

COVID-19 Vaccination and Obesity: Optimism and Challenges

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Researchers have speculated that vaccines to prevent coronavirus disease 2019 (COVID-19) may be less effective for individuals with obesity, a major risk factor for mortality and morbidity from COVID-19. Initial results from the Pfizer-BioNTech and Moderna COVID-19 vaccine trials, though limited by inadequate power to compare subgroups and incomplete stratification of high-risk groups, appear to have similar efficacy among individuals with and without obesity. Careful follow-up in placebo-controlled studies is required to generate data on long-term vaccine immunogenicity, particularly in high-risk groups. Subsequent analyses should stratify safety and efficacy results by each class of obesity. Speculation about variable effectiveness of COVID-19 vaccines in obesity likely increases vaccine hesitancy among individuals with obesity, who face not only a higher risk of severe outcomes from COVID-19 but also weight stigma, which reduces health care engagement at baseline. Clinical and public health messaging must be data driven, transparent, and sensitive to these biological and sociological vulnerabilities.

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Obesity is a major risk factor for morbidity and mortality for patients with coronavirus disease 2019 (COVID-19) (1-3). The effectiveness of COVID-19 vaccines in people with obesity and other high-risk conditions is a critical issue. Researchers have hypothesized that these vaccines would offer reduced protection in those with obesity, drawing on evidence of immune cell dysregulation and alterations in inflammatory signaling pathways (1). Lay media amplified these concerns. We synthesize now-available vaccine trial data, biological evidence of vaccine immunogenicity in obesity, and sociological implications of speculation on vaccine acceptance and health care engagement in the COVID-19 pandemic.

Phase 3 trial results for the Pfizer-BioNTech and Moderna COVID-19 vaccines, authorized for emergency use in December 2020 by the United States Food and Drug Administration (FDA), clarify short-term safety and efficacy (4,5). Obesity (BMI ≥ 30 kg/m²) and severe obesity (BMI ≥ 40 kg/m²) were included among subgroups for analysis in the Pfizer-BioNTech and Moderna studies, respectively. In the Pfizer-BioNTech trial, vaccine efficacy (from 7 days after the second dose) was 95.4% in people with obesity (95% CI: 86.0-99.1%) and 94.8% in people without obesity (95% CI: 87.4%-98.3%) in preventing symptomatic COVID-19 compared with placebo (4). In the Moderna trial, vaccine efficacy (from 14 days after the second dose) was 94.1% overall (95% CI: 89.3%-96.8%) and 91.2% in the subgroup with severe obesity (95% CI: 32.0%-98.9%) (5,6). A post hoc analysis of Moderna vaccine data similarly demonstrated comparable efficacy in participants with obesity (95.8%, 95% CI: 82.6%-99.0%) versus no high-risk comorbidity (94.0%, 95% CI: 83.5%-97.8%) (6). The conspicuous absence of Class 1 (BMI 30.0-34.9 kg/m²) and Class 2 obesity (BMI 35.0-39.9 kg/m²) from the Moderna trial design may be explained by the delayed identification of obesity as a high-risk condition for severe outcomes

from COVID-19; the United States Centers for Disease Control and Prevention did not add this range of obesity to its list of risk factors for severe COVID-19 until late June 2020 (3). Though these two large-scale, randomized, placebo-controlled studies were not powered to detect differences between subgroups, available efficacy data appear similar across subgroups to include age, race/ethnicity, and comorbidities. These findings inspire optimism and assuage concerns about differential vaccine protectiveness in obesity at least across the median follow-up period of 2 months in the two published reports.

The longer-term effectiveness of COVID-19 vaccines in general—and specifically in those with obesity—remains uncertain. Earlier in the COVID-19 pandemic, researchers questioned whether immune memory from COVID-19 vaccines would wane faster in people with obesity (1). In some studies, obesity has been correlated with impaired immunogenicity following hepatitis B, tetanus, rabies, and influenza A vaccination, as measured by suboptimal antibody titers over time (1,7). The first several months of trial data suggest comparably strong short-term vaccine efficacy with higher and lower BMI. We do not yet know how persistent the protection will be for either group nor whether long-term protection will wane more for one group than the other. We also do not yet understand whether antibody titers accurately predict waning immunity or increased susceptibility to severe disease. These are a few of many uncertainties that support the need for thoughtful research questions and ongoing placebo-controlled vaccine trials, which include strata for each class of obesity. The results have implications for post-vaccine risk stratification and public health strategy.

Unfortunately, speculation about COVID-19 vaccine efficacy in people with obesity may cause unintended harm. The benefits of vaccination depend not only on vaccine efficacy but also on public engagement

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with and trust in vaccination efforts. A recent national survey of US adults reveals a stronger reluctance to choose a COVID-19 vaccine the lower its anticipated effectiveness and/or the lower its anticipated protection duration (8). A similar pattern occurs for influenza vaccines: in all demographic groups, perception of reduced vaccine effectiveness is associated with reduced vaccine uptake (9). Although currently available data on COVID-19 vaccine willingness do not report responses by obesity/BMI, the risk of vaccine hesitancy specifically among individuals with obesity is concerning for several reasons. Most obviously, obesity is one of the most significant risk factors for severe outcomes from COVID-19 (1-3). Moreover, weight bias is prevalent and impacts how people with obesity engage with the health care system. Weight stigma, a set of prejudicial attitudes on the basis of body size, marginalizes people with obesity and poses a “threat to quality health care” (10). Importantly, weight stigma is associated with reduced use of recommended preventive care (e.g., breast and gynecologic cancer screening examinations) (2,10).

Multiple academic and lay media sources have publicized speculation that available COVID-19 vaccines may work less well for people with obesity. Pending clear data, this is a perilous message for vaccine acceptance in any group. It is especially hazardous for a group at increased biologic vulnerability for worse outcomes and for whom the medical community has not consistently engendered trust. A headline that questions vaccine efficacy in obesity, even if it reaches only a fraction of the 42.4% of adults with obesity in the United States, sows lasting doubt for millions.

Ultimately, the public health impact of vaccines against COVID-19 relies on both vaccine efficacy and vaccine acceptance. The initial data published by the Pfizer-BioNTech and Moderna groups offer optimism: multiple vaccines with a high level of safety and efficacy for the general population and high-risk subgroups, including individuals with obesity. Careful follow-up in placebo-controlled studies is required to generate data on long-term vaccine immunogenicity, particularly in obesity and other high-risk conditions. For this reason, subsequent analyses of ongoing placebo-controlled vaccine trials must stratify by class of obesity and be appropriately powered to detect any differences in efficacy

across subgroups. As this research is pursued, and as vaccines become available to millions across the world, clinical and public health messaging should clearly delineate the current limits of our knowledge. Speculation about variable effectiveness of COVID-19 vaccines in the absence of robust data must consider the trade-offs of increased vaccine hesitancy. Groups who have faced historical marginalization and stigma in health care, including individuals with obesity, deserve attention in efforts to build trust in current COVID-19 vaccination efforts and beyond. **O**

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