Week in Review: 29 June – 3 July 2020

BRIEF19

A daily review of covid-19 research and policy.

RESEARCH BRIEFING

Excess deaths associated with covid-19. A new study appearing in *JAMA Internal Medicine* indicates that excess deaths between March and May of this year were significantly greater than those directly attributed to covid-19, implying that the burden of disease is far higher than previously thought. The authors of this study attempted to quantify one aspect of the covid-19 disease burden by comparing the excess number of all-cause mortality over these few months as compared to previous years' data, and the known figures for Covid-19 related mortality over that time. All-cause mortality counts the number of total deaths in a particular area, without regard for the specific cause of death. The study looked at the number of deaths in the United States from March 1 to May 30, 2020 with those from previous years. The researchers found that there were approximately 122,000 excess deaths during the study period. This number is 28% higher than the official tally of 95,000 covid-19-related deaths in that time span. In New York City alone, the authors estimated 25,000 excess all-cause deaths occurred during this period versus the reported 18,000 that were attributed to covid-19. While the authors acknowledge the gap between all-cause deaths and covid-19 related deaths could be related to a variety of factors, they conclude that this large increase in all-cause mortality indicates a greater burden of disease due to the pandemic. They emphasize that monitoring excess mortality is a useful tool in evaluating the ongoing effects of the pandemic. *Abbreviated from Brief19 for 2 July 2020.* *–Michael Chary, MD PhD*

Higher viral loads found to be associated with worse covid-19 outcomes. A new study published in *Clinical Infectious Diseases*, an influential medical journal, found a correlation between patients with high SARS-CoV-2 viral loads and increased risks of dying. The study was conducted by researchers at Weill Cornell Medicine in New York and studied patients hospitalized between March 30 and April 30, 2020. The outcomes of the cases were followed through June 8, 2020. While the concept is intuitive, prior to this study there had not been definitive evidence linking higher viral loads to mortality. This is the first study in the United States to show a clear association. 678 patients diagnosed with laboratory-confirmed active SARS-CoV-2 infections were included in the study. Researchers broke down viral loads into three categories: low, medium, and high. There was a clear association between higher viral loads and in-hospital mortality. Among patients with high viral loads, 35% died. For those with medium viral loads, the mortality rate was 17.6%. Patients with low viral loads died only 6% of the time. The authors also assessed the likelihood that a patient would require intubation (mechanical ventilation). 29% of patients with high viral loads required mechanical ventilation intubated, versus 21% of those with medium viral loads, and 15% among those with low viral loads. The authors found an association between high viral loads and heart attacks, congestive heart failure, and kidney damage. The authors did not find any association between use of certain blood pressure medications (ACE-inhibitors or ARBs) and viral load. There was no association with viral load between racial or ethnic groups, suggesting that non-biological factors including "social determinants of health" played a role in differing outcomes in these groups. One limitation of this study was the fact that only a single sample for viral load measuring was taken at the time of hospital admission. Serial testing, in which multiple samples were drawn over time, would have permitted researchers to monitor the changes in viral loads over the course of the disease. The data from this study may be useful for clinicians as it provides confirmation that higher viral loads are associated with worse patient outcomes. For example, this may help physicians determine whether patients need hospitalization in borderline situations and guide hospital care. Knowledge of

a patient's viral load potentially improves upon simple yes/no results by providing a more nuanced view of a patient's disease status. Those with higher viral loads will likely need more frequent assessments and closer monitoring. In situations where hospitals are overwhelmed, quantitative testing may help with decisions on allocating scarce resources. Furthermore, it may help communicate the severity of a patient's infection to family members. *3 July 2020. –Eric Funk, MD*

A new covid-19 resource: The US Gender/Sex Covid-19 Data Tracker by the Harvard GenderSci Lab. On June 24, the Harvard GenderSci Lab released the US Gender/Sex Covid-19 Data Tracker, the most comprehensive collection of state-by-state statistics of covid-19 cases and deaths that have occurred in the United States broken down by sex. The tracker offers a time series of mortality rates that shows how the gap between female and male covid-19 deaths has evolved since mid-April.

Our data show that there is great variability in sex disparities in covid-19 case and mortality rates nationally. Overall, the differences have been narrowing over the eleven-week time period captured by the tracker. The GenderSci Lab findings emphasize that when popular covid-19 trackers and even government agencies exclusively report on covid-19 cases and death counts and percentages without breaking the numbers down by demographics, inaccurate conclusions are more likely: sex disparities in covid-19 should always be contextualized within existing gendered and sexed patterns of disease, aging, and mortality. In particular, data showing mortality rates is far more informative when reported and analyzed in relation to the underlying population's age distribution, sex ratio, as well as baseline mortality rates for women and men (which, even before covid-19, were higher for men). It should also be recognized that data refer to covid-19 among people categorized as female and male, and that the nuances of their sex-linked biology and gender identities are not known and therefore not captured by the tracker.

The main take-aways? It has been widely claimed that sex disparities in covid-19 are related to differences between female and male biology. In a New York Times Op-Ed "What's Really Behind the Gender Gap in Covid-19 Deaths?" the directors of the GenderSci Lab outlined problems with over-reliance on biological explanations only. The essay explains why it is critical to consider the role of gender and other variables in producing apparent sex-differences in covid-19 (and other) outcomes. In past respiratory pandemics, gender-segregated occupations and gender-related comorbidities have, through careful statistical analyses, fully explained similar apparent sex-differences in male to female mortality rates. The substantial variation across time and place captured by the tracker strongly suggests that gender and sex differences in covid-19 too are mediated by social context. However, the extent of these associations are not yet clear. To do so will require further analysis that takes into account both covid-19 data broken down by sex and gender as well as other potentially influential factors including existing medical comorbidities, occupation, race, and living environments. *Abbreviated from Brief19 for 1 July 2020.*

–Ann Caroline Danielsen and Tamara Rushovich for the Harvard GenderSci Lab

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Brief19 is a daily executive summary of covid-19-related medical research, news, and public policy. It was founded and created by frontline emergency medicine physicians with expertise in medical research critique, health policy, and public policy.