Why Sex and Gender Need to be Considered in COVID-19 Research

A Guide for Applicants and Peer Reviewers

First, sex-disaggregated data reveal that more males are dying from COVID-19 than females[1]. Biological factors and/or comorbidities likely play a role.

Second, pandemics can compound differential exposures and outcomes for girls, women, sexual and gender minorities, caregivers, and other essential workers involved in gendered occupations. It is essential that the impacts of COVID-19 are considered through an intersectional lens to create effective, equitable policies and interventions. For example, consider how gendered racism may modify the impacts of COVID-19 on racialized women[2]. Learn more about what intersectionality is and how it can be applied to quantitative health research here[3].

Applicants and peer reviewers should appropriately account for the following in COVID-19 research proposals:

☐ **Molecular Mechanisms of Viral Pathogenesis**
Include both male and female cells. The SARS-CoV-2 receptor, ACE2, is X-linked and escapes X chromosome inactivation[4]. Male sex and increased age are associated with increased co-expression of genes which code for the ACE2 receptor, as well as for proteases required for SARS-CoV-2 cellular entry (TMPRSS2 and CTSL)[5]. Disaggregate results by sex and age.

☐ **Host Immune Response**
Include male and female animals or humans, as sex differences in the host immune response to SARS-CoV[6] and SARS-CoV-2[7] infections have been reported. Disaggregate results by sex and age.

☐ **Diagnostic Tests and Serologic Antibody Testing**
Measure sensitivity and specificity for males and females separately, as sex differences in viral titers and IgG antibodies have been reported for SARS-CoV and SARS-CoV-2 infections in humans and mice[6,8].

☐ **Vaccines and Therapeutics**
Test and report sex-specific dosing of vaccines and other therapeutics. Efficacy, safety and toxicity for males and females differ for some drugs[9], immunotherapies[10] and vaccines[11]. Higher rates of adverse events following COVID-19 vaccination have been reported in women[12].

☐ **Clinical Trials**
Stratify randomization by sex and age, as these variables influence the safety and efficacy of drugs and biologics[13]. If race/ethnicity variables are included in the trial, avoid ascribing racial and ethnic differences to biology[14,15]. Consider how processes like racism may influence recruitment. Disaggregate results by sex, age, race/ethnicity, and other identity and social position variables if applicable.

TIP: In all studies involving human participants, consider how processes of oppression, discrimination, power, and privilege, such as ableism, ageism, classism, and racism may influence health impacts, outcomes, and access to care. Learn more about the definitions of these terms here[16].

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Medical Devices and Personal Protective Equipment

Incorporate sex-specific anatomical differences and gendered user preferences into the design of medical devices and personal protective equipment for COVID-19[17].

Social, Behavioural Observational and Seroprevalence Studies

Consider sex, gender, age, disability, income, Indigeneity, race/ethnicity, and other identity or social position variables in survey questions and sampling strategies.

For gender, in studies of disease susceptibility, investigate:

1) Gendered behaviours, as men are more likely to smoke than women[18] and less likely to seek healthcare[19], whereas older women are more likely to live alone and experience social isolation.

2) Gender roles, as 70% of the paid and unpaid global healthcare workforce are women[20]. The risk of exposure increases for those on the frontline of the COVID-19 pandemic.

For gender, in research on the impact of the pandemic, investigate:

1) Gender relations, as physical distancing puts women and girls at higher risk of domestic violence[21], while transgender and non-binary individuals are at higher risk of feeling unsafe due to heightened tensions and unsupportive environments in the household[22,23].

2) Gender roles, as women disproportionately assume caregiving responsibilities. Lockdown measures and school closures have caused negative impacts on women's wellbeing[24].

Mental Health

Examine how mental health effects vary by sex, gender, sexual orientation and other identity or social position variables, as the triggers, causes, signs and symptoms of depression and anxiety may differ[25].

Implementation Science

Sex, gender, age, disability, income, Indigeneity, race/ethnicity, immigration status, occupation, and other identities or social positions influence the way in which an implementation strategy works, for whom, under what circumstances and why. Consider how messaging should appropriately include and target different groups according to sex, gender, and other identity characteristics[26].

Policy

Consider the unintended impacts of all COVID-19 policies, especially economic recovery policies, on Indigenous Peoples, women, sexual and gender minorities, racialized individuals, single parents, immigrants, unpaid workers, individuals with precarious work status, people with disabilities, the homeless and those living in rural and remote areas[27].

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