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BRIEF19

A daily review of covid-19 research and policy.

RESEARCH BRIEFING

Pre-existing conditions that contribute to mortality in covid-19. What we know.

Most people now understand that a number of pre-existing medical conditions can increase the likelihood that a person will develop serious or critical covid-19. However, just how strong the statistical associations are is less well described and appreciated.

A new systematic review and meta-analysis (SRMA) published in the medical journal *PLOS ONE* looked to estimate the strength of the associations of pre-existing comorbidities and covid-19 mortality. This was a review of the published literature from December 1, 2019 to July 9, 2020. Included studies were required to have at least two cohorts of hospitalized patients both with and without 11 pre-defined comorbidities and required that any included studies had data pertaining to mortality.

The 11 comorbidities chosen were cardiovascular diseases, hypertension, diabetes, congestive heart failure, cerebrovascular disease, chronic kidney disease, chronic liver disease, cancer, chronic obstructive pulmonary disease, asthma and HIV/AIDS. Of 253 papers identified, only 25 studies were included in this SRMA (which is not an unusually low yield for SRMAs). Those 25 studies captured the outcomes of a total of 484 patients with covid-19. When compared to patients without comorbidities, patients with covid-19 and chronic kidney disease were 3.25 times more likely to die (risk ratio (RR) = 3.25) were 2.25 times more likely to die (risk ratio [RR] 2.25). Other significant associations with death were found including cardiovascular disease (RR 2.25), diabetes (RR 1.48), congestive heart failure (RR 2.03), and cancer (RR 1.47).

That said, the studies did not assess the effect of advanced age as an independent risk factor for serious covid-19 or death, which appears to be the strongest single predictor of poor outcomes.

Although relatively few studies were included in this SRMA, the included studies had low publication bias (meaning that the studies were not all "positive studies," which often indicates cherry-picked data) and were of high quality with respect to their methodology. While this study does not necessarily change our understanding of covid-19, it is a helpful synthesis of the literature eight months into this historic pandemic, and reiterates the importance of tailored approaches when considering which covid-19 patients should be prioritized for admission to the hospital. Nevertheless, given how rapidly the literature is growing and evolving, it is likely that this systematic review is already up to two months out of date at the time of its publication yesterday.

—Joshua Niforatos, MD

POLICY BRIEFING

Operation Warp Speed becomes more transparent, but questions still remain.

A pair of researchers involved in Operation Warp Speed (OWS) penned an editorial in the *New England Journal of Medicine* published yesterday, exposing some of the inner workings of government's groundbreaking push to create and distribute a vaccine to fight the SARS-CoV-2 infection responsible for covid-19. Initially announced on May 15, 2020, OWS was a new partnership created between the Department of Defense, Department of Health and Human Services, and the private sector, and the medical community has been clamoring for more details about its progress and goals. Leadership within OWS is drawing upon experience from working for many high-level health organizations such as the National Institutes of Health (NIH) and is taking a page out of the Zika and Ebola response playbooks, but with even more ambitious initiatives.

In the article, the authors describe concrete steps being taken by OWS to develop and deploy hundreds of millions of vaccine doses to the American public by the middle of 2021. They discuss the four types of vaccine platforms which have been chosen as the basis for the vaccine candidates currently being investigated and note that they were chosen not only for their ability to be rapidly developed and manufactured, but also because these methods of immunization are generally known to be safe and effective. To encourage broader chances of success, OWS also plans to support two vaccine candidates in each of the four categories and will further delineate which candidate will best serve various at-risk populations as more data is obtained and becomes available.

Many critics of OWS have raised concerns that the project might forego safety for the sake of speed. The authors attempt to allay these fears by describing the "harmonized end-points" across all Phase 3 trials, as well as the steps that have been taken to give those trials as much time to progress as possible. This includes extensive investment in the infrastructure required to produce and distribute a vaccine as quickly as possible, including building the physical plants, vials, and retaining the workforce necessary to manufacture the eventual vaccines even before any single candidate is approved by the Food and Drug Administration. This will allow vaccine production to occur as soon as possible once a candidate's safety and efficacy are determined. The authors also note that OWS will continue to monitor the long-term safety of any vaccines produced by the project using comprehensive surveillance strategies.

Despite this cursory look into the workings of this extensive and expensive endeavor, it is unlikely to answer all of the questions outside experts will have, not least of which will be expected costs of the vaccine candidates. Other questions remain surrounding regulations imposed on more traditionally developed pharmaceuticals such as how patent protections and exclusivities will be applied.

—Jordan M. Warchol, MD, MPH