

Roundtable Discussion on COVID-19 Through a Sex and Gender Lens

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Abstract

Although the full and lasting impact of the coronavirus disease 2019 (COVID-19) outbreak is yet to be determined, there is evidence that sex and gender play a significant role in determining patient outcomes across the globe. This roundtable discussion is a transcript of a seminar held by several representatives from Johns Hopkins University on the impact of the global pandemic on women's health and well-being. They reported on the various pathophysiological aspects of the disease, as well as the social and financial consequences of this global pandemic. Looking at COVID-19 through a sex and gender lens highlights the vulnerabilities and inequalities of people of different genders, races, and socioeconomic conditions, and how care providers can better respond to those differences.

Keywords

gender, sex, sex differences, female, male, sociocultural and economic, factor

Wendy Bennett, MD, MPH, Director of Research for Johns Hopkins Community Physicians and Codirector of the Johns Hopkins Center for Women's Health, Sex and Gender Research

I am pleased to welcome all of our attendees to this exciting and timely webinar focusing on the implications for sex and gender related to coronavirus disease 2019 (COVID-19).

I'm especially grateful to Dr Sabra Klein, the director of the Johns Hopkins Specialized Center for Research Excellence (SCORE), focused on sex differences research; to Dr Rosemary Morgan, an assistant scientist in the Bloomberg School; and Patrick Shea, the administrator of our SCORE for organizing and coordinating this program.

I also want to announce a special opportunity that we were able to make possible for Johns Hopkins University because of a very generous donation from the Foundation for Gender-Specific Medicine. I'm very pleased today that we're able to announce our 2 outstanding grant awardees for research relating to COVID-19 and I want to take the opportunity to congratulate them.

The first is Dr Fenne Sille, an assistant professor at the Johns Hopkins Bloomberg School of Public Health in the Department of Environmental Health and Engineering. Her project is entitled "Sex Differences and the Cytokine Storm Associated With COVID-19 Mortality."

The second awardee is Dr Shannon Wood, an assistant scientist at the Johns Hopkins Bloomberg School of Public Health in the Department of Population, Family and Reproductive Health. Her project is entitled "COVID-19's Impact on Pregnant Women in Ethiopia: Understanding Unmet Needs for Vulnerable Populations."

Our moderator is Dr Nancy Glass, a professor in the School of Nursing. She has been a core and very involved member in our Center for Women's Health, Sex and Gender Research.

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Nancy Glass, PHD, MPH, MS, RN, Associate Director of Johns Hopkins Center for Global Health and Independence Chair in Nursing Education

Thank you and welcome everyone. I have the pleasure to moderate a panel of global experts in this timely discussion of sex and gender within the context of COVID-19.

It is my great pleasure to introduce our first speaker, Dr Sabra Klein.

Sabra Klein, PhD, Professor of Molecular Microbiology and Immunology at the Johns Hopkins School of Public Health and Codirector of Johns Hopkins Center for Women's Health, Sex and Gender Research

I am going to focus on the biology of sex differences. Sex is a biological variable that affects our immune responses to microbes, like viruses as well as vaccines.

Our biological sex affects the functioning of our immune system, through the presence of our sex chromosome complement. In most of us, there are 2 X chromosomes in biological females and an X and Y chromosome in biological males.

On the Y chromosome is a gene called the SRY gene. This gene encodes for a factor referred to as the testes-determining factor, which contributes to the formation of the testes during embryonic development. This is not to say that other genetic factors are not involved with ovarian or female development. The SRY gene has been most well studied as a major factor contributing to the sex-specific development of the bipotential gonads into either testes or ovaries, which define us as being either male or female, respectively.¹

The second factor that contributes to this definition of sex as a biologic variable pertains to the sex steroid hormones. In XY individuals with testes this would be the androgen testosterone, and in XX individuals with ovaries this would be not only estrogens but progesterone. This hormone-dependent signaling contributes to the development of secondary sex characteristics as well as to sex-specific responses—most of which have often been studied in the context of reproductive development, reproductive physiology, and reproductive behavior.

For our purposes today, I will focus on how sex can impact our immune responses to affect the severity of COVID-19. Some of the best observations of sex impacting immunity are with regard to inflammation and autoimmunity. The observation that 80% of all autoimmune disease patients are female has been used to study and understand how sex-specific differences can be affected not only by our hormones but by the expression of X-linked genes as well as autosomal genes.²

What do we know about sex-disaggregated data pertaining to COVID-19? Many countries are sex-disaggregating data based on cases, hospitalization, and death from COVID-19. Some countries are sex disaggregating all of their data, while other are only giving us partial sex disaggregation, meaning for

example that they may disaggregate deaths but not the number of cases.³

By and large, when we look at COVID-19 cases (ie, those individuals testing positive for exposure to the severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) we see a very mixed response within various countries. Some countries are reporting a female bias, other countries are reporting a male bias. Yet other countries are reporting no sex bias.³ When it comes to exposure, it seems likely that gendered socio-economic factors are contributing to this and will be discussed during this roundtable.

For deaths, however, it is reported that a significant majority of countries are reporting male-biased death rates from COVID-19. Specifically, 87% of countries that have sex disaggregated their case fatality data report having a male bias.³ In contrast, only 2% of countries are reporting a female bias and 11% are reporting no sex bias. It is this male bias in death rates from COVID-19 that I want to focus on for my brief discussion with you today.

Let's begin with data that were published recently from France.⁴ What I liked about these data was that, unlike many of us speaking to you in this webinar, these were not investigators focused on sex- and gender-based research. Rather, they are infectious disease epidemiologists who made an unbiased observation about sex-specific differences in COVID-19 outcomes. In their study, when they reviewed hospitalizations, intensive care unit (ICU) admissions, as well as deaths, there was a dramatic increase in all measures of COVID-19 severity throughout the country and particularly in the regions of France that were most affected. When they broke down their COVID-19 outcome data by sex, they made several important observations. First, across diverse age-groups (broken down into 10-year age groupings), we find that males have increased rates of hospitalization and increased rates of ICU admission. We're seeing this across diverse ages with the majority of the severe cases occurring in older-aged individuals (ie, individuals 50 years and older). And then when we look at deaths, there's a slight skewing in terms of the age distribution, in which the majority of deaths are occurring in individuals 60 years and older, but that male bias is still maintained.⁴ We're still seeing significantly more males experiencing severe disease. Thus, the burden of SARS-CoV-2 virus is worse for men than women.

Next let's look across all countries and consider those that have partitioned their male–female data into age categories. When we look at case fatality rates among countries that have sex disaggregated their data, we find that the case fatality rates are consistently greater for men compared with women.⁵ While some countries may have significantly lower case fatality rates than other countries, this male bias is still true in places like Norway and even South Africa, not just in France. When we look across countries around the globe—those that are reporting sex-disaggregated data broken down by age—we find that males are significantly more likely to die than females, with this being very pronounced among the age 60 years and older, where we are seeing the greatest percentage of deaths around the world.⁵

How can sex as a biological variable results in male biases in the severity of COVID-19? Sex can impact at the level of

SARS-CoV-2 entry into epithelial cells. The primary receptor that SARS-CoV-2 uses for entry into cells, primarily respiratory epithelial cells, is angiotensin-converting enzyme 2 (ACE2), which is X-linked, and is downregulated by estrogen, at least in the kidney; we are still awaiting data from the pulmonary tract.⁶ We also know that there are sex differences in the expression and in the effect of ACE2 genetic variance, at least in the context of diseases associated with the kidney.⁶

The membrane-localized receptor, TMPRSS2 is also used by SARS-CoV-2 for membrane fusion and we know that, at least in the prostate, androgens can regulate the expression of this receptor.⁵ Some early data from Italy compared the likelihood of being infected with SARS-CoV-2 among men with prostate cancer that either were on an androgen deprivation therapy or men who were not.⁷ It is clear from these data that a greater proportion of men who were not on this androgen deprivation therapy became infected with SARS-CoV-2 as compared with those who were not taking this therapy.⁷ This is not definitive by any means, but it is suggested that there could be a role of androgens in impacting virus membrane fusion.

Virus sensing is another sex-specific difference that could contribute to differences in the experience of the illness and to outcome. TLR7 is a pattern recognition receptor that can be used for detecting RNA viruses, including SARS-CoV-2, a gene that has been shown to have biallelic expression in females, meaning that it has been shown to escape X inactivation and contribute to increased antiviral immune responses in other viral infections, including HIV.⁵ Differential expression of pattern recognition receptors can contribute to sex differences in innate immune responses, in which cytokines and chemokine production early during an infection, including with SARS-CoV-2, could be integral in recruiting immune cells to the site of infection to clear the virus. We know that there are sex differences in greater expression of genes associated with innate immunity in females as compared with males.⁸ This is going to lead to induction of an adaptive immune response, the response that's going to be critical for clearing a virus. There are also the types of responses which will be critical for responses to vaccination, all of which have been shown to have sex-specific differences and could contribute to sex differences in case fatality rates that we're seeing around the world.

Collectively, sex differences in virus entry, virus sensing, as well as immune responses can contribute to sex differences in the control of infection. Early data from China, including family studies, have shown that there is prolonged virus shedding in males as compared with females.^{9,10} This is something for us to examine further: prolonged viral shedding may contribute to an inability to control infection, contribute to progressive infection, or induce the cytokines storm which could lead to greater damage and worse outcome in men as compared with women.

Nancy Glass: Thank you, Dr Klein. Now we have the great pleasure of having Dr Jeanne Sheffield join us.

Jeanne Sheffield, MD, Director of the Division of Maternal-Fetal Medicine and Professor of Gynecology and Obstetrics at the Johns Hopkins School of Medicine

I only have 10 minutes to talk about pregnancy and COVID-19, which normally I would say is impossible. However, we still have very little information about how COVID-19 affects pregnancy. In the last couple of weeks though, we at least have a little bit more information that I will present today.

I wanted to talk about the impact of respiratory viruses on pregnancy and why pregnant women may be more susceptible to infection, how COVID-19 is similar but also how it's a little bit different to the 2 others we dealt with in the last couple of decades: severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). Then I'll finally end by briefly addressing racial disparities.

In January of this year, I gave a talk here at Johns Hopkins on the emergence of COVID-19, and how we probably needed to pay attention to this virus. We had our national meeting at the Society of Maternal Fetal Medicine at the end of January and they asked me to touch on this new coronavirus in my talk about emerging infections. It's amazing how much has changed since then.

We received the first reports 3 months ago, when we started trying to figure out how we're going to make recommendations about coronavirus and what we need to do in pregnancy. In the Wuhan case series, there were 9 pregnant women in the course of about a 10-day time period. All of these pregnant women were positive for SARS-CoV-2. All these women were in the third trimester and presented for delivery. All of them had a cesarean delivery, but the authors admitted they performed the cesarean only because they were not sure what the risks of a vaginal delivery with SARS-CoV-2 were in pregnancy and with the possible risk of transmission to the neonate.

The women had no comorbidities, except for one with gestational hypertension, one with severe preeclampsia and one, interestingly, who was co-infected with influenza at the time. Six out of nine received antiviral therapy and empiric antibiotics. All of them had live births. Of the 9, 4 had a preterm birth, all between 36 and 37 weeks unrelated to COVID, for example, delivery for hypertension.

The care workers collected amniotic fluid, breast milk, neonatal throat swabs, and cord blood. All of these were negative for SARS-CoV-2. They mentioned that in another case report, there was a neonate that tested positive for COVID-19 but that was 36 hours after birth, and they suspected it may have been an infection from the mother at the time of delivery.

It's amazing how many papers have come out since that time period. We've learned a lot, but there are still significant gaps in our knowledge. But first I want to talk about what we know about COVID-19 and pregnancy.

First, let's discuss respiratory viruses in general in pregnant women as these have a tendency to cause worse disease during pregnancy.

One of the main reasons for worse disease and more complications is that there are several physiologic changes in pregnancy that affect how a woman responds to a respiratory virus. We see increases in heart rate and cardiac output. Importantly from a pulmonary standpoint, pregnant women have increased oxygen consumption and decreased lung capacity, especially as the uterus increases in size. They are also less able to clear secretions.

Then there are also immunologic changes. There has been a lot of controversy surrounding the level of immunosuppression in pregnancy. However, we do know that there are immunologic changes that allow for tolerance of a genetically distinct fetus. These changes affect how a pregnant woman responds to infectious diseases, particularly some viruses, differently than a nonpregnant individual.

What do we know about other coronavirus in pregnancy? We have some information that has come out of the SARS-CoV-1 and then the MERS epidemics; SARS-CoV-1 had about a 25% case fatality rate. Complications included pneumonia, acute respiratory distress syndrome, and disseminated intravascular coagulation. There was a high risk of miscarriage and preterm delivery. Interestingly, there was no vertical transmission to the fetus. Middle East Respiratory Syndrome was very similar. Middle East Respiratory Syndrome also had a high risk of preterm birth, but no fetal transmission reported. These are different than what we are seeing so far with SARS-CoV-2.

The disease severity categories that we're currently using when we look at pregnancy outcomes lump asymptomatic or presymptomatic together and are classified as mild, moderate, severe, and critical.

The World Health Organization (WHO) recently reviewed the Chinese data. Eight percent of women had severe disease, and 1% critical disease. The WHO data summarize that pregnant women did not seem to be at a higher risk for severe disease than the general population. Since that time, there have been several literature reviews and case reports/series in pregnancy, and it again is reported to be similar to the nonpregnant population. About 80% of pregnant patients are either mild or asymptomatic, about 15% are severe, and only about 5% have critical illness by those guidelines.

There are a couple of studies that have come out in the last month. This first one was a cohort of 64 women from 12 hospitals in the United States. This was by Pierce-Williams and colleagues, published in *American Journal of Obstetrics and Gynecology* last month.¹¹ Of those 64 women, 15 of the 17 who delivered during the actual hospitalization delivered preterm, as one might expect if they're sick enough to be hospitalized. Several were on ventilators.

One patient had a cardiac arrest. Fortunately, there were no maternal or neonatal deaths. There were no cases of cardiomyopathy in those 64 women and there were no cases of vertical transmission of the disease to their babies.

Data from a large New York cohort were also published in the last month, by London and colleagues.¹² Approximately 26% of their symptomatic women required respiratory support. But this was during the time when they had started screening all

women who were presenting for labor and delivery, and the vast majority of those women who screened positive were asymptomatic.

Everyone has been asking about the fetal and neonatal consequences of COVID-19, particularly with reference to the risk of vertical transmission. There are a few case reports concerning possible vertical transmission although the overall risks are low. There was one case of a fetal demise, possibly secondary to COVID-19 infection. There have been placental abnormalities identified: changes concerning for vascular malperfusion which could result in intrauterine growth restriction and fetal death.

There is biological plausibility for vertical transmission as the ACE2 is one of the receptors for SARS-CoV-2, and we do know that this is expressed on fetal membranes, decidua, and placenta, as well as in fetal lung tissue.

So far we have not found evidence of SARS-CoV-2 in vaginal fluid, placenta, cord blood, amniotic fluid, or breast milk.

There were early data from China published in *Journal of the American Medical Association* concerning possible vertical transmission. These reports identified a couple of infants who were immunoglobulin (Ig) M-positive in the first few days of life—and remember, IgG crosses the placenta; IgM does not cross the placenta.^{13,14}

Interestingly, the neonates' COVID-19 RT-PCR tests were negative. The neonates were asymptomatic, and there were questions about the accuracy of the antibody assay that was being used.

However, in June 2020, a paper was published describing a cohort of 427 pregnant women, covering 194 OB units in the United Kingdom. Fifty-six percent of the pregnant women were black or other ethnicities, highlighting the race and ethnicity differences that we are seeing in COVID-19 infections. Sixty-nine percent of their COVID-positive cohort were overweight or obese; 41% were greater than or equal to the age of 35, which is considered advanced maternal age; and 34% had other comorbidities, which is significantly higher than the general population. Ten percent of the cohort required respiratory support and about 1% of the mothers died, a higher mortality rate than we have reported in the United States.

Interestingly, 5% of the 265 delivered infants—not all of this cohort are delivered yet—have tested positive for SARS-CoV-2 RNA, 6 of those within the first 12 hours of life. It is possible this is secondary to colonization at the time of delivery, either through cesarean or more likely through the vagina during a vaginal delivery. More information should be forthcoming regarding these 6 neonates.

Overall, while vertical transmission may be possible, we expect the incidence to be low.

At Johns Hopkins, we have 4 labor and delivery services. We have screened well over 1000 women who have presented to labor and delivery, and so far our overall RNA positive rate for SARS-CoV-2 is about 1%. However, at one of our hospitals which cares for a predominantly Hispanic population, our asymptomatic screen positive rate is 15% to 20%. The

asymptomatic screen positive rate is significantly higher in our Hispanic patients, compared to black, Caucasian, and Asian women.

We now have over 150 people who are COVID-19 positive who have delivered or are currently pregnant. We have had 1 infant test positive, but it was likely a result of transmission after delivery.

I did want to address briefly maternal morbidity and mortality and racial disparity. We know that overall, the maternal mortality rate in the United States is concerning high at 17.4 deaths per 100,000 live births. There are disparate outcomes in non-Hispanic black women compared to both Hispanic and non-Hispanic white women. In the early data from COVID-19 infections, these racial and ethnic discrepancies are again noted, with disproportionately higher rates and worse outcomes reported in the non-Hispanic black and Hispanic patients. Obviously, the reasons for this are multifactorial, but the discrepancy must be addressed. Obviously, there are many confounding factors to this, but I think it is a discrepancy that must be addressed.

Nancy Glass: Thank you, Dr Sheffield. Our next presenter is Rosemary Morgan, an assistant scientist at the Johns Hopkins Bloomberg School of Public Health, who has been leading us at the university in thinking about gender and gender analysis within the context of COVID-19.

Rosemary Morgan, PhD, Assistant Scientist at the Bloomberg School of Public Health

Thank you, Nancy, and welcome everyone. My name is Rosemary Morgan. I'm in the Department of International Health. I currently work on a Canadian Institute for Health Research-funded project, looking at the gender differences in the experience of COVID-19 in Canada, the United Kingdom, Hong Kong, and China. I'm also the director of the Sex and Gender Analysis Core of the U54 SCORE on sex and age differences in immunity to influenza.

We know from past experience that pandemics like COVID-19 are not gender neutral. It is important to think about how men and women, as well as people of other genders, are differently impacted.^{15,16} Some effects are immediate, while others are more long term. Additionally, there will be different health, social, and economic impacts.

While more men are impacted in the short term, more women will likely be impacted in the long term.^{15,17} When discussing gendered impacts of pandemics, we must also look at differences not only between but among men and women and people of other genders, by considering how gender intersects with other social stratifiers like race,¹⁸ as Jeanne mentioned when she was looking at pregnancy and COVID-19; age, as Sabra mentioned when she was showing age and sex-disaggregated data; as well as income, disability, sexual orientation, and others, to know how these intersect to create individual experiences of marginalization and vulnerability.

One point I want to emphasize here is that the response to the gendered impacts of COVID-19 is not a zero-sum game. Talking about how one group is impacted does not mean that the ways in which other groups are impacted are any less important. The evidence clearly shows that everyone is better off when societies themselves are more equitable.

We've heard from a number of speakers already that we do need more data. While we do have some sex-disaggregated data, they are lacking, which is particularly true of data from the beginning of the pandemic. This is surprising due to the initial reports of how men and women are differently affected. Many countries, while they were collecting these data, simply weren't reporting it for a very long time. After about 1000 cases, for example, countries just stopped reporting the sex-disaggregated data and instead combined the infection and mortality rates for men and women.

We're seeing changes as more and more calls come out for sex-disaggregated data. We cannot respond to something if we don't see it, and our current data are inadequate. Not only are there little sex-disaggregated data, there are even less data disaggregated by other social stratifiers like race and disability—not to mention intersectional data, looking at sex and race or disability combined. Having accurate data is so important; if something is not measured and counted, it's often treated as if it doesn't exist.

A lot of the focus on the gendered effects of COVID-19 have also left out an important dimension: how not all men and not all women and not all people of other genders will have the same experiences of marginalization and vulnerability due to the ways in which gender intersects with other social stratifiers.

I'd like to just take a moment to look at the intersection of gender and race here in the United States.

As of May 20th, nearly 23% of reported COVID-19 deaths were among African Americans, even though they make up roughly 13% of the US population.¹⁹ The reasons behind this are not biological but social and structural, and they do include systemic racism. Yes, more men are dying from COVID-19 and women are more affected by long-term social and economic impacts, but not all men and not all women are affected equally.

I want to touch just a little bit here on the effects on men. Sabra discussed biological differences for why more men are dying from COVID-19. The reasons for this, however, are both biological and behavioral. For example, when you look at sex-disaggregated differences in noncommunicable diseases, men engage in higher behavioral risk factors such as smoking and drinking.¹⁷

Globally, men engage in higher smoking and alcohol consumption than women. Such behavioral factors can lead to comorbidities such as diabetes or high blood pressure, which can increase the risk of complications following infection of COVID-19.

We saw similar patterns during the SARS and MERS outbreaks. While more women than men were infected by SARS in Hong Kong, the death rate was higher among men.

We also see that women are more proactive in seeking health care compared to men, which does affect prognosis. There is evidence to suggest that patients whose diagnosis are delayed are at greater risk of dying.

Turning now to the effects on women. While data show that more men are dying from COVID worldwide, we know from past pandemics that the long-term social and economic impacts tend to have a more negative effect on women.²⁰ After Ebola in Sierra Leone, for example, women returned to the health workforce at a much slower rate than men, often due to care responsibilities.

We know that health emergencies also distort local health agendas, with most local capacity and resources diverted to service immediate needs of the pandemic, impacting routine service provision, including maternal care, pregnancy and delivery, and sexual reproductive health services.^{21,22}

During the Ebola outbreak in Sierra Leone, the combination of a diversion of resources and women's fear of hospitals resulted in 3600 additional maternal, neonatal, and still births in 2014 and 2015.²³ This was a number that paralleled all the deaths as a result of the virus that year.

We expect to see, and are already seeing, similar patterns during COVID-19. In the United States, this is evident with pregnant women experiencing a shortage of obstetricians, alongside concerns over supply chain disruptions to contraception and whether abortion is considered an essential service at all.²⁴

As COVID continues to hit low- and middle-income countries, we are only likely to see these issues worsen.

So how are gender inequalities being magnified during the current pandemic? I'd like to highlight 3 key issues, although there's many more that I can talk about. These are women's dual responsibilities, lack of women's representation within leadership, and the risk among health workers.

Dual responsibilities: Evidence shows that the majority of child care and caring of elderly parents is still done by women, and the pandemic is only exacerbating this.²⁵ Women perform on average about 241 minutes of unpaid labor every day, which includes things like cooking, cleaning, and caring.²⁶ Compare this to men's 145 minutes of unpaid labor.

As schools and nurseries closed and remain close, and elderly and vulnerable relatives need more help with errands, women will continue to carry this extra burden.

What are the men saying about this? Well, *The New York Times* recently reported that nearly half of men say that they do most of the homeschooling, while only 3% of women agree with this.²⁷ In fact, 80% of mothers said that that they spent more time than men on homeschooling.

All of this has important implications for women's mental health, as well as gender equality within the workforce. There is a risk that this pandemic will undo a lot of the gender equality gains we've made in recent years.

What about leadership? Currently, women are not equally represented in decision-making roles responding to the COVID-19 pandemic.²⁸ The White House Coronavirus Task Force is over 90% men. In the United Kingdom, the original

task force was all men. And only 20% of the WHO Emergency Committee on COVID-19 are women.

Given women's frontline interaction with communities, it is concerning that women have not been fully incorporated into these decision-making bodies.²⁰ Women's socially prescribed care roles place them in a position to identify trends at the local level that might signal the start of an outbreak and thus improve global security.

When women have less decision-making power than men—either in households, or in the government—women's needs during an epidemic are less likely to be met.

Another key gender-related issue is in relation to health workers. Women make up 75% of the health and social care workforce worldwide.²⁹ However, they have been disproportionately infected by COVID-19. In some countries, COVID-19 infections among women are twice than among men.

In Italy, the United States, Spain, and Germany, a higher proportion of health care workers who are infected with COVID-19 are women.

So why are women health care workers infected more frequently? There are likely to be multiple reasons for this, but one I'd like to highlight here is in relation to personal protective equipment (PPE) and how PPE historically has been made for the male body or uses the male body as the norm.³⁰ There are increasing reports of women health care workers failing their respiratory mask fit tests, which show whether PPE is effective or not. Sometimes health care workers don't have equipment at all, which makes them more vulnerable to infection.

We know that the viral load that one is exposed to affects the seriousness of infection, so workers in health facilities are more likely to be exposed to higher viral loads. Health care workers, including nurses, which are predominantly women, must have adequate protection.

Much attention on the gendered effects of COVID-19 has been focused on men and women. However, we must not forget that gender is not binary and nor should our response to it be. Gender minorities across the globe are being negatively impacted by the pandemic and the response to it.

In an effort to maintain social distancing, some governments have instigated gender-based rules which dictate which days of the week men and women are allowed to go outside. This has had negative impacts on transgender men and women, who are already extremely marginalized.³¹ Coronavirus disease 2019 has also caused a delay in gender-confirmation surgeries, which is likely to have severe mental health implications on the transgender community.³²

Many of us who study gender and health systems, particularly health systems in fragile and conflict-affected states, speak about the need to “build back better”³³, i.e. to build structures and responses which take into account gender and other inequities and respond to them accordingly. How can we expect to have equitable outcomes if the structures and processes in which we ourselves work are inequitable?

We currently have an opportunity to shine light on the inequalities within our societies and the structures in which we live and work.¹⁶ We can also ensure that our emergency

preparedness response and plans are gender responsive and consider the specific needs and vulnerabilities between and among women, men, and people of other genders. We have an opportunity now to build back better. Thank you.

Nancy Glass: Great. Thank you, Dr Morgan. Another excellent presentation. I now have the honor to introduce Dr Michele Decker.

Michele Decker, ScD, MPH, Associate Professor at Johns Hopkins Bloomberg School of Public Health in the Department of Population, Family and Reproductive Health

I'm going to build on the foundation that Dr Morgan laid out and really extend discussion on that social impact piece to discuss the social and economic impact of the virus and also some of the mitigation measures—how this can differentially affect women and men, and critically, how it can impact women's safety and risk for violence.

Globally, there are 2 leading forms of violence against women. Intimate partner violence (IPV) is a pattern of physical violence. Sexual violence (SV), stalking by a current or former partner, affects approximately 1 in 3 women in her lifetime. Sexual violence is defined as nonconsensual sexual contact through force, coercion, or other measures. It is essential to address women's safety within the broader lens of women's health. While all genders experience violence, women are consistently at the highest risk for severe partner violence, including partner violence homicide and SV by any perpetrator. This evidence base is more robust for cisgender women, though emergent data suggest that transgender women similarly suffer violence disproportionately. There are also racial/ethnic disparities in the burden of IPV/SV, with African American women in particularly disproportionately affected—the very communities most affected by COVID-19. These epidemics of gender-based violence, and their implications for women's morbidity and mortality, form a critical part of the backdrop to what women are experiencing during the COVID-19 pandemic.

The discussion on COVID-19 amplifying risk for gender-based violence is really well founded. The combination of isolation with an abusive partner coupled with social and economic disruption presents a host of risks for women's safety.

First, we must consider this situation within the broader gendered economic context, meaning the gender wage gap that persists both in the United States and globally. When we add additional dimensions such as race/ethnicity, that wage gap can become even greater. This wage gap means that the impact of any economic disruption, including COVID-19, will be amplified for women, where there is less of an economic buffer with which to create options. For those experiencing IPV, the wage gap in the background coupled with economic disruption can amplify dependence on an abusive partner, leaving women with less leverage with which to create additional options in situations of abuse.

The social and economic disruption features of the COVID-19 epidemic have been observed in other humanitarian crises and can amplify stress and enable conflict. Economic insecurity through a job loss, a furlough, a layoff, lack of work within the informal economy, a fear of job loss in the future, or fear of economic insecurity in the future can amplify stress and conflict and erode resilience. All of these features can create and extend risk for IPV/SV.

Stay-at-home orders and restrictions on movement can create more time at home with potential abusers which can create risk for violence. Where alcohol or firearms are also part of the home environment, coupled with the stress of the pandemic, risk for violence and risk for severe violence can increase even further. Stay-at-home orders also reduce opportunity to leave home to create space from a partner who may be abusive. Even some of the most mundane daily activities like going to work, taking children to school, or going out for groceries can be used strategically by women in danger to create space where tension and risk for conflict and violence exist. The natural movements of other individuals who might otherwise visit the home or interrupt a potential conflict are similarly inaccessible with restrictions on movement. So these natural buffers and opportunities for conflict de-escalation and potentially IPV de-escalation have been tremendously disrupted by restrictions on movement.

Partners who use violence may also be engaging in additional abuse tactics specific to COVID-19, in that abusive partners may be taking advantage of stay-at-home orders, and more limited access to public spaces and transport, to exert more power or control. Controlling movement, controlling mobility, and controlling access to transportation, can all become tools to manipulate those stay-at-home orders to exert additional power and control. Other examples include refusing to purchase needed cleaning and health supplies, not sharing information about the virus, or sharing misinformation, amplifying fear intentionally, and preventing access to health services and medications. These context-specific forms of abuse are ones that we have seen all over the world in other types of scenarios. Around HIV, around sexual and reproductive health, where there is control within the relationship around access to preventive measures or manipulation of stigma or misinformation. There's a great concern that this is happening as well for COVID.

Against that backdrop around amplified risk, there's also a disruption to accessing support services. Where there are limitations on privacy within the home, where partners are ever-present within the home, contacting service providers safely and privately becomes increasingly challenging. There is concern right now for forgone health services and health care due to fear of COVID-related health risk to themselves, their children, or other family members. This may also be true for partner violence survivors who may not be coming forward for emergency services or other types of care.

Changes to the service delivery infrastructure can also present challenges to learning about and connecting with IPV/SV support services. The closure of many in-person services, including IPV/SV outreach supports, can also create risk and

make it more difficult to connect to care. When operational, health clinics and educational spaces are critical points of connection for violence-related screenings, referrals, and access to resource information. When those services are not operating as regular, that flow of information, screening, and referral is disrupted, and we are not as able to access people who may be at risk for IPV/SV or who may be in need of support services.

The news media have focused heavily on IPV crisis call volume of late, and this is an important metric to monitor. I do want to remind us that it is actually a tricky indicator—in that, in some places the concern is for *increased* call volume and other places the concern is for *decreased* call volume, which may reflect gaps in knowledge of services, as well as closures of those referral sites that make people aware of the supports that are available. Anecdotally within Baltimore City, there is a concern for decreases in call volume to IPV crisis supports, yet this is coupled with an increase in severity of violence among those individuals coming forward for services. Severity, forgone care, and unmet needs all must be considered when we interpret changes to indicators such as call volume to crisis hotlines.

What are some of the support needs for IPV survivors right now? There is a lot of discussion in the news media about shelter for IPV survivors. I want to take this moment to clarify that shelter is an important part of this picture, but it is not the only piece. Shelter often functions as a very last resort for those experiencing IPV and for those experiencing particularly severe IPV. It may actually not be one of the most fundamental or immediate needs for all women at risk. I want to encourage us to consider some of the other needs, which include economic supports for basic needs. This can reduce dependence on potential abusers and give people that sense of stability that they can then extend to their families and children around meeting basic needs—and by that I mean food and other types of fundamental basic needs. While IPV shelter is often necessary in especially severe cases, it would be shortsighted to focus only there, and we do not want to risk overlooking other essential support that are less disruptive for women and their families.

There is a critical need for discreet and accessible support services, particularly psychosocial support for counseling and support. In many parts of the world, even pre-COVID, we are starting to see an uptake of texting-based systems around survivor support. Sometimes it can lower the barrier to entry. Even the difference between speaking out loud on the phone and texting allows a little bit more anonymity. The texting option is even more where auditory privacy is not possible due to some of the stay-at-home orders that we just discussed.

I'll turn next to safety planning, which is a cornerstone of IPV prevention and response. It's a personalized, practical plan to stay safe and cope with abuse—either while in a relationship, making a plan to leave, or after leaving—and laying out the steps that can be taken to preserve safety, given their own individual priorities and needs. Safety planning is a core competency for support services, including national domestic violence hotline and all of the local crisis hotlines. It is important to note that this process can also help to mitigate the added

stress of COVID-19 when we consider some of the ways in which we can reduce stress and meet support needs, even in this time of crisis.

New innovations have showcased how technology can be leveraged for safety planning. The myPlan safety decision-aid app developed and evaluated by Dr Nancy Glass over the past decade is an app-based system that helps people identify and make decisions about safety in abusive relationships and can help friends and family who may be experiencing abuse. This tool has been found to improve safety planning and safety preparedness, and reduce IPV in some settings. More recently, it was adapted and tested in a low- and middle-income setting in Nairobi, Kenya. The tool takes stock of users' personal safety priorities and preferences and generates a tailored, personalized plan for safety that can be completed individually and anonymously. In the Nairobi example, lay professionals (community health volunteers) implemented the myPlan app with women. So, this is a tool that is flexible and can be administered over the phone or in person or completely anonymously online through the web interface or via the app itself on a smart phone. There is a real opportunity for expanding this resource in the COVID era because it is providing that information, anonymous access to resources, and safety planning, without the risks of being overheard or other types of auditory privacy issues.

I want to close with action steps that can be undertaken by national and local leadership in the COVID-19 response. It is clear that local and national responses to COVID-19 have an imperative to address the safety issues that are underlying for women in their communities and amplified in the COVID era. One immediately actionable step is simply helping connect survivors with services. Given what is suspected about the increased risk of violence, COVID-19 response sites including testing sites, food, and emergency supply distribution sites should at a minimum provide information on IPV/SV supports alongside other referrals and information to basic services. Helping survivors learn about services and normalizing that service use is a core function for public health and public service professionals and is something that can be readily and rapidly integrated into a COVID-19 response. Having the information at hand in nonjudgmental and nonstigmatizing language allows survivors to make decisions on their own about when and how to contact IPV/SV support services. The universal approach, "In case you or anybody you know might need this information," is an effective way to get information out about IPV/SV and normalize use of services.

The national domestic violence hotline (1-800-799-7233) provides connection to local support services. There's an online chat option (thehotline.org) and there's also an SMS line system (1-866-331-9474), which can further support accessibility and discretion in accessing care.

Nancy Glass: Thank you, Dr Decker. Moving to our last presentation. Let me introduce my colleague, Dr Phyllis Sharps.

**Phyllis Sharps, PhD, RN, FAAN, Professor,
Associate Dean for Community Programs
and Initiatives and Elsie Lawler Endowed
Chair for the Johns Hopkins University
School of Nursing**

Good morning. The one thing about being last is that you get to summarize everything that people said that was in your presentation.

When we talk about domestic abuse, we're talking about a pattern of behavior an intimate partner uses to control the other partner in the relationship. So, the abuser attempts to have power and dominate the other one.

You will also hear people talk about it as "domestic violence," "intimate partner violence," "domestic abuse," and "relationship abuse." I will use primarily "domestic" and "intimate partner violence" as it is the relationship between 2 people in an intimate relationship.

As you have heard before, there are many forms of violence. There is physical violence, SV, emotional violence, stalking, reproductive, and financial abuse.

When we look at families in Baltimore, the things that have been designed to mitigate violence also increases the household stress; for example if a partner—regardless of which partner—needs to have isolation or to be in quarantine.

Baltimore is a city that has pockets of poverty and people living in high-density housing, often with limited number of rooms and bathroom facilities. So just doing that—isolating someone or having a private space in the home—can be challenging and increase the stress as well, especially for an abused partner.

As for physical distancing, there are high rates of unemployment. Since March 14, more than 400,000 claims of unemployment benefits have been filed. And as we have clearly seen and come to appreciate, often it is communities of color that are employed in essential jobs: nursing assistants, housekeeping, facilities, truck drivers, delivery, and checkout cashiers in stores. So, these people, even if they need to stay at home, often don't have the option; it's a decision between working or staying at home and caring for your family.

Although this is a presentation on women's health, we have children at home who may be living in a situation where there is violence and are not able to at least escape child maltreatment and abuse a few hours a day while they attend school or to be away from other resources they can access while in schools.

As we've heard from Dr Morgan, women are most often caregivers. We know that culturally in communities of color, families are not necessarily putting elder members in nursing homes—although that may be a blessing given what we are learning about nursing homes. But it increases responsibility for caring for individuals, if there is a COVID-positive person in a household, as well as responsibility for child care and the additional burden of trying to do some aspect of homeschooling.

And as we have heard, women are often—and particularly women of color—employed in essential jobs. Many of these

essential jobs that women hold are more secure than perhaps some of the jobs those in which their male partner may have been employed, and so she may be working and her partner may not be working. That causes status inequality and increases the risk for violence in the home.

We should also understand that COVID-19 does not trigger abuse. But if the pattern was there already, then it is likely to exacerbate the pattern of abuse. The abuser will use the stress created by COVID-19 to further control and use more abusive tactics against a partner. We should be clear that generally, if the pattern was not there before, losing a job or staying at home is not suddenly going to turn someone into an abusive partner.

What we have learned from other pandemics like Ebola and other natural disasters like the earthquake in Haiti, is that people living in high-density areas are at increased risk for domestic violence and there are increased domestic violence calls to helping agencies. At the same time, as we see this happening in Baltimore, a lot of effort is being directed at mitigating the pandemic and not as much attention to its social consequences, such as domestic violence in the home.

There are not many statistics about what is happening at home. Lifebridge, a major insurance company in the Baltimore region, has reported that there were 70% fewer calls to their services early on in the pandemic, but that doesn't mean that domestic violence has gone away. It's more likely that women are afraid to call, are not able to call, or are prevented from calling or from or leaving their homes to access other resources.

Also, as we heard earlier, both partners are at home. If you're in a small home or don't have enough rooms or places to be private, it's much harder to make phone calls and abusers may have control of technologies that could be used. From data gathered from hotline calls, the calls are shorter often frantic, or aborted.

The Able Foundation did a recent report of digital technology access and Internet in Baltimore.³⁴ They used a sample of 33 urban cities; Baltimore was number 29 and thus near the bottom of the list, and Baltimore is not necessarily the poorest city. But there are other cities that have done much better in getting Internet accessibility and access to devices. This digital divide is also impacting people's resources or access to resources when much of what is available is through apps online and other digital resources. This poses a challenge for families that don't have access to the Internet or to digital devices.

The other context, and it becomes very salient as we are in this critical juncture with police, is where women may have in the past reluctantly called the police for help, women of color (and particularly African American women) are now afraid to call the police. They understand that reporting a male partner (particularly if he's an African American man) means he's likely to be mistreated at the hands of the police.

Of course there is existing bias and stigma toward any African American woman who calls the police, as well as immigrant women who fear being reported to immigration authorities.

Often in my work at the House of Blues Maryland I hear women talk about, even before the pandemic, how they didn't

want to call because they didn't want to be responsible for the mistreatment of their partner. Basically, they just wanted the abuse to stop. So this is a very difficult dilemma insofar as reaching out for other resources to help or staying in a violent relationship. African American women are keenly aware that resource entities and agencies are not necessarily going to provide the help they seek.

So I think for those of us that are providers or in helping professions, when we assess for safety, we need to continue to assess not only safety in terms of COVID-19 but also safety in terms of partner violence issues and safety in the home.

There are at least 5 shelters in the Baltimore area that are available and providing both shelter space and outreach services. One of the things that we've done in our community centers is to not only have internet resources available but telephone numbers, because if a person can get to a phone, they may be able to call in for help.

Nancy Glass: Thank you, Dr Sharps. We have now completed the presentations from our panelists and we do have some questions that have already come in.

Let me ask the first question of Dr Klein. Early in your presentation, a question came in related to information—if there's any information at this point—about COVID-19 and intersex variations.

Sabra Klein: That's an excellent question. To the anonymous attendee as well as Nancy, there are no data pertaining to this. I think this speaks to broader lack of data, not just in connection with COVID-19 but about how some of the biology associated with intersex impacts our immune system and our susceptibility to not only infectious diseases, but even autoimmune diseases.

I think there is an absolute need, not just in the context of this pandemic, to better understand both the immunological implications of intersex and even transgender. I think in these cases, there can be intersection between sex and gender. We know very little in terms of what that does to the immune system and biological susceptibility to infectious diseases.

So, thank you for that question. Let's keep pushing our policy-makers and funders to care more about these issues.

Nancy Glass: Thank you. So let me ask Dr Sheffield: Let's go back to the UK study. Do you have information about those who had vertical transmissions, if they were delivered by vaginal or C-section?

Jeanne Sheffield: There were 6 infants who tested positive for SARS-CoV-2 RNA within the first 12 hours of life and another 6 who were positive prior to discharge.

Of the 6 neonates who were diagnosed in the first 12 hours of life, 2 delivered vaginally and 4 delivered by cesarean. Three of the 4 women delivered by cesarean had not undergone labor.

Of the 6 neonates who were diagnosed in the first 12 hours of life, only 1 was admitted to the neonatal intensive care unit as compared to 5 of the 6 who were diagnosed after 12 hours of life. There was unfortunately limited data on the evaluation. There were also limited data on whether these babies were separated at birth from the parents, if these infants were breastfed and if these infants came into contact with another positive individual.

Nancy Glass: To follow-up with you with 1 question that came in really linked to that as well. Studies have indicated that for COVID-positive mothers, that the baby is separated from them at delivery and not allowed skin-to-skin contact nor initiation of breastfeeding. Is there research that you're aware of? Are you or any of our colleagues investigating that at this time?

Jeanne Sheffield: This is being investigated and has been probably the most controversial aspect that we have had to deal with in the COVID recommendations.

The initial recommendations were, if feasible, to separate the mother from the baby. The reason was that COVID-19 is found in the respiratory secretions so they were worried about the respiratory secretions of the mother infecting the neonate during the skin-to-skin contact with breastfeeding. COVID-19 was not found in the breast milk.

As you would expect, this has caused a lot of angst for parents and physicians. The WHO does not recommend separation due to the benefits outweighing the potential risk of transmission,

Many places here in the United States, including Johns Hopkins, have moved to a shared decision model—the potential risks of transmission are discussed with the parents as well as methods to decrease that transmission risk.

Our pediatricians counsel that the best way to make sure the baby is not going to get infected after delivery is to separate the mom and the child. However, in a shared-decision model they talk through pros and cons with the moms. If a mother chooses to have the baby stay with her, which is perfectly acceptable, then we teach the mothers how to safely care for the infant and ways to decrease the risk as much as possible.

Nancy Glass: Dr Morgan, there's a question related to behavioral differences in men and women in presenting for COVID-19 symptoms. Do we see some differences in their presentation to the health care services?

Rosemary Morgan: Thanks, Nancy. I think that is a great question. We are seeing—and

there are data and some studies coming out now—that show that there are distinct behavioral differences between men and women, both in terms of disease severity and risk of getting infected. Then, of course, these considerations are impacted by whether or not you take preventive measures. So that might be wearing a mask or washing your hands, for example.

With that question specifically, about coming to the health facility at a later date. We do know from evidence from other diseases like HIV/AIDS and Ebola, that men do tend to—and I'm generalizing here, of course it's not all men, but when we're looking at the aggregate level, men generally tend to present at health care facilities when they are sicker, so later on in their illness. This we think is really tied to masculinities and norms about what it means to be a man, that is, this idea of needing to be healthy, robust, and strong. Showing vulnerability, showing illness, and showing sickness goes against that.

Gender norms harm both men and women. If we have more equitable gender norms, we can break these cycles and know that for men, it's okay to be vulnerable and it's okay to present at the health facility earlier on, it's okay to take preventative measures like wearing a mask. You're not going to be seen like any less of a man if you do that.

Nancy Glass: Great, thank you. I have a question for Dr Sharps and Dr Decker that I think is very interesting. We do often times ask women to take on the responsibility of calling for help, seeking services, and planning for escape. We aren't necessarily holding or advocating for holding the abusive partner accountable.

Dr Sharps, you did an excellent job of talking about some of the hesitancy, especially for African American women, to reach out to police services. But what are other strategies that we can use to support and help men get the help that they need and reduce violence in the community?

Phyllis Sharps: In times past, which I think is one of the things that's coming out in the current environment is that there probably needs to be a differential response as police are called on domestic violence scenes and that it should not always be shoot and kill and ask questions later situation. If men had the opportunity to be directed to other resources that many shelters have, that would be important.

I think the other thing is that particularly women of color, are often reluctant to leave their homes and to go into shelter situations. So many of the shelters have outreach or other kinds

of services that they could avail themselves to, that would be helpful.

Michele Decker: Thanks. It's a great question.

Just to add, we typically think about a comprehensive response to violence against women as: (1) prevention, (2) survivors supports, and (3) accountability and access to justice—and not necessarily meaning only the criminal justice system. We often hear from survivors that their definition of justice is the peaceful end to violence and that the abusive person will not go on to abuse anyone else.

In a crisis situation, one of the first things that we can do is make sure that immediate needs are met and safety is improved, for women and for anyone experiencing violence. A comprehensive and sustainable response is absolutely going to include violence prevention, and we have some great examples of this as well-being achieved including through incremental changes in norms and behavior, and other methods of holding individuals accountable.

I will say that many of the batterer intervention programs typically involve meeting in small groups—so the disruptive features of the prevention and response environment are being felt there as well. And I completely agree with Dr Sharps; the conversations that we are having right now about the justice system really must include the needs of women and the ways in which police brutality has undermined women's ability to access the justice system including following IPV/SV.

We must keep women's health in the conversation when we talk about justice reform, both in COVID-19 era and beyond. That's another webinar—so I'll stop there.

Nancy Glass: We have just one more minute and I want to ask Dr Klein one last question related to men. What about men who have had prostatectomies? What do we know about that?

Sabra Klein: I have not seen data indicating or suggesting that does or does not impact COVID-19. But what could be relevant whether or not these men are on any type of hormone therapy following this type of surgical procedure. That's where we don't have a lot of evidence.

I gave you data from the Italian study. There are a number of studies ongoing. Not just thinking about hormone modulation in men, but also thinking about how both estrogen and progesterone could influence outcomes of COVID-19. There are trials going on around the United States administering either a form of estrogen and/or a form of progesterone to people with severe COVID-19.

Nancy Glass: I want to thank our panelists for the information they provided, a thoughtful conversation and responses to questions. We look forward to future leadership from our center here in Women's Health, Sex and Gender.

Editor's Note

Just as we were sending off this transcript for publication, we received the following message from Dr Margarethe Hochleitner, who established the Women's Health Center at Innsbruck Medical University in Austria, concerning her experience during the COVID pandemic. She says in part:

“... for research it was a good time because everybody had time to do research work but in the end this was only true for men, because in Austria we fell back to the 1960's; women did all the house-keeping, all the childcare, all the homeschooling and men had time to do scientific work. For me the most astonishing and really dramatic thing was women accepted this role silently: corona was a massive backlash in women's emancipation and of course with the same effects for all diversity-groups; they were not even mentioned in all these weeks. So, we have a lot to do in gender and diversity, but we will do it-hopefully.”

We share the same experiences all over the world! (MJL).

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