Transgender Women’s Health

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The feature story of this issue of In Focus describes health concerns unique to or more prevalent in transgender women (i.e., individuals who identify as women but were assigned male at birth). Estimates suggest that 1 million to 1.4 million transgender individuals—possibly many more—live in the United States. Transgender women experience high rates of cardiovascular disease, HIV infection, and mental health problems, including depression, anxiety, and suicidality. Transgender women also face discrimination, social stigma, and victimization by violence. We discuss these health concerns as well as efforts by the White House, the U.S. Department of Health and Human Services, including NIH and the researchers it supports, to understand, prevent, and treat the health problems of this underrepresented population.

This issue also discusses ongoing efforts on several major ORWH initiatives, including the follow-up to last year’s “Advancing NIH Research on the Health of Women: A 2021 Conference.” This conference, requested by the U.S. Congress, explored rising rates of maternal morbidity and mortality, stagnant cervical cancer survival rates, and increasing rates of chronic debilitating conditions in women. Other articles examine applications of the NIH Policy on Sex as a Biological Variable, sex and gender considerations in research, and issues facing women in biomedical careers.

I hope you find this issue of In Focus informative. Please share it with your colleagues and subscribe by clicking the link on the front or back cover. Make sure to get your COVID-19 vaccines and booster shots as recommended by the Centers for Disease Control and Prevention.
NIH Supports Research on the Health of Transgender Women

Transgender women, individuals who identify as women but were assigned male at birth, experience higher rates of illness and premature mortality than their cisgender peers.1,2 (See Glossary on p. 11 for definitions of italicized words and other terms related to transgender health.) Transgender women experience the same health issues as cisgender men and women as well as physical and mental health problems unique to or more prevalent among trans women. A recent Dutch study involving almost 3,000 transgender women showed that, over the study period, they were almost twice as likely to die as cisgender men and three times as likely to die as cisgender women.2 The researchers cited cardiovascular disease, HIV-related problems, and suicide as common causes of death.2 Other health concerns prevalent among transgender women include victimization by violence, depression, anxiety, and substance use disorders.

Estimates on the size of the transgender population vary. Both stigma and inconsistent data collection methods make obtaining accurate numbers difficult. Commonly cited estimates indicate that there are between 1 million and 1.4 million transgender adults currently living in the United States.3,4 The population of transgender children and adolescents as well as uncounted transgender adults would appreciably increase these numbers. Indeed, some population-based studies show that up to 2.7% of the global population may be transgender.5 A population of this size, coupled with its high rates of morbidity and mortality, warrants dedicated biomedical and biobehavioral research into the causes, prevention, and treatment of its health problems.

ORWH recognizes that a discussion of transgender and gender-nonbinary individuals can touch upon sensitive issues. As a Federal research agency, NIH takes no position on such issues. ORWH remains committed to the vision articulated in the 2019–2023 Trans-NIH Strategic Plan for Women’s Health Research: a world in which every woman—including every transgender woman—receives evidence-based disease prevention and treatment tailored to her own needs, circumstances, and goals. Below, we describe the prevalent health issues of transgender women and efforts by NIH and NIH-supported researchers to address them.

Physical Health Issues Prevalent in Transgender Women

Violence. NIH-supported researcher Nadia L. Dowshen, M.D., M.S.H.P., specializes in adolescent medicine and serves as both the Director of Adolescent HIV Services and the Co-Director of the Gender and Sexuality Development Clinic at the Children’s Hospital of Philadelphia. She says, “The greatest threat to the health and well-being of trans women is the violence and victimization they face.” Regardless of sex assigned at birth, transgender people experience more hate crime and intimate partner violence than cisgender individuals.6 Half of transgender adults report having experienced at least one lifetime instance of physical or sexual assault.7
The White House and the U.S. Department of Health and Human Services (HHS) have prioritized improving transgender safety and well-being. (See The White House and HHS Address Trans Discrimination on p. 9.) On November 20, 2021, the White House issued the following statement: “This year, at least 46 transgender individuals in this country—and hundreds more around the world—were killed in horrifying acts of violence. Each of these lives was precious. Each of them deserved freedom, justice, and joy. Today, on Transgender Day of Remembrance, we mourn those we lost in the deadliest year on record for transgender Americans, as well as the countless other transgender people—disproportionately Black and brown transgender women and girls—who face brutal violence, discrimination, and harassment.”

Between 2013 and 2020, over 200 trans and other gender-nonconforming people were killed in the United States. Stigma and discrimination limit employment opportunities for transgender individuals, and many trans women become sex workers and experience associated violence. Researchers led by Rob Stephenson, Ph.D., and supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) are currently studying the risks and health effects of partner violence in transgender populations (Project Number 1R21HD097234-01A1).

HIV. Transgender women represent the fastest-growing population of people living with HIV and face an almost 50-fold greater risk of HIV infection than other adults of reproductive age. This risk is even greater among transgender women of color, and one study found that 25% of transgender women of color in their 20s report living with HIV. The 2019–2020 National HIV Behavioral Surveillance (NHBS) of the Centers for Disease Control and Prevention (CDC) found that 42% of transgender women in seven major U.S. cities were living with HIV. CDC also reported significant racial and ethnic differences among respondents (e.g., HIV prevalence was 62% in Black/African American trans women, 35% in Hispanic/Latina trans women, 17% in White trans women). Only 32% of those surveyed without HIV reported using pre-exposure prophylaxis (PrEP). Medical professionals recommend that individuals at high risk for HIV exposure take PrEP medications (e.g., Truvada, Descovy) to prevent infection. CDC data also show that adult and adolescent transgender individuals constitute a disproportionately high percentage of new HIV diagnoses in the U.S.

NIH supports several programs and research efforts to address the rates of HIV and other sexually transmitted infections (STIs) among transgender women. Rona Siskind, M.H.S., a Health Sciences Specialist in the Division of AIDS at the National Institute of Allergy and Infectious Diseases (NIAID), explains, “NIH established the Cross-Network Transgender Working Group (CNTWG) to foster coordination, collaboration, and an exchange of information related to transgender issues across the NIH-funded HIV/AIDS clinical trials research networks.” She adds, “Transgender women represent a priority population for HIV prevention and treatment research, given the high burden and increasing rates of HIV among this population.”

Sari Reisner, Sc.D., M.A., is the Director of Transgender Research at Brigham and Women's Hospital, an Assistant Professor in the Department of Medicine at Harvard Medical School, an Assistant Professor in the Department of Epidemiology at the Harvard T.H. Chan School of Public Health, and the Director of Transgender Health Research at The Fenway Institute at Fenway Health. Much of his research has involved the prevention and treatment of HIV and other STIs in transgender women and men. The NIH-funded LITE (Leading Innovation for Transgender Women’s Health and Empowerment) Study, co-led by Dr. Reisner and Andrea Wirtz, Ph.D., follows a racially and ethnically diverse cohort of more than 1,200 HIV-negative transgender women in the eastern and southern United States to estimate HIV incidence and understand HIV-related risks and resiliencies in this health disparity population. Over the course of this ongoing longitudinal study—the first large cohort study to focus only on transgender women—the researchers have reported successes in methodologies for recruiting this hard-to-reach population and for engaging study participants through social networking apps commonly used by transgender women. Dr. Reisner explains that the study has also examined PrEP indication/uptake and situated HIV vulnerability alongside other psychosocial health concerns, such as transgender-specific violence.
Transgender individuals face higher risk of cardiovascular disease than their cisgender peers. An analysis of data from CDC's Behavioral Risk Factor Surveillance System (BRFSS) demonstrated that transgender women have more than twice the prevalence of myocardial infarction as cisgender women. Health risk behaviors, such as tobacco use (three in five transgender adults smoke cigarettes) and low levels of physical activity compared with cisgender peers as well as disparities in access to health care contribute to the increased risk of cardiovascular disease among transgender women. However, evidence suggests that these risk factors do not fully account for these disparities and that lifelong psychosocial stressors also contribute to cardiovascular morbidity in transgender people.

Transgender adults are also more likely to have asthma than their cisgender peers, with 22% of transgender and 14% of cisgender individuals having been diagnosed with asthma. Asthma, smoking, and disproportionate representation in industries such as food service, hospital work, retail, and education have also made transgender populations more vulnerable to severe cases of COVID-19.

Related NIH-supported studies include Improving PrEP Protection of Transgender Women Through Mechanistic Pharmacokinetic Understanding (Project Number 5R01AI145675-03), Feminizing Sex Hormones' Impact on PrEP Pharmacology in Transgender Women (Project Number 1R21AI145646-01), several research projects associated with the NIH-funded Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN), and the forthcoming Get IT Right Study, which is being planned by the AIDS Clinical Trials Group (ACTG) to evaluate possible drug interactions between antiretroviral and estrogen hormone therapies.

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that they were currently experiencing serious psychological distress, a rate nearly eight times higher than that of the U.S. population. These findings were consistent with those of the BRFSS, which showed that three in five transgender people reported 1 or more days of poor mental health in the previous month (23 percentage points higher than cisgender respondents). Transgender children and adolescents also struggle with depressive disorders, self-harm behaviors, attention deficit disorder, and suicidality at rates much higher than those of their cisgender peers.11

Below, we examine several of the mental health issues of transgender women and girls in greater detail.

**The Minority Stress Model.** Dr. Poteat says, “Our ongoing study gauges the overall stress levels of transgender people by measuring their blood pressure, levels of salivary cortisol, and other biomarkers. We hypothesize that trans people have more stress than the general population, leading to higher allostatic loads.” The effects of stress are cumulative, and high allostatic loads can damage the body’s immune system, metabolism, and cardiovascular health. Many of the health disparities experienced by transgender people, particularly transgender women and those of color, likely stem from the pervasive stress of gender nonaffirmation, external and internalized stigma, discrimination and transphobia, rejection, victimization, and other stressors.10 The Minority Stress Model suggests that minoritized groups experience negative health outcomes as a result of excess stress and that individuals with multiple, intersectional minoritized identities, such as transgender women from underrepresented racial and ethnic groups, experience even more stress. Many researchers believe the Minority Stress Model explains the high rates of mental health disorders and cardiovascular disease among transgender women.10

Financial insecurity and difficulties in finding and sustaining employment among transgender people also contribute to their allostatic loads. “Transgender health researchers tend to focus on HIV prevention and treatment, but that’s not the primary complaint of the transgender community,” says Dr. Poteat. “They want jobs, economic stability, and material resources that allow them to live healthy, stable lives.” Responding to the transgender community, Dr. Poteat and colleagues are developing an intervention that provides both gender-affirming care and financial support to transgender study participants and will track the intervention’s impact on mental health. Dr. Poteat says, “The stress particular to minoritized groups can be great, but general stressors like poverty are enormous. We hope that by mitigating economic concerns and providing access to gender-affirming care, we will improve mental health outcomes.”

**Substance Use.** “We see high rates of substance use among the transgender population as a way of coping with minority stress and trauma,” says Dr. Poteat. Several studies have demonstrated a high prevalence of substance use among transgender people compared with cisgender peers.11,12 Much of the research conducted to date on substance use among transgender individuals has studied LGBTQ+ people as one group. Data from the Substance Abuse and Mental Health Services Administration (SAMHSA) show that 20–30% of LGBTQ+ and 9% of heterosexual individuals meet criteria for substance use disorder. Some research suggests that transgender people may experience higher rates of substance use disorder than their lesbian, gay, and bisexual cisgender peers.12 Transgender youth are more likely than cisgender youth to report lifetime alcohol use.10 High rates of tobacco use among transgender people were discussed above.

**Gender Dysphoria.** The controversial term gender dysphoria refers to the distress transgender individuals may feel as a result of the disparity between their gender identity and their sex assigned at birth. The latest edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) specifies that a diagnosis of gender dysphoria must include a sense of gender incongruence lasting at least 6 months and must meet additional criteria, such as clinical distress and an intense desire to change secondary sexual characteristics.13

In 2013, with the publication of the DSM-5, the American Psychiatric Association (APA) adopted the term gender dysphoria in favor of the older gender identity disorder. This strategic change suggested that the patient’s distress—rather than her, his, or their gender identity—was the source of the mental health problem. In 2019, the World Health Organization (WHO) followed APA’s example, removed gender identity disorder from its manual of diagnoses, and classified gender dysphoria as a sexual health concern rather than a mental disorder.

Although some welcome these changes, others object to the inclusion of gender dysphoria in the DSM-5 and similar manuals. “There’s an ongoing effort to separate trans identities from gender dysphoria and mental disorders,” says Dr. Poteat. “Not everyone who identifies as trans has gender dysphoria. Some are fine with the bodies they were born with.”
Dr. Dowshen resists pathologizing and overmedicalizing transgender identities. “I find this in general to be problematic in the biomedical model—that in order to treat someone and support their health, we have to find some diagnosis,” she says. She adds that many of the transgender children and adolescents whom she treats in her clinic live in loving, supportive households and experience little to no distress about their gender identities.

Dr. Poteat says, “Some researchers are looking at whether gender dysphoria is an innate phenomenon tied to one’s body and gender identity; whether the distress stems from social factors, such as how others interact with the transgender individual; or both.”

**Suicidality.** Death by suicide, suicide attempts, and suicidal ideation are common among transgender individuals, and 40% of transgender adults have attempted suicide in their lifetimes. Transgender adults are four times more likely to attempt suicide than cisgender heterosexual adults. Transgender adolescents are more likely to die by suicide, attempt suicide, and have suicidal ideation than cisgender teens.

The COVID-19 pandemic has exacerbated suicidality and other mental health concerns of transgender individuals. One in three transgender participants in a recent study reported suicidal ideation during the pandemic, and one in two reported problems accessing hormone therapies and other gender-affirming treatments and that these problems had proved detrimental to their mental health.

**Gender Affirmation and the Health of Transgender Women**

*Gender affirmation* is a complex interpersonal process of recognizing an individual’s gender identity. Dr. Reisner explains that gender affirmation may involve “social (e.g., name, pronoun), psychological (e.g., internal, felt self), medical (e.g., cross-sex hormones, surgical intervention, other body modification), and legal (e.g., legal gender markers, name change)” components. He also emphasizes that the process of gender affirmation can be as varied and individual as gender identity itself and that there is “no one-size-fits-all approach to gender affirmation.”

Dr. Dowshen has schematized the gender affirmation process into three categories: reversible, partially reversible, or irreversible changes. An individual’s gender affirmation process may include some, all, or none of these types of changes. Reversible changes include steps such as changing one’s name and preferred pronouns or adopting hair and clothing styles aligned with one’s gender identity. Some transgender youth may also take puberty-blocking medications (e.g., GnRH analogues, androgen blockers) to delay the development of secondary sexual characteristics.

Feminizing or masculinizing hormone therapies constitute partially reversible changes. Dr. Poteat states that 83–90% of transgender women take some form of hormone therapy (e.g., oral, injectable, or patch estrogens). Therapy regimens may also include antiandrogens to allow for feminization at lower doses of estrogen or progesterone. Hormone therapy can be an on-again/off-again process. “We have this narrative that people start hormone therapies and stay on them,” Dr. Poteat says. “We have found that people go on and off of hormones—sometimes because of barriers to care, sometimes on their own because of side effects or other self-management of health concerns. It’s not always a straight trajectory.”

The final category includes largely irreversible changes brought about through gender-affirming “top” and “bottom” surgeries and other procedures.

**Health Benefits of Social, Medical, and Psychological Gender Affirmation.** A seminal study by Kristina R. Olson, Ph.D., NIH-supported researcher Katie A. McLaughlin, Ph.D., and colleagues demonstrated that transgender children ages 3–12 whose gender identities were affirmed and supported by their families had rates of depression comparable to those of the general population and only slightly elevated anxiety symptoms. Further, socially gender-affirmed transgender children had much lower rates of psychopathology than had been reported for transgender children with gender dysphoria living with a gender identity aligned with their sex assigned at birth. Dr. Olson was awarded a MacArthur Fellowship for her research demonstrating the health benefits of social gender affirmation for transgender children.

Research has also shown that medical gender affirmation—achieved through puberty blockers, hormone therapies, surgeries, mental health support, and other interventions—can reduce health risks. “Overall, the evidence suggests that medical gender affirmation improves the mental health and quality of life of transgender women and men,” says Dr. Reisner. Indeed, several studies link gender-affirming hormone therapy with decreased depression and anxiety, increased quality of life, greater likelihood of engaging in physical exercise, higher body satisfaction, reduction of psychosocial and behavioral risk factors for cardiovascular disease, and improved mental health.
formal protocols for transgender care involving puberty blockers, hormone therapy, genital reassignment surgery, and other interventions and are following a cohort of transgender youth into early adulthood. The researchers report that the well-being of the transgender youth treated with these protocols is comparable to or better than that of same-age controls from the general population.17 Currently, NICHD supports a large study on the impact of early gender-affirming medical treatment in transgender youth at four U.S. pediatric gender clinics (Project Number 2R01HD082554-06A1).

Dr. Sevelius says that medical gender affirmation “has been shown to reduce gender dysphoria and mitigate some of the downstream negative health effects of marginalization of transgender and gender-diverse people.” They explain that medical gender affirmation can complement social gender affirmation (which is important for people of all genders, not only transgender people) as well as psychological gender affirmation. Dr. Sevelius says, “Psychological gender affirmation is an internal sense of valuing oneself as a transgender or gender-diverse person, being comfortable with one’s own gender identity, and having a sense of satisfaction with one’s body and gender expression.” Research shows that these three types of gender affirmation improve health outcomes, though most research has focused only on social and medical gender affirmation.18

Dr. Sevelius stresses the importance of psychological gender affirmation for transgender women to ensure their well-being and to help them build resilience to transphobia. “It is critical that we understand the full impact of intersectional stigma and discrimination on the health of transgender women,” they say. “Internalized transphobia is the negative appraisal of self and other transgender people due to an acceptance of rigid and binary social gender norms. Psychological gender affirmation describes the positive and potentially stress-buffering aspects of comfort and satisfaction with one’s gender identity and expression, without regard to congruence or conformity to society’s gendered expectations and judgments.”

**Medical Gender Affirmation Involves Minimal Risk.** As with most medical interventions, medical gender affirmation involves a small measure of risk. Puberty-blocking medications are associated with some developmental concerns, and feminizing hormone therapy may increase the risk for cardiovascular issues such as stroke, heart attack, and blood clots. One study identified an increase in suicidal thoughts after initiation of hormone therapy but before physiological changes began or resolved.19

“There are risks when taking any medication or having any surgical procedure,” says Dr. Dowshen. “However, the medicines used in gender affirmation are the standard of care today, have been used for decades, and are safe when used as directed and monitored by a medical practitioner.” Concerns over drug interactions between feminizing hormone medications and HIV antiretroviral therapies have resulted in some medication adherence issues among trans women living with HIV. Ms. Siskind says, “Transgender women often prioritize their hormonal therapy over receipt of other care and services, including HIV treatment and prevention. That may be due to concerns over the interaction between gender-affirming hormonal therapy and antiretrovirals, a lack of resources/access to these services, or both.” Many trans women hesitate to discuss these concerns with their health care providers. Ms. Siskind adds, “Access to comprehensive and integrated gender transition care—including safe, medically supervised feminizing hormone therapy and surgical procedures—is a problem for many transgender people, and many obtain and self-administer them outside of the medical system.” A primary goal of the I AM study is to integrate HIV treatment and hormone therapy into a safe, effective model of care.

Dr. Dowshen articulates the overall consensus of the medical literature and of providers of transgender care: “The small risks are greatly outweighed by the tremendous benefits of medical gender affirmation for overall health and well-being.” Dr. Poteat adds, “The stress of not receiving hormone therapy and the perception that one’s body does not align with one’s authentic gender can cause damage to the body. Our hypothesis is that the benefits of accessing hormone therapy reduce allostatic load and outweigh the cardiovascular risks of estrogen use.”

**Systemic Barriers to Better Health for Transgender Women**

“Transgender women experience health disparities in almost all facets of health and access to health care due to systemic marginalization throughout our society,” says Dr. Sevelius. Transgender women—whether they are seeking routine medical care or medical gender affirmation—face several daunting barriers in the health care system.

**Discrimination in Health Care Settings.** Transphobia and homophobia remain deeply culturally entrenched—so much so that two in three transgender adults report concerns that their sexual orientation or gender identity may negatively affect their health evaluations.7 Almost half of transgender adults report discriminatory experiences with a clinician.7 “Trans women often forgo or avoid health care because of personal experiences of transphobia with providers and on an institutional level,” says Dr. Dowshen.

“A lack of cultural awareness and responsiveness among health care providers and researchers can lead to negative and sometimes traumatizing health care experiences,” says Ms. Siskind. “As a result, transgender people are
Financial Barriers. Low income, lack of health insurance, and high rates of homelessness contribute to health disparities among transgender women. Transgender adults are more likely to be uninsured and to report financial barriers to health care than cisgender adults. The 2019-2020 NHBS found that 63% of transgender women lived at or below Federal poverty levels, 42% had experienced past-year homelessness, 17% had experienced past-year incarceration, and 17% had no health insurance.

Transgender women with health insurance may face exclusions when seeking coverage for gender-affirming care, and almost half of transgender adults have been denied coverage for these procedures. A study by Dr. Dowshen and colleagues published in 2019 analyzed 36 major insurance plans and found numerous transgender-specific exclusions for puberty blockers, hormone therapies, masculinizing chest surgery, and counseling. Dr. Dowshen says that since this study was published, “there have been significant improvements, but we still struggle with a very arduous process for approval for puberty blockers, which are expensive medications, and top surgeries for minors.” She adds, “While insurance companies now provide coverage more frequently for bottom surgery, few, if any, trained providers in many geographic areas will accept Medicaid, creating challenges to access.”

Dr. Poteat adds, “Most larger insurance companies will cover hormone therapy. It’s harder to get reimbursement for surgery through private insurance, but Medicare and Medicaid do cover some procedures. Insurance coverage is increasing but still restricted.”

Limited Knowledge of Medical Providers. Although gender-affirming treatments and surgeries have become available at an increasing number of facilities across the United States, many localities lack providers and facilities that provide these services. A review article by Dr. Sevelius; Joshua D. Safer, M.D.; and colleagues explains that standard medical...
school curricula do not train physicians to treat transgender patients. Thus, practitioners interested in transgender medicine must seek out additional training or mentoring. A lack of familiarity in interacting with transgender people may create additional barriers to effective patient-physician communication and quality care, even for routine medical services not involving gender affirmation.

Trans-Responsive Data Collection and Electronic Health Records. Medical forms that have only two options for gender stand out among the many gender-normative structural barriers in the health care system. To ensure accurate data collection for research and quality continuity of care for individual patients, patient medical records, referral forms, survey research forms, and other documents must accommodate all gender identities. Many research studies, particularly HIV studies, have omitted transgender women or misclassified them as “men who have sex with men,” in part because paper and electronic forms did not list “transgender woman” and other gender identities as options.

Ms. Siskind says, “Recognizing that research networks were not regularly collecting information about the gender identity of study participants in a unified, systematic, and affirming manner, the CNTWG recommended the use of the two-step method and produced a template to facilitate implementation.” The two-step method, originally developed by the Center of Excellence for Transgender Health, captures gender identity and sex assigned at birth as two discrete parameters, both distinct from sexual orientation.

Dr. Dowshen and colleagues developed a patient-oriented template for the ubiquitous Electronic medical record (EMR) system. This template, designed for clinical rather than research applications, captures gender identity, sex assigned at birth, current and former names, an anatomical inventory, preferred pronouns, and other gender-related information. Simple, low-cost, easily implemented practices and tools such as the two-step method and this trans-inclusive EMR template can improve patient care, data collection, research validity, and applicability of findings.

Future Research on Transgender Women's Health at NIH

Researching and improving the health of transgender women present many challenges to the medical community, particularly to its historical assumptions and traditional clinical practices. However, through the funding opportunities and programs described above and many others, NIH, other funding agencies, researchers, and clinicians strive to improve the knowledge base on the health of transgender women; to develop safe and effective preventive interventions and treatments for the health problems prevalent among this population; and to effect trans-responsive changes to gender-normative medical practices. By doing so, we take steps to realize NIH’s vision of a world in which every transgender and cisgender woman receives evidence-based disease prevention and treatment tailored to her own needs, circumstances, and goals.

ORWH thanks the researchers pictured above; Ronna Popkin, Ph.D., NICHD; Pablo Belaunzardin-Zamudio, M.D., M.Sc., NIAID; Wairimu Chege, Dr.P.H., NIAID; Gerald Sharp, Dr.P.H., NIAID; Kimberly Seigfreid, HHS; and Shyam Patel, NIH Sexual and Gender Minority Research Office, for their help in preparing this article.

References

Transgender offensive. male (FTM), but these terms are dated and may be considered as transgender male-to-female (MTF) or transgender female-to-birth. Transgender individuals have sometimes been described a person who identifies as a man but was assigned female at birth, or trans woman, that usually refers to individuals whose gender identities do not match their sex assigned at birth. These people are sometimes described by the shortened forms “cis men” and “cis women.”

**Sex** and **gender** are often used interchangeably. However, in precise scientific usage, **sex** refers to biological differences—including chromosomes, sex organs, and endogenous hormonal profiles—and **gender** refers to socially constructed and enacted roles and behaviors that occur in a historical and cultural context and vary across societies and over time. Both sex and gender—and the interaction of the two—are major determinants of mental and physical health.

**Sex assigned at birth** refers to the biological sex ascribed to a newborn—male/boy or female/girl—based on phenotypic presentation (i.e., appearance of the genitals).

**Differences in sex development (DSD)** broadly describes congenital variations in anatomical, gonadal, or chromosomal development. Genital physiology may not align with an individual’s chromosomes. For example, individuals with XX (female) chromosomes can have testes. Many individuals with DSD identify as intersex. Currently, no U.S. State assigns intersex on original birth certificates, though some allow changes later in life.

**Gender identity** describes one’s sense of self as a woman, girl, man, boy, or individual who is gender-nonbinary, gender-nonconforming, gender-diverse, or intersex. Gender identity is a largely psychosocial construct. However, some biological factors—including genetic and hormonal influences as well as brain differences—can also affect gender identity.5

**Gender expression** refers to how individuals present their gender through social markers such as names, hairstyles, clothing, pronouns, speech, and mannerisms.

**Cisgender** describes individuals whose gender identities match their sex assigned at birth. These people are sometimes described by the shortened forms “cis men” and “cis women.”

**Transgender woman** and **transgender man** are broad terms that usually refer to individuals whose gender identities do not match their sex assigned at birth. A **transgender woman**, or **trans woman**, is a person who identifies as a woman but was assigned male at birth. A **transgender man**, or **trans man**, is a person who identifies as a man but was assigned female at birth. Transgender individuals have sometimes been described as transgender male-to-female (MTF) or transgender female-to-male (FTM), but these terms are dated and may be considered offensive.

**Transfeminine** and **transmasculine** can describe individuals with gender identities on a feminine or masculine spectrum, respectively, but their gender identities do not fit neatly into traditional gender categories.

**Gender-nonconforming (GNC), gender-diverse, gender-nonbinary, and genderqueer** are other terms used to describe individuals with diverse or nonbinary gender identities.

**Transgender, trans, and variations on these terms sometimes describe individuals with GNC identities. Gender-fluid individuals can have a shifting or evolving gender identity over time. Others may describe themselves as agender (i.e., having no gender expression), bigender (i.e., identifying as two genders), or pangender (i.e., identifying as all genders). Transsexual** is an older term with origins in the medical literature. The word refers to individuals who have changed or who seek to change their bodies through hormonal, surgical, or other treatments to better align with their gender identities. Not all transgender people identify as transsexual, and the term is falling out of use.

**Sexual attraction** describes an individual’s sexual desire for women, men, both, or neither. **Pansexual** individuals experience sexual attraction to others without regard for sex or gender identity. **Sexual orientation** is a more inclusive term that encompasses sexual attraction, behavior (e.g., dating), and identity (e.g., lesbian, gay, bisexual, heterosexual). Sexual preference, once used as a synonym for sexual orientation, has fallen out of use and may be considered insensitive.

**LGBTQ+ and variations of this abbreviation (e.g., LGBT, LGBTQIA)** represent blanket terms to refer to sexual and gender minorities, which include lesbian, gay, bisexual, transgender, queer, questioning, intersex, and asexual people. In this context, **queer** can describe a broad range of sexual orientations and gender identities, though the term has had and continues to have pejorative uses as well.

**Transphobia** and **homophobia** refer to fear, discrimination, and hatred of transgender and homosexual/bisexual individuals, respectively.

**Gender minority** refers to people, including transgender, intersex, and other GNC individuals, whose gender identities are incongruous with their sex assigned at birth.

**Gender affirmation** refers to the complex interpersonal process of recognizing an individual’s gender identity, involving social, psychological, medical, and/or legal components.7

**Transitioning** is an older term used to describe the process of taking steps to affirm one’s gender.

**Misgendering** describes referring to an individual, particularly a transgender or gender-nonbinary person, with a pronoun or another word that does not reflect the person’s gender identity. Although it can result from confusion, misgendering can be intended or perceived to be impolite, offensive, or transphobic. Many gender-nonbinary people prefer the pronouns they/them rather than she/her or he/him.

**People with childbearing/reproductive potential** is an inclusive term acknowledging that individuals of all genders and sexes may have the potential to reproduce. Terms like **pregnant person and chestfeeding** are increasingly common.
The Future of Women’s Health Research After the 2021 Women’s Health Consensus Conference

Between ORWH’s many contributions to the NIH COVID-19 response, our office has continued to support advancements in research on women’s health with several major initiatives. In February of last year, ORWH staff members, grantees, and other colleagues contributed over 20 scholarly articles to a special issue of the Journal of Women’s Health focusing on the persistent problem of maternal morbidity and mortality (MMM) in the U.S. Complementing this effort, ORWH created and regularly updates the MMM Web Portal to lead the discussion of MMM both within and outside of NIH and to serve as a centralized hub for current, reliable information on this public health crisis.

ORWH also addressed MMM, along with rising rates of chronic debilitating conditions in women and stagnant cervical cancer survival rates, at the recent “Advancing NIH Research on the Health of Women: A 2021 Conference.” This event, organized in response to a congressional request for a women’s health conference (WHC) and hosted in conjunction with the Advisory Committee on Research on Women’s Health, convened biomedical researchers and policy experts to characterize these public health concerns and consider future directions for the NIH women’s health research agenda. ORWH will collect specific recommendations from the WHC in a forthcoming report. Here, I describe the broader themes and ideas that emerged from discussions among NIH subject matter experts, panelists, and participants.

**Improve Implementation Research.** Researchers and clinicians have already developed effective, evidence-based practices and preventive interventions for several of the medical issues addressed at the WHC—notably, MMM and cervical cancer. Estimates indicate that between half and two-thirds of the deaths resulting from pregnancy or delivery complications in the U.S. are preventable with appropriate medical interventions. Despite availability of effective screening and prevention interventions, incidence of cervical cancer has declined minimally over the past two decades. Regular screening with Pap or HPV (human papillomavirus) testing can detect premalignant, treatable cervical lesions. Vaccines against HPV, the virus that causes virtually all cervical cancers, have been available since 2006. Although discovery research and clinical trials could potentially improve outcomes for patients diagnosed with cervical cancer, proper and thorough implementation of existing interventions remains a challenge. Multiple social and health care delivery barriers prevent large numbers of women with cervical cancer from receiving standard-of-care treatments, including surgery, brachytherapy, and targeted therapies. Implementation research to improve uptake of known interventions is a top public health priority.

**Increase Diversity.** WHC participants commented that diversity, equity, and inclusion (DEI) concerns must be integrated into all aspects of the biomedical enterprise. Research relevant to the 70-kg White man—historically considered the medical norm in health research—may not align with the clinical needs of women. In the interest of robust science, biomedical and biobehavioral research and clinical practice must account for implicit biases as well as health disparities associated with race, ethnicity, geographic location, socioeconomic status, age, sex, gender, and other demographic factors as well as the intersection of these factors. Equity science must inform all aspects of the research process—from the development of funding opportunities to the designing of studies to recruitment practices to data collection and analysis to reporting—for everyone to benefit equitably from our investment in medical discovery.

**Intentional Research on Women.** Chronic conditions affect more women than men, and women develop a broader range of chronic disease types than men. As a clinical framework specific to chronic debilitating conditions in women did not exist, one had to be developed to describe NIH research on this topic. WHC participants also called for research centered around women from representative populations, support of a broader and more diverse group of universities and research institutions, and enhanced research on female-specific conditions and on the health concerns of women and individuals from underrepresented populations.

**Successful Programs Can Lead the Way.** These ambitious suggestions from the WHC present imposing challenges to funders, administrators, researchers, and others. However, the successes of individual programs and initiatives demonstrate that thoughtful, equity-minded research can advance DEI, allow implementation of best practices, and improve public health. Initiatives and institutions such as the New Mexico HPV Pap Registry, the California Perinatal Quality Care Collaborative, and the Stephenson Cancer Center provide examples of strategies and approaches suggested by WHC participants that can realize positive systemic changes and, ultimately, improve outcomes for all patients.
Nature Editorial Calls for Expanded Definition of “Women’s Health”


A recent Nature editorial advocates expanding the definition of women’s health to include not only issues related to reproductive health but the totality of the health of women, including diseases that affect both men and women. This view is consistent with NIH’s definition of women’s health, one that encompasses the health of women from head to toe and the internal and external factors that affect the health of women across the lifespan. Historically, medical research has focused on men and male animals. For instance, only one-third of participants in clinical trials related to cardiovascular disease are women. An analysis of articles published in six leading journals in 2014 shows that 40% of neuroscientific studies used only male animals.

The Nature editorial argues that the “study of health and disease in women should not be limited to conditions that affect only women.” Many diseases, such as Alzheimer’s disease and type 2 diabetes, present and progress differently in men than they do in women and, as such, should be studied in both. The editorial points to important sex differences often overlooked by researchers and clinicians alike. For instance, men and women have different heart attack symptoms, and guidelines for treatments to prevent subsequent heart attacks are also sex-specific.

The editorial concludes by calling for more women on grant review panels and advisory boards to help ensure more equitable consideration of sex differences in research. The piece also cites the NIH Policy on Sex as a Biological Variable and challenges funding organizations, researchers, and journal publishers to incorporate this policy to promote more biomedical studies with the potential to benefit all.

COVID-19 Studies Lack Data on Sex and Gender


A recent Science editorial by STEMM journalist Cathleen O’Grady states that most COVID-19 studies do not disaggregate data by sex and gender. Only 8 of 45 randomized controlled trials on COVID-19 completed by December 2020 reported sex or gender effects. Although the Pfizer–BioNTech and Moderna vaccine trials demonstrated more than 90% efficacy in both men and women, neither group of researchers published study results distinguishing the risks of adverse effects by sex or gender. Ms. O’Grady finds this trend troubling, as a large body of evidence indicates that the disease does not affect men and women in the same way. For instance, global COVID-19 statistics show higher rates of hospitalization and mortality in men. Ms. O’Grady quotes several researchers lamenting how COVID-19 studies that fail to consider sex and gender are missing “an evident piece of the puzzle” and thereby overlook an opportunity to understand how the disease functions.

Study Shows Gender Gap in Pandemic-Era Scholarly Publishing

(Original article by Squazzoni et al. 2021. PLOS One. PMID: 34669713.)

Academics submitted an unusually high number of articles to scholarly journals through the early stages of the COVID-19 pandemic. However, during this period, women, particularly those in junior academic positions and those in medical disciplines, submitted proportionately fewer articles than men. Flaminio Squazzoni, Ph.D., and colleagues discovered this gender gap in their analysis of data on over 5 million authors and reviewers of manuscripts submitted to over 2,300 Elsevier journals between January 2018 and May 2020. The researchers attribute this trend, in part, to women’s increased child care and other domestic responsibilities during lockdowns. In their discussion, Dr. Squazzoni and colleagues make several recommendations for mitigating this gender gap. The researchers recommend that grant, hiring, and promotion committees adjust policies and assessment guidelines to account for pandemic-related career disruptions. For instance, such committees could consider COVID-19 impact statements as part of their decision-making processes. The authors also suggest institutional initiatives to bolster retention; to create more diverse, equitable, and inclusive workplaces; and to improve family-friendly policies.

Research Suggests Strategies to Improve Equity for Mothers in Academic Research


In response to the pandemic’s conspicuous exposure of gender inequalities in the STEMM research field, Robinson W. Fulweiler, Ph.D.; Sarah W. Davies, Ph.D.; and colleagues suggest strategies for “building back better” and increasing equity for academic women,
particularly working mothers. The authors make recommendations to mentors of women with child care responsibilities as well as to institutions, scientific societies, publishers, and funding organizations. Mentors should create an accepting environment and ensure a healthy work-life balance for academic mothers; involve them in all lab interactions and decisions; develop short- and long-term flexible schedules; and fully understand and adhere to parental leave policies. Institutions and administrators should invest in on-campus day care or subsidize off-site care, create gender-specific (rather than gender-neutral) policies to address systemic gender inequalities, dedicate flexible funds to support productivity of researcher-mothers, decrease teaching loads and service responsibilities of academic mothers, adapt tenure review processes and schedules, and account for COVID-19 disruptions in tenure and promotion reviews. Scientific societies should plan hybrid virtual/in-person conferences, diversify their governing boards, provide small grants to early-career members, and improve networking opportunities for mothers. Publishers could expedite submissions from women, waive open-access publication fees, recruit women to editorial boards, and invite women to write review articles. Funding agencies could reduce the paperwork of sequential applications and provide supplemental funds and other accommodations to account for pandemic-related delays. The authors argue that these strategies would mitigate the impact of COVID-19 on academic women and the scientific community as a whole.

Blanca Himes, Ph.D., completed her undergraduate degree in physics and obtained a Ph.D. in medical physics and bioinformatics from the Division of Health Sciences and Technology at the Massachusetts Institute of Technology. She was a biomedical informatics research fellow at Harvard Medical School in the Computational Health Informatics Program under the guidance of Isaac Kohane, M.D., Ph.D., and Scott Weiss, M.D. She served as a faculty member at Brigham and Women’s Hospital and Harvard Medical School prior to moving to the University of Pennsylvania, where she has been a tenured Associate Professor of Informatics in Biostatistics and Epidemiology since 2020.

**What are your primary research interests?**
My lab studies asthma and common asthma drugs (e.g., β2 agonists, glucocorticoids). We identify genetic traits associated with asthma and characterize changes in gene expression by analyzing molecular biology data from human and in vitro studies. We also use data from electronic health records to understand characteristics of real-life populations with asthma and chronic obstructive pulmonary disease and incorporate social, economic, and environmental factor data obtained from secondary sources.

**How does the biomedical informatics approach help you to pursue these interests?**
My background in biomedical informatics has been key in the design and execution of studies that require analysis of large datasets, which, these days, are part of most health studies. My biomedical background has been particularly helpful. Having data science skills, along with some relevant domain knowledge, helps me design studies that yield helpful insights and improves my ability to communicate with experimental researchers and physicians who have different areas of expertise.

**What are the barriers for women in science?**
Women, particularly those from underrepresented groups, are underestimated by some colleagues and people in leadership positions. Other people’s fears that women will not succeed can result in women scientists receiving fewer opportunities and resources that could foster research independence. These fears can become self-fulfilling prophecies when women are deprived of opportunities at early career stages.

**What advice would you give to young women scientists?**
Make sure that you do what is necessary to remain fulfilled. If you find that you are losing your joy for science because of your environment, change your environment! There are plenty of supportive, enthusiastic, and devoted scientists who do amazing work without sacrificing their physical or mental health.

**Of which career achievement are you most proud?**
There have been salient moments of happiness and relief as I have progressed through my career, but I most associate feelings of pride with students and trainees reaching milestones. A special part of being an academic is seeing trainees master difficult material, successfully complete conference talks, publish papers, graduate, and move on to their next career stage. Each trainee achievement is a source of pride.
ORWH and NIGMS Support Women’s Health Research in States with Low NIH Funding

A recent funding opportunity from the National Institute of General Medical Sciences (NIGMS) and ORWH will expand and complement the development of innovative, state-of-the-art women’s health research through the Centers of Biomedical Research Excellence (COBRE) program in Institutional Development Award (IDeA) States, areas that have historically received low levels of NIH funding. More information on this funding opportunity —Supporting Women’s Health Research in the IDeA States Through the Centers of Biomedical Research Excellence (COBRE) Phase I Program (NOT-GM-21-056)—is available here.

NIH Director Francis S. Collins Steps Down

Francis S. Collins, M.D., Ph.D., the longest-serving presidentially appointed NIH Director, stepped down from his role late last year. A physician-geneticist, former leader of the Human Genome Project, and former Director of the National Human Genome Research Institute, Dr. Collins took office as the 16th NIH Director in August 2009, after being appointed by President Barack Obama and confirmed by the Senate. He was asked to continue in his role by President Donald Trump in 2017 and again in 2021 by President Joe Biden. In addition to leading NIH during the COVID-19 pandemic, Dr. Collins accomplished much to advance research on the health of women and to support women in biomedical careers, such as helping to include more women in NIH-supported clinical trials; co-authoring a seminal Nature article with ORWH Director Janine A. Clayton, M.D., that announced the NIH Policy on Sex as a Biological Variable; working to end sexual harassment in the scientific workplace; and conspicuously refusing to serve on academic panels without equitable gender representation. ORWH thanks Dr. Collins for his leadership, service, and many accomplishments, particularly those in the field of women’s health. You can read more about Dr. Collins’ contributions and leadership here.
New ORWH Video Series Complements E-Learning Course on Sex as a Biological Variable

ORWH recently released a series of videos that complement the e-learning course “Sex as a Biological Variable (SABV): A Primer.” The SABV primer gives users a thorough and up-to-date understanding of NIH requirements for factoring SABV into research designs. Users will be able to apply this knowledge when designing studies, conducting research, and interpreting evidence. The videos introduce SABV and the NIH SABV policy, summarize the e-learning course and its four modules, and share insights on SABV and sex differences research from principal investigators in the Specialized Centers of Research Excellence on Sex Differences (SCORE) program. ORWH has also developed two other e-learning courses: “Bench to Bedside: Integrating Sex and Gender to Improve Human Health” and “Introduction: Sex- and Gender-Related Differences in Health.” All of the courses and videos are available at no cost to the public.

Study Demonstrates Efficacy of Pfizer-BioNTech COVID-19 Vaccine in Pregnant Women

A recent retrospective observational study of over 15,000 pregnant Israeli women—half of whom were vaccinated with the Pfizer-BioNTech mRNA vaccine (BNT162b2) and half of whom were not vaccinated—demonstrated 78% vaccine efficacy. At follow-up 28 days or more after the first vaccine dose, 10 SARS-CoV-2 infections had occurred in the vaccinated women, as opposed to 46 in the unvaccinated women. Pregnant individuals and recently postpartum people face additional risks of complications from SARS-CoV-2 infection but were not included in the Phase III clinical trials. Currently, the Centers for Disease Control and Prevention recommends COVID-19 vaccines for people who are “pregnant, breastfeeding, trying to get pregnant now, or might become pregnant in the future.”

NIH Supports Research on Possible Link Between COVID-19 Vaccines and Minor Menstrual Abnormalities

ORWH and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) have awarded grants totaling $1.67 million to five institutions to explore potential links between vaccination against COVID-19 and menstrual changes. Some anecdotal evidence connects vaccination against COVID-19 with subsequent menstrual irregularities. Patients have reported missing or having irregular menstrual periods, heavier bleeding, and longer menstrual periods. Some postmenopausal women report having experienced vaginal bleeding after receiving a COVID-19 vaccine. An initial publication from one team of NIH-supported researchers reported that, for a small number of patients, COVID-19 vaccines were associated with a short delay in the start of their next menses. The study participants most likely to experience an increase in cycle length were those who received both vaccine doses within a single menstrual cycle. Most vaccinated participants did not have a clinically significant change in their menstrual cycles.

NIH Scientific Workforce Diversity Office Hosts New Seminar Series

The Scientific Workforce Diversity Seminar Series (SWDSS), hosted by the NIH Scientific Workforce Diversity Office, features renowned researchers who have contributed to the growing body of knowledge on pressing topics relevant to scientific workforce diversity. SWDSS serves to keep scientific workforce diversity issues at the forefront, to share the latest research on these topics, and to engage with professionals and researchers within and outside of NIH. Seminars have discussed the efficacy of implicit bias training and outcomes from “Addressing Diversity, Equity, Inclusion, and Anti-Racism in 21st Century STEMM Organizations: A Summit,” hosted by the National Academies of Sciences, Engineering, and Medicine (NASEM). More information and recordings of past seminars are available on the SWDSS webpage.