

First, I want to acknowledge that today is the 19th anniversary of 9/11 and the memory of all who lost their lives that day.

Today I have chosen 4 articles. The first is an RCT on steroids for patients infected with SARS-CoV-2. The results only saw benefit among patients older than 60 years of age (mortality 46.6% vs. 61.9%). This is a much smaller trial than RECOVERY and I do not think this changes current guidance. The second article highlights that infection with SARS-CoV-2 has increased in younger adults and underscore the importance of education and prevention measures in this age group especially with underlying medical conditions [especially morbid obesity and DM]. This article also shows the value of using large deidentified datasets to answer important questions rapidly. The third article looked at community and close contact exposures associated with COVID-19 among symptomatic adults. They found people who tested positive were more likely to have reported dining at a restaurant in the two weeks before they became ill. The last article is from colleagues in Boston who reported that nosocomial COVID-19 was rare during the height of the pandemic in Boston.

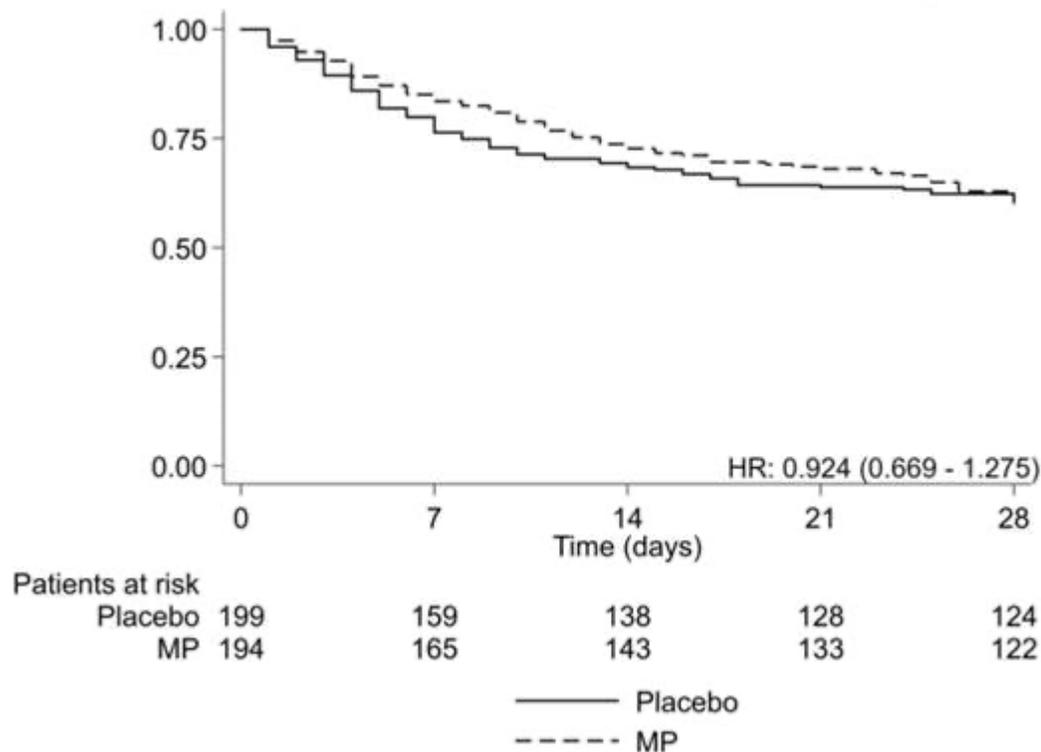
Have a great weekend

Ed

**Methylprednisolone as Adjunctive Therapy for Patients Hospitalized With COVID-19 (Metcovid):
A Randomised, Double-Blind, Phase IIb, Placebo-Controlled Trial**

Clin Infect Dis published online September 9, 2020

This clinical trial evaluated the efficacy of a 5-day course of methylprednisolone (MP 0.5 mg/kg/day) at reducing the mortality of patients hospitalized with COVID-19. This was a double-blind placebo-control trial. 416 patients randomized, 393 (mean age, 55 years) completed follow-up: 194 in the MP arm and 199 in the placebo arm. No patient received remdesivir, anti-IL-6, or anti-IL-1 agents. The most common comorbidities were diabetes, hypertension, and alcohol use disorder. One third of patients were mechanically ventilated. Mortality at day 28 was 37.1% in the MP group and 38.2% in the placebo group. No between-group differences were apparent in mortality at 7 days or 14 days, viral clearance in the upper airways, or need for mechanical ventilation at 7 days. In a subgroup analysis, day-28 mortality was significantly lower with MP versus placebo among patients older than 60 years of age (46.6% vs. 61.9%). Below is survival rates-time randomization to death.



Comment: The findings in this trial contrasts with the RECOVERY Trial. There are several different methodologic differences between the two trials. The duration of treatment and steroid agent were different. Mortality rates were much higher than reported in the US. Sample size was small in this report compared to the RECOVERY Trial: in current publication MP was given to 194 patients compared to over 2000 receiving dexamethasone in the RECOVERY Trial with over 4000 in control group, in addition, some patients received MP late in their course. In my opinion absent additional data, dexamethasone remains appropriate for patients infected with SARS-CoV-2 who require supplemental oxygen especially patients who require mechanical ventilation.

Clinical Outcomes in Young US Adults Hospitalized With COVID-19

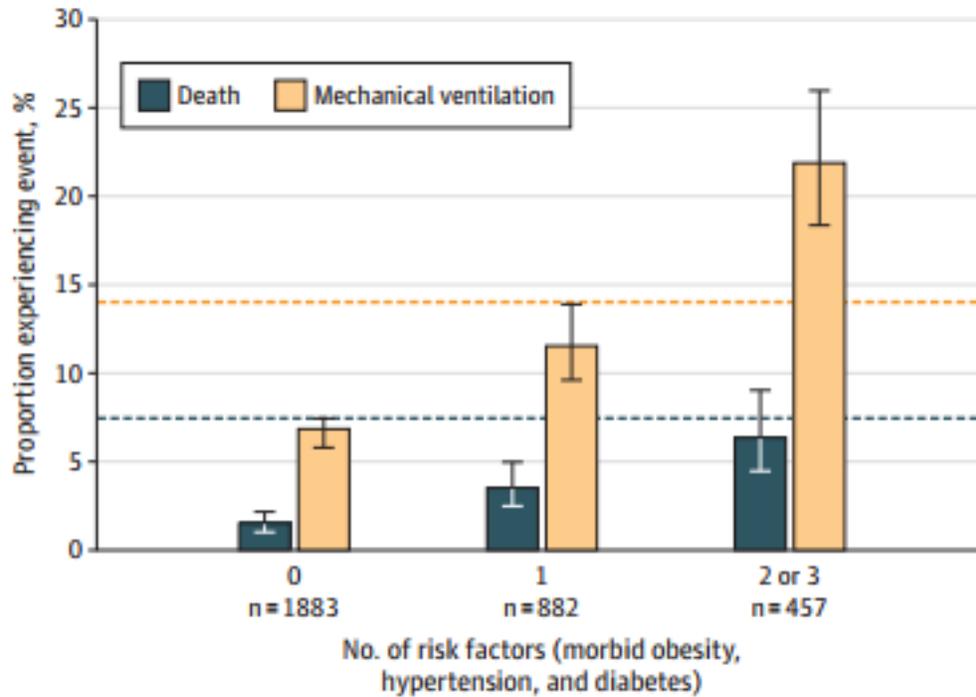
JAMA Intern Med published online September 9, 2020

This study was conducted by investigators in Boston which identified and collected data on 3,222 young adults ages 18 to 34 diagnosed with COVID-19 and discharged from the hospital from Apr 1 to Jun 30. Data was collected and deidentified by Premier and transferred and analyzed at Brigham and Women's Hospital. Young adults age 18 to 34 years with the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) code U07.1 (COVID-19, virus identified) were identified for analysis.

During hospitalization, 684 of these young adult patients (21%) required intensive care, 331 (10%) required mechanical ventilation, and 88 (2.7%) died. Morbid obesity was present in 140 patients (41%) who died or required mechanical ventilation. More than half of the patients requiring hospitalization were black or Hispanic. Using multivariable logistics regression analysis, the researchers determined that morbid obesity (adjusted odds ratio [aOR], 2.30; 95% confidence interval [CI], 1.77 to 2.98; $P < .001$), hypertension (aOR, 2.36; 95% CI, 1.79 to 3.12; $P < .001$), and male sex (aOR, 1.53; 95% CI, 1.20 to 1.95; $P = .001$) were associated with greater risk of death or mechanical ventilation. Diabetes was

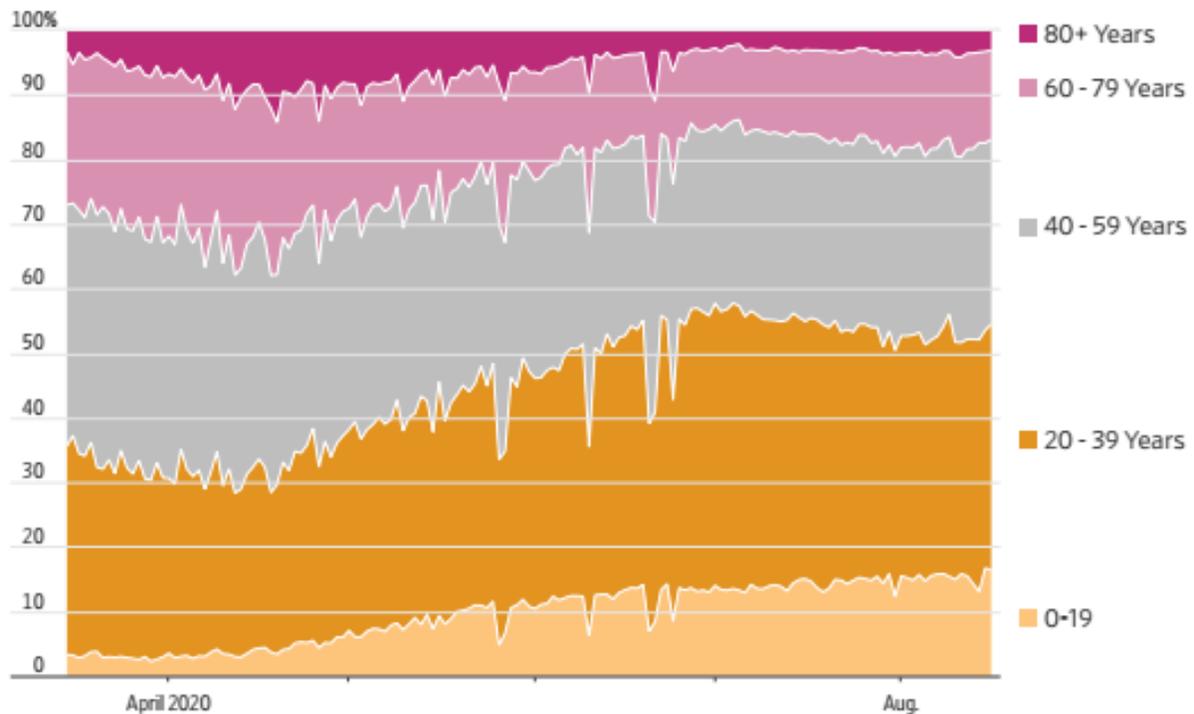
associated with increased risk of these outcomes on univariable analysis but did not reach statistical significance after adjustment (aOR, 1.31; 95% CI, 0.99 to 1.73; $P = .06$). Odds of death or mechanical ventilation did not vary significantly with race or ethnicity. Patients with multiple risk factors (morbid obesity, hypertension, and diabetes) faced risks similar to 8,862 middle-aged adults (ages 35 to 64) without these conditions.

Figure. Death and Mechanical Ventilation in Young Adults With and Without Morbid Obesity, Hypertension, and Diabetes



Comment: This study included defining COVID-19 infection and comorbidities by ICD-10 codes, which may be subject to misclassification, however, given the sharply rising rates of COVID-19 infection in young adults, these findings underscore the importance of education and prevention measures in this age group especially with underlying medical conditions. The graph below published in the WSJ from CDC highlights new COVID-19 cases over time by age.

New confirmed Covid-19 cases, by age



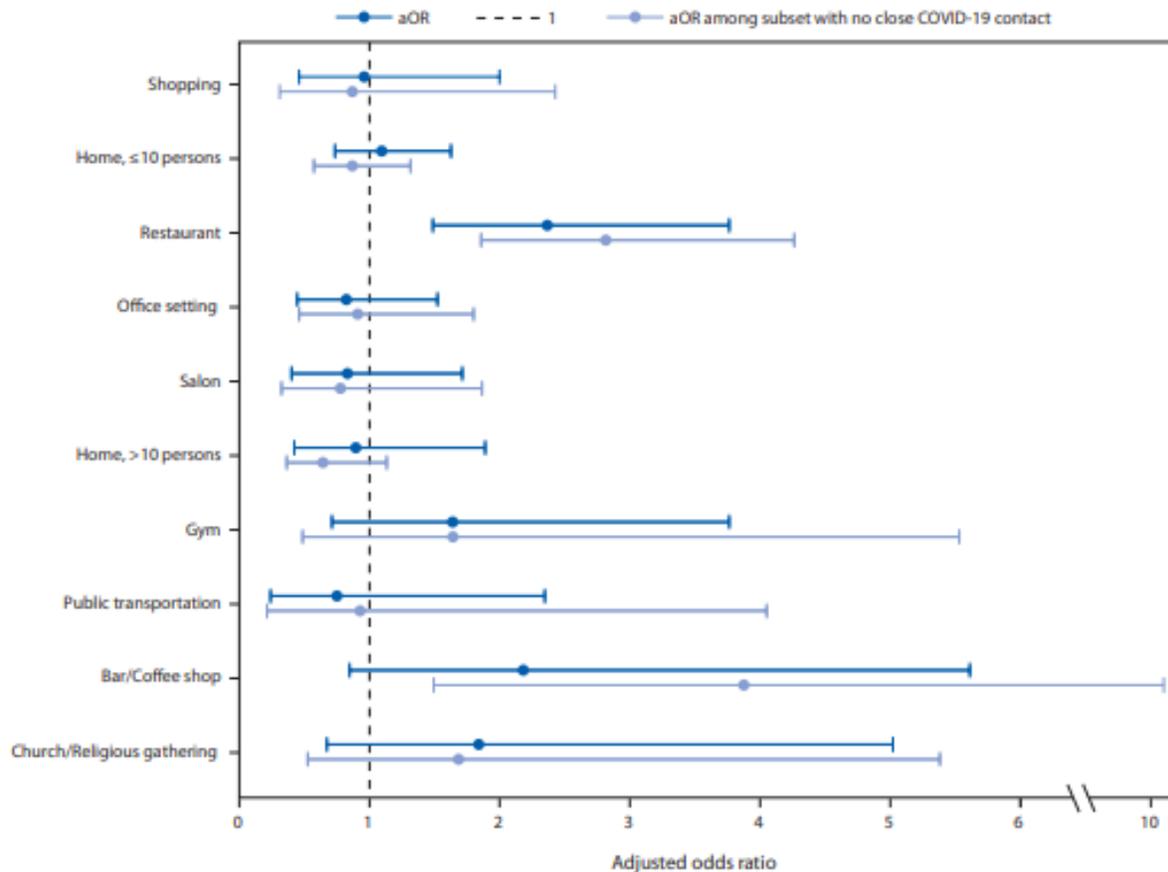
Note: Date is by reported date; cases where age unknown are not included.
Source: Centers for Disease Control and Prevention

Community and Close Contact Exposures Associated with COVID-19 Among Symptomatic Adults ≥ 18 Years in 11 Outpatient Health Care Facilities — United States, July 2020

MMWR 2020; 69:1258-1264

This study included data on 314 adults who were tested for Covid-19 in July because they were experiencing symptoms: 154 tested positive and 160 tested negative. The tests were administered at 11 different health care facilities across 10 US states: California, Colorado, Maryland, Massachusetts, Minnesota, North Carolina, Ohio, Tennessee, Utah and Washington. Investigators took a close look at whether patients were wearing masks and various activities in the community, including whether they recently dined at a restaurant, hung out a bar or went to a gym.

42% of the adults who tested positive reported having close contact with at least one person known to have Covid-19, compared with 14% of those who tested negative -- and most of the close contacts, 51%, were family members [c/w many other studies]. The investigators also found that 71% of the adults with Covid-19 and 74% of those who tested negative reported always using a face covering while in public. There were no significant differences between those who tested positive versus negative when it came to shopping, gathering with fewer than 10 people in a home, going to an office, going to a gym, going to a salon, using public transportation or attending religious gatherings, according to the study [some had wide CI]. However, people who tested positive were more likely to have reported dining at a restaurant in the two weeks before they became ill.



Comment: One of the major limitations of the study was assessing dining at a restaurant did not distinguish between indoor versus outdoor dining. Reports of exposures in restaurants have been linked to ventilation. Direction, ventilation, and intensity of airflow might affect virus transmission, even if social distancing measures and mask use are implemented according to current guidance. In addition, masks cannot be effectively worn while eating and drinking, whereas shopping and numerous other indoor activities do not preclude mask use. Implementing safe practices to reduce exposures to SARS-CoV-2 during on-site eating and drinking should be considered to protect customers, employees, and communities [Sound public health limitations in bars, taverns, and restaurants include limiting alcohol service to accompanying food orders, not allowing hours of operation to extend into the late nights, and limiting occupancy levels and table arrangements to those levels which allow for social distancing.]. CDC guidance for restaurants and bars by risk:

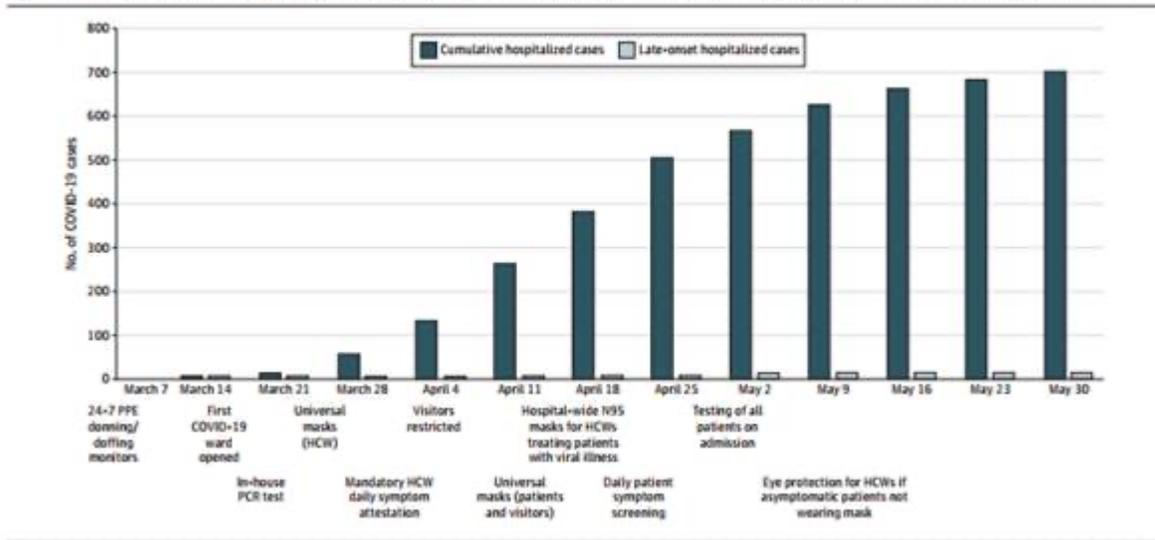
- **Lowest risk:** Food service limited to drive-through, delivery, takeout and curbside pickup.
- **More risk:** On-site dining limited to outdoor seating. Seating capacity reduced to allow tables to be spaced at least 6 feet apart.
- **Even more risk:** On-site dining with both indoor and outdoor seating. Seating capacity reduced to allow tables to be spaced at least 6 feet apart.
- **Highest risk:** On-site dining with both indoor and outdoor seating. Seating capacity not reduced, and tables not spaced at least 6 feet apart.

Incidence of Nosocomial COVID-19 in Patients Hospitalized at a Large US Academic Medical Center
 JAMA Netw Open published online September 9, 2020

The objective was to assess the incidence of COVID-19 among patients hospitalized at a large US academic medical center in Boston. This cohort study included all patients admitted to between March 7 and May 30, 2020. Follow-up occurred through June 17, 2020. Medical records for all patients who first tested positive for SARS-CoV-2 by PCR on hospital day 3 or later or within 14 days of discharge were reviewed. A robust infection prevention program was implemented that included dedicated COVID-19 units with airborne infection isolation rooms, personal protective equipment in accordance with CDC recommendations, personal protective equipment donning and doffing monitors, universal masking, restriction of visitors, and liberal PCR testing of symptomatic and asymptomatic patients.

Over the 12-week period, 9149 patients (mean [SD] age, 46.1 [26.4] years; median [IQR] age, 51 years [30-67 years]; 5243 female [57.3%]) were admitted to the hospital, for whom 7394 SARS-CoV-2 PCR tests were performed; 697 COVID-19 cases were confirmed, translating into 8656 days of COVID-19-related care. Twelve of the 697 hospitalized patients with COVID-19 (1.7%) first tested positive on hospital day 3 or later (median, 4 days; range, 3-15 days). Of these, only 1 case was deemed to be hospital acquired, most likely from a presymptomatic spouse who was visiting daily and diagnosed with COVID-19 before visitor restrictions and masking were implemented. Among 8370 patients with non-COVID-19-related hospitalizations discharged through June 17, 11 (0.1%) tested positive within 14 days (median time to diagnosis, 6 days; range, 1-14 days). Only 1 case was deemed likely to be hospital acquired, but with no known exposures.

Figure. Cumulative Number of Total and Late-Onset Hospitalized Coronavirus Disease 2019 (COVID-19) Cases by Week and Associated With Infection Control Policies



Comment: It is reassuring that nosocomial COVID-19 was rare during the height of the pandemic in the Boston area if strict infection preventions practices are implemented. The authors admit it is difficult to know the source of infection in every case. Viral genome sequencing could potentially have helped in some cases, such as for the patient exposed to both a COVID-positive staff member and spouse; however, this was not available. There may have been additional undetected nosocomial cases related to false-negative PCR test, but I doubt this changes the overall conclusions of this publication. This same group of Investigators published another important article reviewed in last Monday's Briefing which showed only 1 clear case of SARS-CoV-2 transmission from an HCW to a patient (<1%). This event occurred prior to implementation of universal masking for patients and providers. Both of these articles

demonstrate the importance of a robust infection prevention and control team that executes on the science.