Focus](#) for details.) *Lancet* journals also regularly publish profiles of “remarkable women from around the world whose work helps advance gender equity in science, medicine, and global health.” Recently, *The Lancet* featured the late Wendy Sheila Atkin, Ph.D., M.P.H., who developed new screening methods for bowel cancer. A complete list of the profiles is available on the [website of The Lancet](#).

The “Fourth Trimester” Garner Increasing Attention from Physicians and Researchers

Pregnancy and the perinatal period pose acute health risks for many women and may result in long-term health effects that can endure throughout the lifespan. Many physicians and biomedical researchers posit that the so-called “fourth trimester,” the 3-month period after birth, warrants particular scrutiny, especially after complicated pregnancies. Possible health outcomes after pregnancy include chronic pain, mental health problems, and increased risk of cardiovascular disease. Lisa M. Hollier, M.D., President of [The American College of Obstetricians and Gynecologists \(ACOG\)](#), has indicated that health care integrating mental and physical health services is particularly important during the fourth trimester. [National Institute of Nursing Research \(NINR\)](#)-funded researcher Susan Groth, Ph.D., of the University of Rochester School of Nursing is studying the effects of pregnancy beyond the fourth trimester. Her longitudinal study aims to identify and clarify health effects of pregnancy up to 3 years after delivery. More information on the fourth trimester is available in the previous issue of [In Focus \(Women’s Health in Focus at NIH 2.1: 11–12\)](#) and National Public Radio article titled “‘4th Trimester’ Problems Can Have Long-Term Effects on a Mom’s Health” (<https://www.npr.org/sections/healthshots/2019/01/24/686790727/fourth-trimester-problems-can-have-long-term-effects-on-a-moms-health>).



A microscopic image of a cervical polyp.

Artificial Intelligence (AI) Accurately Identifies Cervical Precancer

A new computer algorithm can analyze digital images of a woman’s cervix, identify precancerous changes requiring medical intervention, and do so with greater accuracy than human physicians. Known as automated visual evaluation, the new AI technology may revolutionize cervical cancer screening, particularly in low-resource settings where Pap tests and colposcopies are unavailable. The algorithm emerged from a collaboration of researchers from the [National Cancer Institute \(NCI\)](#) and [Global Good](#), a humanitarian partnership between the Bill & Melinda Gates Foundation and Intellectual Ventures. Experts at the [National Library of Medicine \(NLM\)](#) confirmed the developers’ findings. The investigators used large datasets to “train” a machine learning the algorithm to identify features associated with precancerous changes from the digital images. The original research article reporting these findings appeared in the *Journal of the National Cancer Institute* ([Hu et al. 2019. J. Natl. Cancer Inst. doi: 10.1093/jnci/djy225](#)).

NIH-Funded Researchers Test Artificial Pancreas in Pregnant Women with Type 1 Diabetes

A consortium of NIH-funded clinical research specialists with support from algorithm experts from Harvard University have commenced clinical trials of a closed-loop insulin delivery system—or artificial pancreas—adapted to treat pregnant women with type 1 diabetes. The [U.S. Food and Drug Administration \(FDA\)](#) has approved one artificial pancreas for treating diabetes, but this device was not designed for pregnant women. The adapted artificial pancreas uses a new algorithm and functions to maintain blood glucose levels appropriate for healthy pregnant women. Investigators hope that their work will eventually lead to an effective at-home treatment for pregnant women with diabetes. The consortium includes researchers from the Icahn School of Medicine at Mount Sinai, the Mayo Clinic, and the Sansum Diabetes Research Institute.

Women's Health Organizations Announce New Leadership



Dorothy Fink, M.D.

[U.S. Department of Health and Human Services \(HHS\) Office on Women's Health \(OWH\).](#)

Earlier this year, Dorothy Fink, M.D., became the Director of OWH, bringing her extensive experience in treating women's health issues to the organization. Dr. Fink also serves as the Deputy Assistant Secretary for Women's Health. Dr. Fink is board-certified in endocrinology,

internal medicine, and pediatrics and is recognized as a physician leader on topics such as diabetes, nutrition, and bone health. Previously, her clinical practice focused on girls and women from adolescence through menopause and beyond. She is a nationally certified menopause practitioner and an expert on estrogen. Dr. Fink has done extensive research related to women's health, including evaluation of blood markers to assist in the diagnosis of hypothalamic amenorrhea and investigating the role of diabetes in women's skeletal health.



Noni H. Byrnes, Ph.D.

[NIH Center for Scientific Review \(CSR\).](#) After serving as the Acting Director of CSR since the retirement of Richard Nakamura, Ph.D., last year, Noni H. Byrnes, Ph.D., became the Director of CSR on February 17. With almost two decades of experience with NIH peer review, Dr. Byrnes oversees more than 500 personnel, who manage the receipt and

referral of all grant proposals for NIH and other parts of the U.S. Department of Health and Human Services (HHS), including the Centers for Disease Control and Prevention (CDC) and the U.S. Food and Drug Administration (FDA). CSR oversees the peer review of approximately 75% of the nearly 50,000 grant applications received by NIH each year. Prior to joining NIH, Dr. Byrnes worked in the pharmaceutical industry, where she conducted research to support new drug submissions. Dr. Byrnes earned her B.S. in chemistry from Allegheny College and her Ph.D. in analytical chemistry from Emory University.

[U.S. Food and Drug Administration \(FDA\) OWH.](#) The FDA's OWH welcomed Kaveeta Vasisht, M.D., Pharm.D., as a Deputy Director and Director of Research and Development. Dr. Vasisht began her career at the FDA in 2011, where she served as the clinical expert on multidisciplinary teams in the review and evaluation of scientific data to assess the safety, efficacy,

and approvability of drugs for the U.S. market. Subsequently, she joined the Office of Medical Policy at the Center for Drug Evaluation and Research, where she most recently served as the Deputy Director of the Division of Clinical Trial Quality. In her current role at OWH, she combines her extensive academic and clinical training with her diverse regulatory background to protect and advance the health of women. Dr. Vasisht is board-certified in both internal medicine and adult endocrinology.



Kaveeta P. Vasisht, M.D., Pharm.D.

[Organization for the Study of Sex Differences \(OSSD\).](#) In 2018, the OSSD membership elected an all-woman leadership team: President Sabra L. Klein, Ph.D., Immediate Past-President Margaret M. McCarthy, Ph.D., President-Elect Rhonda R. Voskuhl, M.D., Treasurer Nancy G. Forger, Ph.D., and Secretary Anne Z. Murphy, Ph.D. Founded in 2006 by staff members of the Society for Women's Health Research and other scientists, OSSD is an independent nonprofit educational organization that promotes the study of sex differences in biomedical research. Information on the 2020 meeting of OSSD is available [here](#).

[The American College of Obstetricians and Gynecologists \(ACOG\).](#) On May 6, Ted L. Anderson, M.D., Ph.D., began his term as President of ACOG after being announced as President-Elect in November of last year. Dr. Anderson is the Betty and Lonnie S. Burnett Professor of Obstetrics and Gynecology at Vanderbilt University Medical Center and has served in leadership roles at The Mary Parrish Center, A Step Ahead Foundation, the American Association of Gynecologic Laparoscopists, the Middle Tennessee Ob-Gyn Society, and the Lonnie S. Burnett Alumni Society. Dr. Anderson's clinical and research interests include gynecological surgery, alternatives to hysterectomy, and the impact of technology on medical practice.

ORWH Director Speaks at 14th Annual Kenneth Austin Rheumatology Symposium

ORWH Director Janine Austin Clayton, M.D., and fellow ophthalmologist Claude Cowan, M.D., spoke on inflammatory eye disease at the 14th Annual Kenneth Austin Rheumatology Symposium at Howard University Hospital on April 6. Howard University sponsors this symposium, which honors Dr. Clayton's father, Kenneth Austin, M.D., a noted rheumatologist and Howard University College of Medicine alumnus. In addition to eye disease, speakers explored the role of the microbiome in rheumatic diseases, clinical research efforts at the Howard University Hospital Division of Rheumatology, and the evaluation of patients with elevated creatine phosphokinase (CPK) levels.

Reyna Gordon Wins New Innovator Award for Research on Health, Speech, and Rhythm



Reyna Gordon, Ph.D.

Last year, Reyna Gordon, Ph.D., Assistant Professor of Otolaryngology and Psychology and Director of the Music Cognition Lab in the Department of Otolaryngology at the Vanderbilt Bill Wilkerson Center, received an NIH Director's [New Innovator Award](#) (DP2-HD098859) for her study "Biomarkers of Rhythmic Communication: Integrating

Foundational and Translational Approaches." Established in 2007, New Innovator Awards support early-career investigators conducting exceptional, innovative biomedical research. Dr. Gordon investigates the biomarkers associated with rhythm at genetic, neural, and behavioral levels and how they relate to speech and risk factors for childhood language disorders.

Sara Bares Presents Research on Sex Differences, HIV Antiretroviral Therapy (ART), and Weight Gain

NIH-funded researcher Sara Bares, M.D., of the University of Nebraska Medical Center, a winner of a Minority HIV Investigator Award from the [AIDS Clinical Trials Group \(ACTG\)](#), presented her work titled "[The Impact of Weight Gain and Sex on Immune Activation Following Initiation of ART](#)" at the Conference on Retroviruses and Opportunistic Infections, held in Seattle on March 4–7. Her research explored the connection between HIV-related weight gain and immune activation and how the two may amplify each other, particularly in women with HIV. This research was supported, in part, by an [ORWH Administrative Supplement for Research on Sex/Gender Differences](#) and was published in the *Journal of Women's Health* ([Bares et al. 2018. *J. Womens Health \(Larchmt\)*. 27: 1162-1169](#)). Earlier in her career, Dr. Bares worked with mentor Grace A. McComsey, M.D., of the Case Western Reserve University School of Medicine through an ORWH Administrative Supplement research grant to Michael Lederman, M.D., also of Case Western.

Anna Levinsson Receives ORWH's Inaugural Science Policy Scholar Travel Award

Anna Levinsson, Ph.D., received the 2019 ORWH Science Policy Scholar Travel Award to support her attendance and participation in the 2019 Annual Meeting of the Organization for the Study of Sex Differences (OSSD) on May 5–8 in Washington, DC. Dr. Levinsson is a cardiovascular epidemiologist, currently a postdoctoral research fellow at the Montreal Heart Institute. She conducts cardiovascular research involving sex pharmacogenomics and social determinants of health. Her OSSD presentation, titled "Sex Differences in Hypertension: Insights from Pharmacogenomics," detailed how women experience more adverse events from cardiovascular drugs than men. As women are often underrepresented in randomized clinical drug trials testing safety and efficacy, currently no antihypertensive treatment guidelines specifically for women exist.

The ORWH Science Policy Scholar Travel Award was developed to support the development of junior investigators focused on women's health and sex/gender differences research who also have an interest in research policy. The award supports the travel of the selected scholar, whose abstract has been accepted to be presented at OSSD's annual meeting. ORWH encourages applications for the 2020 OSSD meeting (May 4–7, Marina del Rey, CA, <https://www.ossdweb.org/future-meetings>). For more information, visit the ORWH website (<https://orwh.od.nih.gov/science-policy>).



ORWH Science Policy Scholar Travel Award Recipient Anna Levinsson, Ph.D., with ORWH Associate Director for Science Policy, Planning, and Analysis Samia Noursi, Ph.D.



The U.S. Preventive Services Task Force (Task Force) recommends that clinicians provide or refer pregnant and postpartum people who are at increased risk for perinatal depression to counseling interventions.

Perinatal depression, which is depression that develops during pregnancy or after childbirth, is one of the most common complications of pregnancy and the postpartum period. Perinatal depression affects as many as one in seven pregnant women and can result in negative short- and long-term consequences for both the mother and her baby, such as moms having difficulty bonding with their babies and babies getting fewer preventive health services.

“Effective counseling interventions can help prevent perinatal depression before it develops,” says Task Force member Karina Davidson, Ph.D., M.A.Sc. “We can

help prevent one of the most common and serious complications of having a baby.”

The Task Force reviewed evidence on interventions to prevent perinatal depression and found that counseling is effective in pregnant and postpartum women who are at increased risk. Two types of counseling interventions that were shown to be effective are:

- Cognitive behavioral therapy, which addresses negative thoughts and increases positive activities; and
- Interpersonal therapy, which focuses on an individual's relationships with other people to improve communication and address problems that contribute to depression.

This recommendation is for people at increased risk for perinatal depression, not those who have already been diagnosed with the condition. Currently, there is no accurate screening tool available to assess risk of perinatal depression, but there are certain factors that clinicians can use to



determine risk. People with a history of depression, symptoms of depression, and certain socioeconomic risk factors, such as being a young or single parent, may be at increased risk and benefit from intervention.

“Clinicians should use patient history and risk factors to identify pregnant or postpartum individuals who are most likely to benefit from counseling,” says Task Force member Aaron B. Caughey, M.D., Ph.D., M.P.P., M.P.H. “Patients who are pregnant and concerned about depression should talk to their doctor.”

STAFF UPDATES

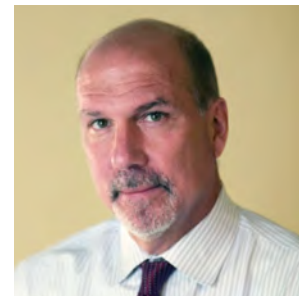


Katrina Serrano, Ph.D.

Katrina Serrano, Ph.D., is a Health Scientist Administrator at ORWH. She joined the editorial board of *PLOS One* in September of last year. *PLOS One* is a multidisciplinary journal dedicated to accelerating the pace of scientific advancement and making rigorous science “discoverable, widely disseminated, and freely

accessible to all.” *PLOS One* accepts submissions from over 200 subject areas, including science, medicine, engineering, and the humanities. Throughout her initial 3-year appointment, Dr. Serrano will conduct initial assessments of submissions in her subject area, oversee the peer review process, coordinate peer reviewers, evaluate reviewer feedback, and make editorial decisions. ORWH congratulates Dr. Serrano on this prestigious appointment.

David Thomas, Ph.D., joined ORWH in May as a Special Advisor to the Director, specializing in opioids and pain research. Dr. Thomas began his career at the National Institute of Dental Research (NIDR), which is now known as the [National Institute of Dental and Craniofacial Research \(NIDCR\)](#), researching the impact of opioids on pain and pruritus, followed by 2 years of research on opioid and pain at the University of Chicago. In 1995, Dr. Thomas joined the [National Institute on Drug Abuse \(NIDA\)](#), where he managed pain and opioid research efforts and cochaired the NIDA Prescription Opioid and Pain Workgroup. He is a member of numerous national committees and consortia throughout the organizations of the U.S. Department of Health and Human Services (HHS). Earlier this year, Dr. Thomas was awarded the John and Emma Bonica Public Service Award by the American Pain Society.



David Thomas, Ph.D.

UPCOMING EVENTS

49th Meeting of the NIH Advisory Committee on Research on Women's Health
October 23, 2019
9:00 a.m.–4:00 p.m. (Eastern Time)
NIH Main Campus
Natcher Conference Center

Building Interdisciplinary Research Careers in Women's Health Annual Meeting
December 11, 2019
NIH Main Campus
Natcher Conference Center

For up-to-date information, visit www.nih.gov/women.

FUNDING OPPORTUNITIES

Discovery of Biomarkers, Biomarker Signatures, and Endpoints for Pain

This funding opportunity announcement (FOA) promotes the discovery of strong candidate biomarkers and endpoints for pain that can be used to facilitate the development of nonopioid pain therapeutics, from discovery through phase 2 clinical trials. Specifically, the focus of this FOA is on the identification and initial biological, analytical, and clinical validation of pain biomarkers, biomarker signatures, and/or endpoints. Although research supported by this FOA can include animal studies, it must also include preliminary human validation using carefully standardized human samples or human clinical studies. The goal of this initiative is to deliver candidate biomarkers, biomarker signatures, and/or endpoints for pain that are ready for advanced clinical and analytical validation research. Upcoming application due dates are November 2019 and March 2020. For more information, see FOA number RFA-NS-18-041 or contact ORWH at ORWHinfo@nih.gov.

Analytical and/or Clinical Validation of a Candidate Biomarker for Pain

This FOA promotes the validation of strong candidate biomarkers and endpoints for pain that can be used to facilitate the development of nonopioid pain therapeutics from discovery through phase 2 clinical trials. Specifically, the focus of this FOA is on advanced analytical and clinical validation of pain biomarkers, biomarker signatures, and/or endpoints using retrospective and/or prospective methods. Research supported by this FOA will ultimately demonstrate that biomarker or endpoint change is reliably correlated with variables such as clinical outcome, pathophysiologic subsets of pain, therapeutic target engagement, or response to a pain therapeutic. In addition, biomarker response will demonstrate specificity to the pain condition or therapeutic as demonstrated at multiple clinical sites. The goal of this FOA is to facilitate the advancement of robust and reliable biomarkers, biomarker signatures, and endpoints of pain to application in clinical trials (phase 2 clinical trials and beyond) and in the spectrum of clinical practice. Upcoming application due dates are November 2019 and March 2020. For more information, see FOA number RFA-NS-18-046 or contact ORWH at ORWHinfo@nih.gov.

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