

TGIF 😊

I start with a correction from the Briefing last Tuesday.

Under COVID-19 News the most talked about topic concerns when and if we should start offering a third dose or booster.

Under Journal Review I start with three articles all published Wednesday in MMWR. The first studied the VE in nursing home residents. The second study evaluated the duration of mRNA VE against COVID-19 hospitalization in patients 18 years and older. The last in this series is a study from New York which estimated rates of new adult COVID-19 infections and hospitalizations by vaccine status from May 3 to Jul 25. The next article looks at a study on the use of CP in the outpatient setting to reduce progression and hospitalizations. [Hint – another negative study] The last article looks at the use of HCQ, RDV, and dexamethasone from February 2020 to February 2021.

I hope everyone has a relaxing weekend

Ed

## **Correction**

Thanks to Robert Atmar – I used a double negative in my comments in the N Engl J Med article about adolescent vaccination – see correction thus, it was unlikely that these events would ~~not~~ be detected in this trial.

Sorry for the oversight.

## **COVID-19 News**

### **COVID-19 Booster Shots**

The U.S. said on Wednesday that it is prepared to offer booster shots for all Americans who received two doses of Pfizer or Moderna's COVID-19 vaccine beginning the week of Sept. 20 and starting eight months after an individual's second dose.

HHS said "the individuals who were fully vaccinated earliest in the vaccination rollout" will likely be the first ones who are eligible for boosters, including nursing homes residents, healthcare workers and Americans  $\geq 65$ .

HHS said its plan is contingent upon FDA approval for COVID-19 boosters, which hasn't been granted yet. The agency amended the emergency use authorizations for Pfizer's and Moderna's COVID-19 vaccines Aug. 12<sup>th</sup>, authorizing a third dose in immunocompromised people, but not yet for the rest of the population. We are still waiting for a decision on the J&J vaccine.

Early data from Israel suggests a booster shot of Pfizer Covid-19 vaccine can significantly improve immunity in those aged 60 and above, as the U.S. and other countries plan additional doses to increase protection against the delta variant. The booster shot reduced the risk of infection in the 60-plus age group by 86% and against severe infection by 92%, according to this observational study from Israel.

[this is during the delta surge] Early data from CDC show that 74 percent of breakthrough cases are among adults 65 or older.

**Comment:** While I do believe some vaccinated people may benefit from a third dose over the next few months, let us not forget the 30% who have not been vaccinated at all! What is clear – the only way to contain and eventually end the pandemic is for more people to get vaccinated.

## Journal Review

### **Effectiveness of Pfizer-BioNTech and Moderna Vaccines in Preventing SARS-CoV-2 Infection Among Nursing Home Residents Before and During Widespread Circulation of the SARS-CoV-2 B.1.617.2 (Delta) Variant — National Healthcare Safety Network, March 1–August 1, 2021**

MMWR published online August 18, 2021

Of all nursing home residents, 14.7% were unvaccinated, 49.6% were fully vaccinated with Pfizer, 25.3% were vaccinated with Moderna, and 10.4% had "other" vaccination status.

Before Delta predominated, data from 17,407 reports from 3,862 nursing homes showed that adjusted VE was 74.7%. But after, it fell to 53.1%, according to 85,593 reports from 14,917 facilities.

Pre-Delta, adjusted VE against infection among those fully vaccinated (vs unvaccinated) was 74.7% for either mRNA vaccine, 74.2% for Pfizer, and 74.7% for Moderna. After the emergence of Delta, adjusted VE against infection among fully vaccinated residents was 53.1% for either vaccine, 52.4% for Pfizer, and 50.6% for Moderna.

A total of 6,879 COVID-19 asymptomatic and symptomatic infections were identified, 30.7% of them in unvaccinated residents, 37.8% in those fully vaccinated with Pfizer, 18.9% in those fully vaccinated with Moderna. [Remember the over 80% were vaccinated]

**Comment:** Two doses of mRNA vaccines were 74.7% effective against infection among nursing home residents early in the vaccination program (March-May 2021). During June-July 2021, when Delta variant circulation predominated, effectiveness declined significantly to 53.1%. This analysis could not control for potential confounders, such as age, presence of underlying health conditions, or the influence of previous SARS-CoV-2 infections on VE. Vaccination dates were not available and time since vaccination could not be measured to evaluate potential waning of protection. Last, staff member vaccination data were not sufficiently complete to assess as a potential confounder. I am astonished that staff members were not required to be vaccinated given they are working with a highly vulnerable population. Additional doses of COVID-19 vaccine might be considered for nursing home and long-term care facility residents along with mandating staff to be vaccinated. Wednesday the White House announced a requirement mandating all nursing home workers be vaccinated against COVID-19 as a condition for receiving federal funds.

### **Sustained Effectiveness of Pfizer-BioNTech and Moderna Vaccines Against COVID-19 Associated Hospitalizations Among Adults — United States, March-July 2021**

MMWR published online August 18, 2021

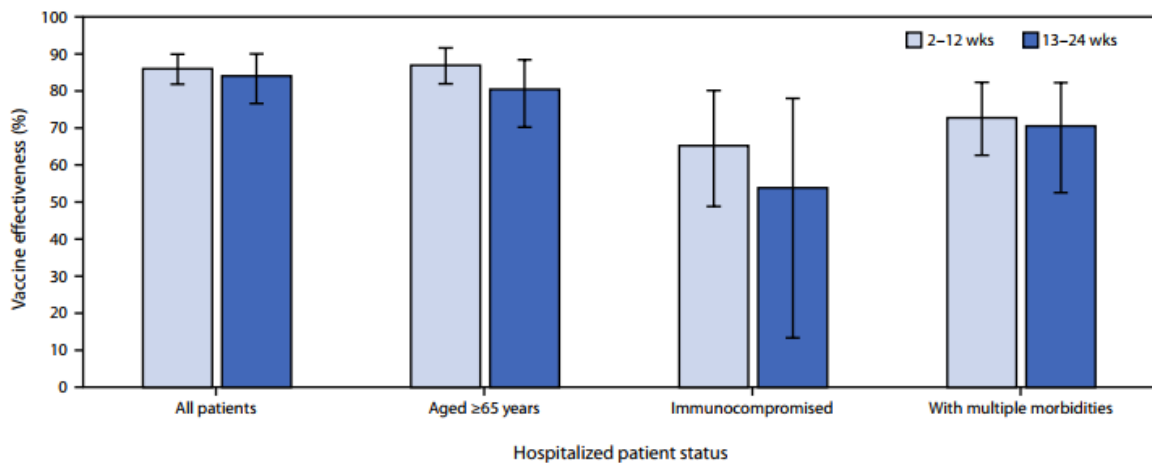
This study evaluated the duration of mRNA VE against COVID-19 hospitalization in patients 18 years and older. Of 3,089 hospitalized adults (1,194 COVID-19 patients and 1,895 uninfected control patients),

11.8% of case-patients and 52.1% of controls had received two doses of the Pfizer or Moderna vaccine 14 days or more before symptom onset. 21.1% were classified as immunocompromised.

Two to 12 weeks after the second dose, VE against SARS-CoV-2 hospitalization was 86% overall, but only 63% in immunocompromised patients versus 90% in those with healthy immune systems. After 13 to 24 weeks, VE was 84%, a nonsignificant change. Whole-genome sequencing of specimens from 454 case patients showed that 53.3% were caused by the Alpha variant, and 16.3% were due to Delta.

Among patients with symptom onset from March to May, before Delta became predominant, VE against hospitalization was 87%, decreasing to 84% in June and July. The results were consistent among subgroups of participants at high risk of severe COVID-19, including older adults, those with at least three underlying illnesses, and those with compromised immune systems.

**FIGURE 2. Sustained vaccine effectiveness\* against COVID-19 among hospitalized adults, by patient status<sup>†,§</sup> and interval since vaccination — 21 medical centers in 18 states,<sup>¶</sup> March–July 2021**



**Comment:** Effectiveness of mRNA vaccines against COVID-19–associated hospitalization was sustained over this 24-week period, including among groups at higher risk for severe COVID-19. However as expected VE was lower in immunocompromised persons. Additional analyses with longer duration of follow-up since vaccination are needed. Ongoing monitoring is needed as new SARS-CoV-2 variants emerge. Delta did emerge at the end of this evaluation but only identified in 16% of isolates.

### **New COVID-19 Cases and Hospitalizations Among Adults, by Vaccination Status — New York, May 3–July 25, 2021**

MMWR published online August 18, 2021

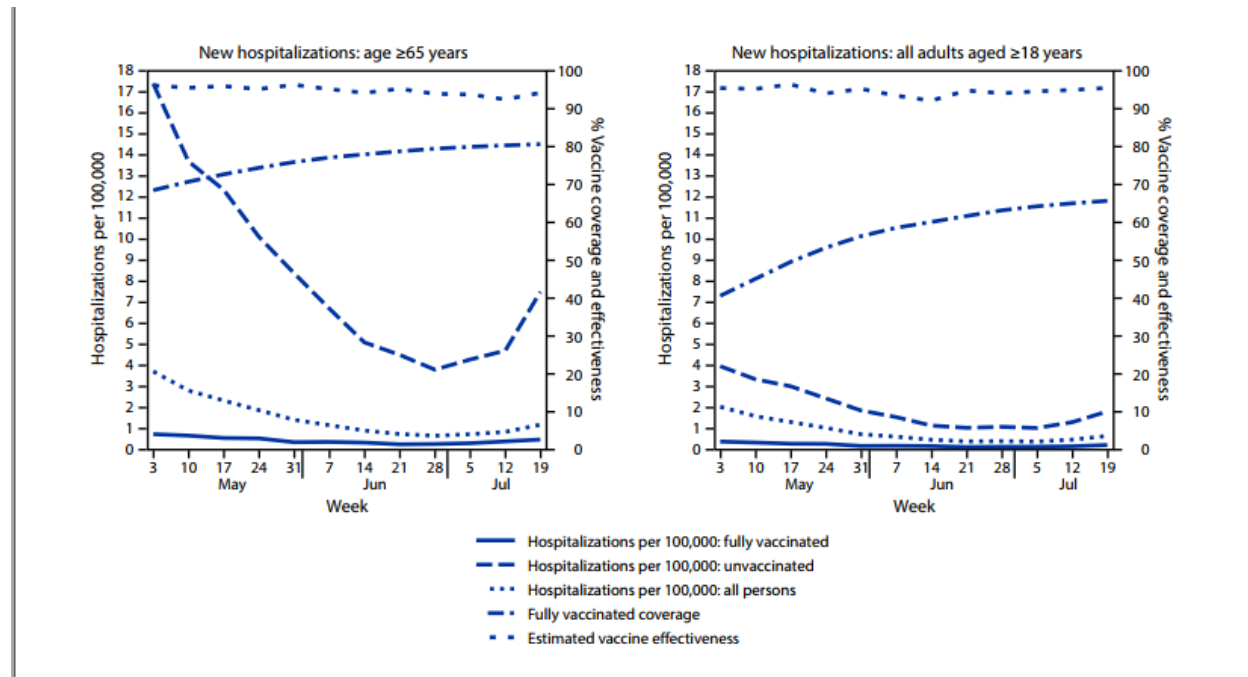
In this study the New York State DOH estimated rates of new adult COVID-19 infections and hospitalizations by vaccine status from May 3 to Jul 25. By the end of the study, 65.8% of adult New Yorkers were fully vaccinated, and 10.4% had received one dose. Of fully vaccinated adults, 51.3% had been given the Pfizer vaccine, 39.8% received Moderna, and 8.9% received J&J.

Over the study period, age-adjusted VE against COVID-related hospitalization was relatively steady, from 91.9% to 95.3%. But the VE against infection fell from 91.7% to 79.8%. Weekly VE against infection dropped in all age-groups during the study, declining from 90.6% to 74.6% in adults 18 to 49 years, 93.5% to 83.4% for those 50 to 64, and 92.3% to 88.9% for those 65 and older.

By Jul 25, 1,271 fully vaccinated adults had been hospitalized with COVID-19 (0.17 per 100,000 person-days), versus 7,308 (2.03) among the unvaccinated. The ratio of hospitalizations to cases was lower among the fully vaccinated than among the unvaccinated (13.1 per 100 cases and 19.0, respectively).

The overall age adjusted VE against hospitalization ranged from 91.9% to 85.3% over the study period. VE against hospitalization stayed steady, at 90.8% to 97.5% for adults 18 to 49 years, 92.4% to 97.0% for those 50 to 64, and 92.3% to 96.1% for those 65 and older.

By the end of the study, 9,675 new infections occurred (1.31 per 100,000 person-days) in fully vaccinated adults, versus 38,505 (10.69) in the unvaccinated.



**Comment:** During May 3-July 25, 2021, the overall age-adjusted vaccine effectiveness against hospitalization in New York was relatively stable (91.9%-95.3%). The overall age-adjusted vaccine effectiveness against infection for all New York adults declined from 91.7% to 79.8% meaning as has been reported there have been vaccine breakthroughs, but vaccination is still remarkably effective against severe disease. In addition, VE against infection appears to have declined coinciding with a relaxation of public health social measures and increasing Delta variant. This analysis excluded partially vaccinated persons, to robustly assess VE for fully vaccinated compared with that of unvaccinated persons. The study did not estimate VE by vaccine product. Recent data in some locations show a clear increase in breakthrough rate in persons >65.

### Early Convalescent Plasma for High-Risk Outpatients with Covid-19

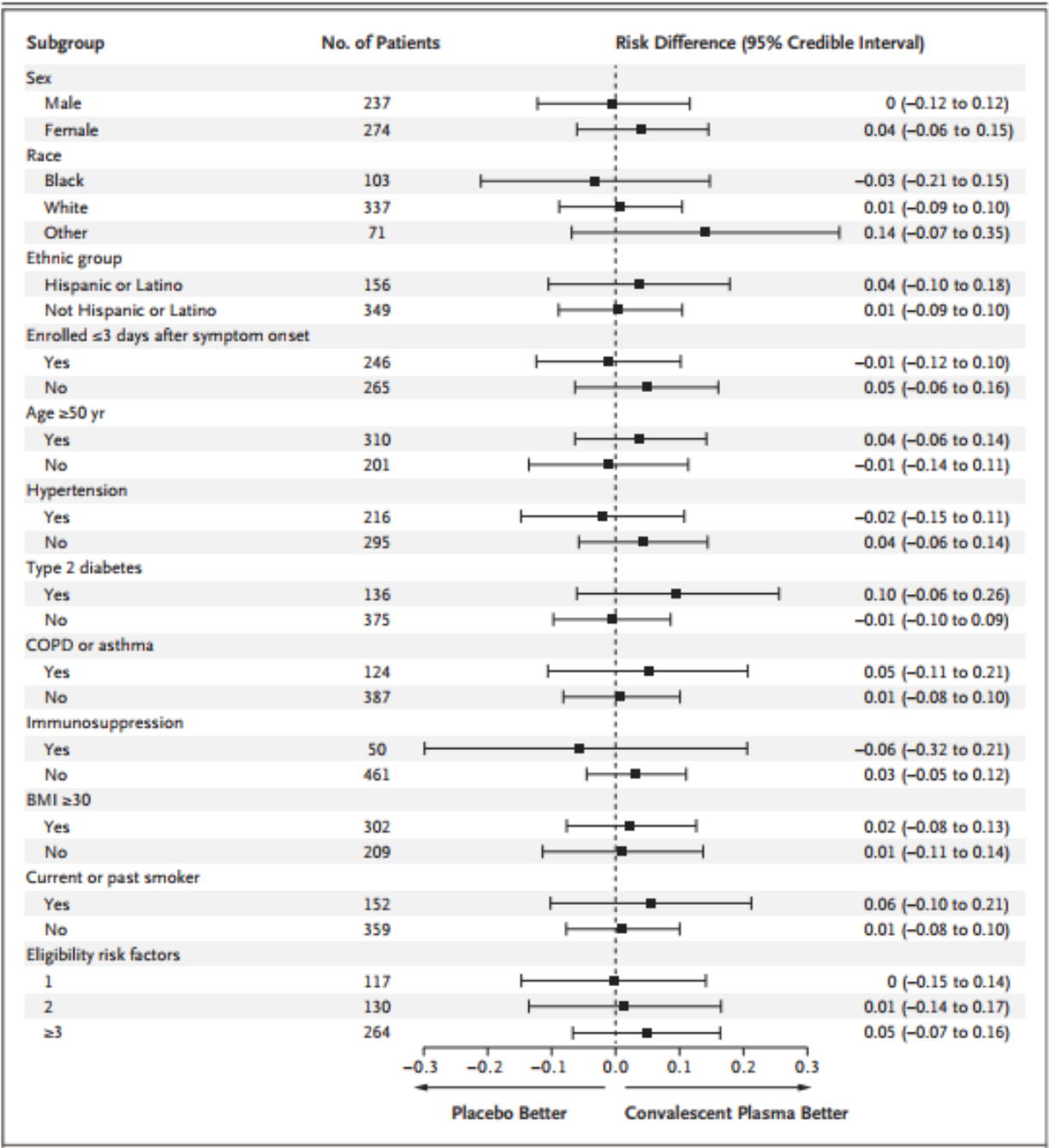
N Engl J Med published online August 18, 2021

DOI: [10.1056/NEJMoa2103784](https://doi.org/10.1056/NEJMoa2103784)

This is a randomized, multicenter, single-blind trial, in which patients who were being treated in an emergency department for Covid-19 symptoms were randomized to receive either one unit of high titer convalescent plasma (CP) against SARS-CoV-2 or placebo. All the patients were either 50 years of age or older or had one or more risk factors for disease progression. In addition, all the patients presented to

the emergency department within 7 days after symptom onset and were in stable condition for outpatient management. The primary outcome was disease progression within 15 days after randomization, which was a composite of hospital admission for any reason, seeking emergency or urgent care, or death without hospitalization. Secondary outcomes included the worst severity of illness on an 8-category ordinal scale, hospital-free days within 30 days after randomization, and death from any cause.

A total of 511 patients were enrolled in the trial (257 in the CP group and 254 in the placebo group). The median age of the patients was 54 years; the median symptom duration was 4 days. Disease progression occurred in 77 patients (30.0%) in the CP group and in 81 patients (31.9%) in the placebo group (p 0.68). Five patients in the plasma group and 1 patient in the placebo group died. Outcomes regarding worst illness severity and hospital-free days were similar in the two groups.



**Comment:** The results here are similar to those from three randomized, controlled trials involving hospitalized patients that showed no improvement in clinical outcome in those who received CP. The use of CP in this trial is like the use of monoclonal antibodies (MCA) in the outpatient setting. MCA has clearly shown a benefit in disease progression and hospitalizations. With the availability of MCA, I see very little justification for CP.

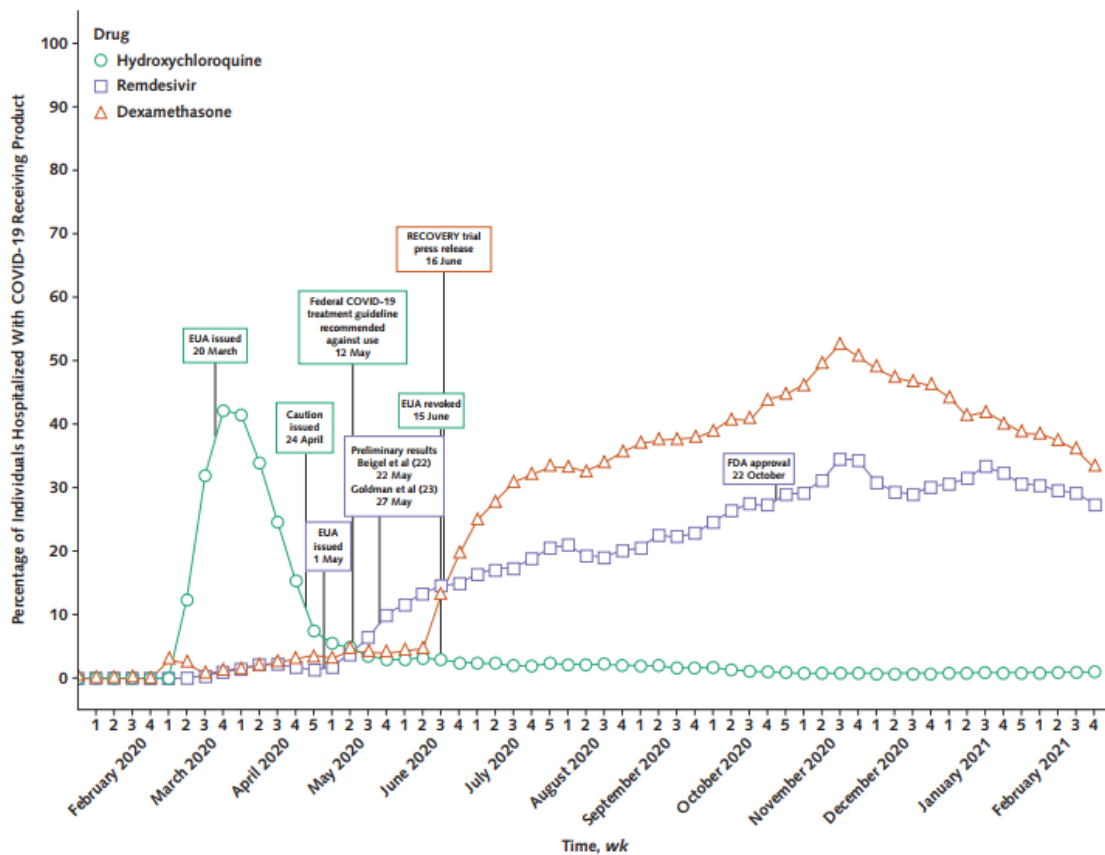
**Use of Hydroxychloroquine, Remdesivir, and Dexamethasone Among Adults Hospitalized With COVID-19 in the United States**

Ann Intern Med published online August 17, 2021

doi:10.7326/M21-0857

The authors used the National COVID Cohort Collaborative (N3C), a large, multicenter, longitudinal cohort, to characterize the use of hydroxychloroquine, remdesivir, and dexamethasone, overall as well as across individuals, health systems, and time. This is a retrospective cohort review of 43 health systems in the United States.

137,870 adults hospitalized between 1 February 2020 and 28 February 2021 with confirmed or suspected COVID-19 were included. 8754 (6.3%) received hydroxychloroquine, 29,272 (21.2%) remdesivir (RDV), and 53,909 (39.1%) dexamethasone during the study period. Since the release of results from the RECOVERY trial in mid-June, approximately 78% to 84% of people who have had invasive mechanical ventilation have received dexamethasone or other corticosteroids. The use of hydroxychloroquine increased during March 2020, peaking at 42%, and started declining by April 2020. By contrast, RDV and dexamethasone use gradually increased over the study period. Dexamethasone and RDV use varied substantially across health centers. See below.



**Comment:** As you can see there was brisk uptake and abandonment of hydroxychloroquine early in the pandemic and then increases in use of RDV and, to an even greater degree, dexamethasone. Dexamethasone, an evidence-based treatment of COVID-19 [AI from NIH], may be underused among persons not only on mechanical ventilation (MV), but especially in non MV patients who require oxygen. As many as one fifth of mechanically ventilated patients potentially eligible for dexamethasone did not receive it. The use of RDV and dexamethasone varied across health systems, suggesting variation in patient case mix, drug access, treatment protocols, and quality of care. I can understand the decreased

use of RDV as the science evolved, but I am perplexed about the use of dexamethasone. Most patients were from academic medical centers. Findings may not reflect the experience of community hospitals. There was no baseline inpatient or outpatient information available for about one third of individuals, and their data probably underestimated comorbidity conditions. In addition, dexamethasone before admission was not captured.