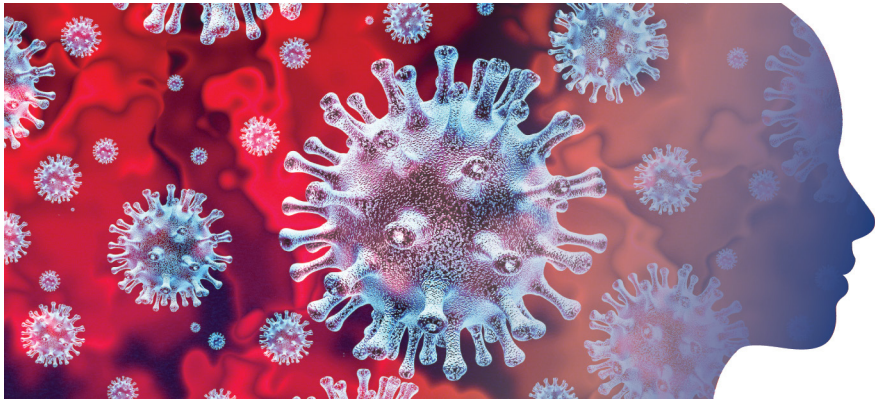




# Guiding Principles: Sex and gender influences in COVID-19 and the health of women



**The COVID-19 pandemic underscores the need to systematically consider sex and social determinants of health, including gender, to strengthen our collective capacity to respond equitably to COVID-19 and any threats related to future outbreaks and pandemics. Accounting for sex without also accounting for gender (and other social determinants of health) would limit the development and deployment of effective, equitable diagnostics, treatments, and interventions that are relevant to the entire population.**

**The principles:** Incorporating a sex-and-gender lens into the NIH COVID-19 research response offers several unique opportunities to promote rigorous research and advance health equity, including<sup>1</sup>:

- Strengthening vaccine efficacy and optimizing dosing for all sexes
- Enhancing investigations of novel therapeutics
- Exploring sex differences in medication risk profiles
- Further elucidating gender-related factors that act as a barrier to treatment and self-management, access to health care, and health-seeking behaviors
- Understanding the long-term mental and physical health consequences of COVID-19 for everyone

**Sex as a biological variable (SABV) policy requirements and COVID-19:** The need to consider sex for research to be reproducible and relevant for all people warranted a separate NIH policy, [Consideration of Sex as a Biological Variable in NIH-funded Research](#).

- **Sex differences in immune response** cause COVID-19 to affect women and men differently,<sup>2</sup> and SABV data are critical to inform an effective public health response to the pandemic.
- **Sex differences in mental health** were already linked to a gender gap, particularly for affective disorders, in the United States pre-pandemic, but the gap has significantly widened as a result of COVID-19.<sup>3</sup>



**NIH inclusion and COVID-19:** The [NIH Policy and Guidelines on The Inclusion of Women and Minorities as Subjects in Clinical Research](#)

require that women, minorities, and individuals of all ages be included in NIH-funded clinical research and, particularly for NIH-defined Phase III clinical trials, that differential effects by sex/gender, race, and ethnicity be examined.

- **Clinical trial design, analysis, and reporting issues:** Rigorous and reproducible research is the foundation for improving health outcomes amid the COVID-19 crisis and public health emergency. It is essential to factor sex and gender into study design, data collection, analysis, and reporting, including publications, and to explore innovative methodologies that could generate valid evidence to inform sex- and gender-aware clinical practices.
- **Safety and efficacy concerns:** Different organs, hormones, and metabolic and clearance pathways could lead to variability in responses to treatment and vaccines. These differences may also lead to diverse responses to treatment and vaccines. It is critical that data from women be available when decisions on dosing, safety, and efficacy of therapeutic agents are being made.



**COVID-19 and the health of women:**

- **Pregnancy** is associated with alterations in the immune system, and pregnant women are susceptible to respiratory pathogens and to the development of severe pneumonia, which may make them more susceptible to COVID-19 infection or its consequences than the general population, especially if they have chronic diseases or pregnancy-related complications.<sup>4</sup>
- **Understudied, underrepresented, and underreported (U3) populations** of women are uniquely situated within overlapping systems of oppression to sustain disproportionate losses of both life and livelihood during this pandemic.<sup>5</sup>
- **Gendered experiences and inequalities** impact COVID-19 risk, progression, and outcomes (directly and indirectly).

**Consequences of COVID-19 on the biomedical workforce:** Women represent the majority of health care and other essential workers, resulting in increased risk of exposure. The effects of COVID-19 on the biomedical research workforce are staggering. The impact is even more devastating for early-career investigators, as the research interruption comes at a period when their productivity is critical in defining the trajectories of their careers.<sup>6</sup>

- **Women scientists** are further challenged because they are disproportionately the principal caregivers and homeschooling teachers in their families.<sup>7</sup>



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