Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Association of Obesity With More Critical Illness in COVID-19

To the Editor: In follow-up to a recent major state-of-the-art review on obesity and outcomes in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (coronavirus disease 19 [COVID-19]),[1] we have additional data regarding the relationship of obesity with outcomes in patients with COVID-19. Clearly, obesity and metabolic syndrome affect both innate and adaptive immunity, leading to increased infection severity.[1,2]

This association is very important because current statistics indicate that three-fourths of the US population are either overweight or obese by body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) criteria, and currently over 42% meet criteria for obesity by a BMI of 30 kg/m^2 or greater. More alarmingly, currently over 9% of the US population meet criteria for severe or morbid obesity (class III obesity) by a BMI of 40 kg/m^2 or greater.[1,2] Certainly, many other countries across the globe are experiencing marked increases in the prevalence and severity of obesity,[1,2] which may be particularly problematic in COVID-19 and other such pandemics. We performed a rapid review and meta-analysis to evaluate whether obesity is associated with worse outcomes in patients with COVID-19.

The present study was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. We performed a comprehensive search in the MEDLINE and medRxiv.org databases for studies published between January 1, 2019, and May 31, 2020. The following key words were used for the search in different combinations: *coronavirus 2019*, *Covid-19*, *SARS-CoV2*, *obesity*, *body mass index*, and *outcomes*. Studies reporting the relationship between BMI (nonobese vs obese) and outcomes among hospitalized patients with COVID-19 were included for analysis. Three reviewers (A.S., A.G., A.R.) screened the study titles and abstracts for relevance, followed by full manuscript evaluation. The following data were collected from included studies: baseline characteristics, proportion of patients classified by BMI categories (<30 kg/m^2 vs >30 kg/m^2), and percentage of hospitalized patients. The primary outcome was critical illness (need for intensive care unit [ICU] admission, invasive mechanical ventilation [IMV], or mortality) as defined per individual study protocol. We used Cochrane Review Manager 5.3 (Cochrane Collaboration) for study analysis. Pooled odds ratios and 95% CIs were calculated using random-effects models and the Mantel-Haenszel method. Heterogeneity was assessed using the I^2 statistic. The initial search resulted in 266

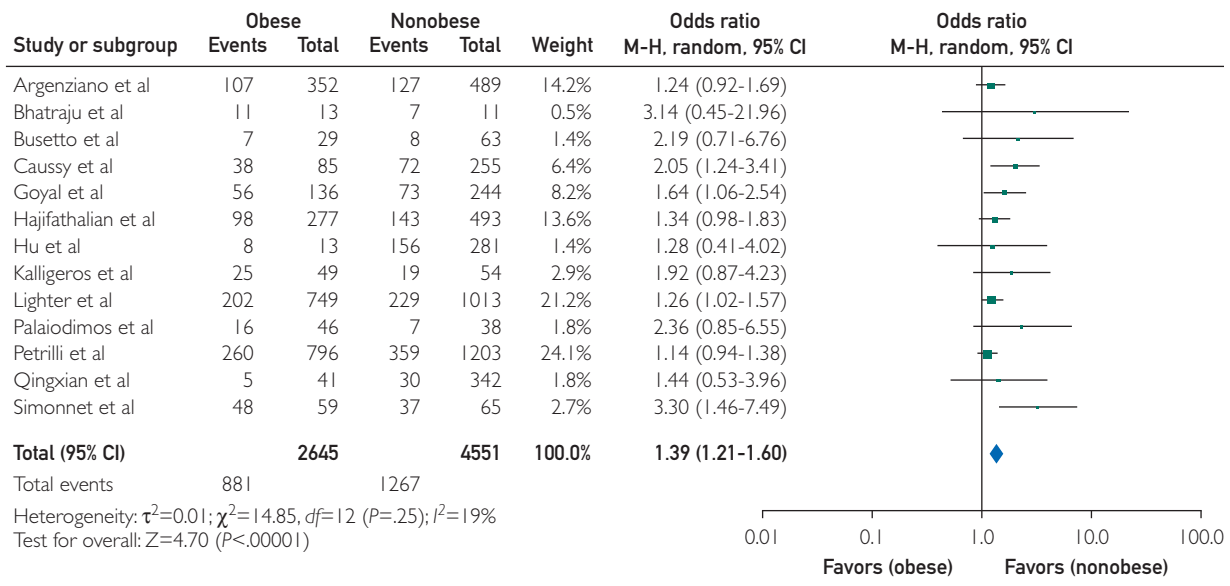

FIGURE. Forest plot comparing the odds of critical illness between obese (body mass index >30 kg/m^2) vs nonobese (body mass index <30 kg/m^2) patients hospitalized with coronavirus disease 19 infection. M-H = Mantel-Haenszel test.

studies, 13 of which (7196 patients) reported outcomes in patients with COVID-19 based on BMI.[3-15] Critical illness was defined as the need for ICU care or IMV or a composite of ICU care, IMV, hospice, or death. Pooled analysis revealed that obesity was associated with increased odds of critical illness among patients hospitalized with COVID-19 (odds ratio, 1.39; 95% CI, 1.21-1.60) (Figure). Low heterogeneity was evident across studies (I^2=19%) (Figure).

In this rapid review and meta-analysis, obesity was associated with a 39% increased risk of critical illness, defined by individual study protocol as ICU admission, need for IMV, or hospice admission or death. Considering the very high prevalence of obesity among adults in the United States and worldwide, and even severe obesity approaching nearly a tenth in US adults, this increased critical illness is a worrisome sign.[2]

Patients with obesity also have more endothelial dysfunction, as well as respiratory and renal diseases that could worsen COVID-19 outcomes. However, probably most importantly, COVID-19 coronavirus attaches to the angiotensin-converting enzyme 2 receptors in the lungs and organs.[1] Obese patients have insulin resistance and activation of the renin-angiotensin-aldosterone system.[1] The presence of angiotensin-converting enzyme 2 may enable the entry of SARS-CoV-2 into adipocytes, which makes adipose tissue an important viral reservoir.[1] Therefore, adipose tissue, which is more abundant in obesity, might also be infected by SARS-CoV-2 and allow spread to other organs, thus explaining the more severe COVID-19 disease in obesity.[1] The prevention of obesity in the first place, and especially its progression to more severe forms, is desperately needed for future pandemics, as well as for the primary and secondary prevention of diabetes mellitus and cardiovascular disease.[2] In this COVID-19 pandemic, clinicians should recognize the marked increased risks associated with obesity, and these patients need more aggressive triage and treatment.

Our study has several limitations. Because patient-level data were not available, the results in our study were not adjusted to baseline patient characteristics. Several studies analyzing the relationship between obesity and clinical outcomes have reported results after adjusting for different confounders. Because of differences in the variables used to adjust results in these studies, we have not performed the pooled analysis of those adjusted confidence intervals and odds ratios. Further, the studies did not have long-term follow-up data and most patients were still hospitalized without a definite outcome (ie, mortality), and thus caution should be exercised before extrapolation of our results to long-term outcomes.

Despite these study limitations, however, our data of a 39% increase in worse outcomes associated with obesity strongly supports the recent article in *Mayo Clinic Proceedings*.[1]

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Serious Illness Conversations

To the Editor: Discussing prognosis is an important but challenging aspect of clinical care with limited evidence to guide best practices. Lu et al[1] should be commended for their perspective article that proposes a three-stage protocol which may prove useful for providers and trainees who are leading goals of care conversations for patients with highly predictable prognoses, such as those who are hospitalized with irreversible multiorgan failure. However, we are concerned about the blanket application of this protocol to include the many cancer patients with high-risk disease but who may still be early in their clinical course. First, the protocol is built upon the disclosure of the patient's prognosis. But even when cancer is incurable there are often multiple lines of therapy available with variable chances of attaining a durable response, which makes it difficult even for oncologists to give an early prognosis that is both accurate and meaningfully specific.[2] Second, there is a significant number of cancer patients (likely 20% to 30%)[3,4] who are not interested in hearing an estimate of their life expectancy; but this protocol offers no recourse for this when it occurs. Finally, we agree that the protocol's emphasis on "negotiating" treatment options and requiring that the provider "make a recommendation" for advance care planning may be appropriate for situations where there is a firm short-term prognosis based on severe illness and declining trajectory. However, for patients without a firm short-term prognosis, this approach potentially conflicts with the palliative care guidelines published by the National Comprehensive Cancer Network (v1.2020)[5] which make a distinction between cancer which has longer versus shorter life expectancy, with only the latter being an indication for the provider to actively recommend de-escalation of code status. For those cancer patients who have serious illness but also a reasonable chance of living with it for many years, it is better to reinforce their sense of control by assisting them in making informed decisions for advanced care planning (ie, naming a health