

### [Remdesivir for the Treatment of Covid-19 — Final Report \(NEJM\)](#)

**Bottom Line:** A randomized control trial shows that remdesivir is associated with shorter recovery time in adults hospitalized for COVID-19 and lower respiratory tract infection.

**Details:** In this double-blind randomized control trial of Remdesivir across several countries, 1062 patients were randomly assigned to remdesivir (541 patients) or placebo (521 patients). Remdesivir was given intravenously as 200mg on day 1, followed by 100mg daily on days 2 through 10 or until hospital discharge or death. Patients who received remdesivir had a shorter median recovery time of 10 days compared to 15 days among patients who received placebo (RR: 1.29; 95% CI, 1.12-1.49; P<0.001). At day 15, patients who received remdesivir showed clinical improvement compared to those who received placebo (OR: 1.5; 95% CI, 1.2-1.9). Though not clinically significant, day 15 and 29 mortality rates (Kaplan–Meier estimates) were lower with remdesivir compared to placebo (6.7% vs. 11.9% on day 15 and 11.4% vs. 15.2% on day 29, respectively). Serious adverse events were reported in 24.6% of patients who received remdesivir and 31.6% who received placebo. Remdesivir may be effective in reducing recovery time among hospitalized COVID-19 patients. However, treatment with an antiviral drug alone may not be sufficient for all patients and a variety of therapeutic approaches (novel antivirals, modifiers of immune response or pathways, or combination) are needed given the high mortality rates with remdesivir in this study.

**Key Takeaways:** Remdesivir is a promising antiviral drug in reducing recovery time from COVID-19. Remdesivir alone may not be effective in reducing mortality from COVID-19; thus additional therapeutic approaches should be studied.

### [Remdesivir for 5 or 10 Days in Patients with Severe Covid-19 \(NEJM\)](#)

**Bottom Line:** For patients hospitalized with COVID-19, this study found no significant difference in clinical outcomes at 14 days between patients treated with remdesivir for 5 days or 10 days.

**Details:** In this open-label phase 3 trial, 397 patients were randomized to receive remdesivir for either 5 days or 10 days. Patients were hospitalized with confirmed COVID-19, oxygen saturation of 94% or less on room air, and with radiologic evidence of pneumonia. At 14 days, clinical status was assessed using a 7-point ordinal scale. The median duration of treatment was 5 days in the 5-day treatment group, and 9 days in the 10-day treatment group. At baseline, patients randomized to 10 days of treatment had significantly worse clinical status than those assigned to 5 days of treatment. After adjusting for baseline status, at 14 days the clinical status of patients receiving 10 days of remdesivir was not significantly different from patients receiving 5 days of treatment (p=0.14). At baseline, very few patients were receiving mechanical ventilation (n=13), making results difficult to extrapolate for critically ill patients.

**Key Takeaways:**

- In patients with severe COVID-19 not requiring mechanical ventilation, there was no significant difference between a 5-day course and a 10-day course of remdesivir.
- Further studies are needed to evaluate efficacy for patients requiring mechanical ventilation, and high-risk groups such as immunocompromised patients.

[A Framework to Triage Older Adults with Covid-19 to Provide Patient-Centered Care \(NEJM\)](#)

**Bottom Line:** Clinicians at one Massachusetts hospital developed a frailty-based geriatric triage framework in the Emergency Department (ED) to provide better patient centered care and appropriate use of intensive care resources during COVID-19 surge. The framework utilized the Clinical Frailty Scale (CFS) to triage COVID-19 patients age 70+.

**Details:** This commentary highlights an ED frailty-based triage framework developed to direct limited geriatric and palliative care resources and provide patient-centered care during the COVID-19 surge to COVID-19 patients age 70 and older. It utilized the CFS, a 9-point scale used to classify patients from “very fit” to “terminally ill,” and deployed palliative care clinicians to a new inpatient palliative care unit in the ED to assess and triage eligible patients.

From April 7 to May 22 a triage clinician triaged 40 patients age 70 and older and provided recommendations for medication management, fall risk reduction, delirium prevention and advance care planning. Patients with a CFS of 1-3 were triaged to usual care (n=8, 20%), those with a CFS of 4-6 to geriatric co-management (n=6, 15%), those with a CFS of 7-9 to palliative care triage (n=23, 57.5%) and an additional 3 patients (7.5%) to palliative and geriatric care. Of those triaged, 72.5% (n=29) had a code status change during their admission and 48.3% of those had a change in the ED (n=14). The ED triage framework help provide structured, goal-concordant care and personalized care and appropriate use of intensive care resources during the COVID-19 surge. The broader utilization of this framework could potentially reduce delirium and unnecessary testing in the ED, but additional research is needed.

**Key Takeaways:** The Clinical Frailty Scale (CFS) could be a useful tool to triage COVID-19 patients age 70 and older to provide patient-centered care and appropriate use of intensive care resources during the COVID-19 surge.

[CPAP Management of COVID-19 Respiratory Failure: a First Quantitative Analysis from an Inpatient Service Evaluation \(BMJ\)](#)

**Bottom Line:** Early use of CPAP (continuous positive airway pressure), a type of non-invasive positive pressure ventilation, may improve outcomes in severe COVID-19

**Details:** In this retrospective case control study in 2 inpatient units in the UK, 206 patients with severe COVID-19 admitted during two periods (early and mid-pandemic) to reflect changing treatment protocols were evaluated to determine if the use and/or timing of CPAP was associated with mortality. They found that use of CPAP within 7 days of hospital admission was associated with lower risk of death (HR 0.38), whereas later use of CPAP beyond 7 days of hospital admission was associated with higher risk of death (HR 1.72). The survival benefit was most notable when CPAP was initiated within 4 days of hospital admission. This study is limited by small numbers (only 18 patients total on CPAP) and retrospective comparison.

**Key Takeaways:** Use of CPAP early in the hospital course may improve chances of survival for patients with severe COVID-19.

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### [Mobility Network Models of COVID-19 Explain Inequities and Inform Reopening \(Nature\)](#)

**Bottom Line:** An infectious disease model incorporating cell phone data to track the hourly movements of 98 million people in 10 U.S. cities from March 1 – May 2 suggests that most SARS-CoV-2 transmission occurred in crowded settings where people spend extended amounts of time, and higher infection rates among lower income populations were predicted by mobility patterns.

**Details:** In this study, researchers developed a model that integrates infectious disease dynamics with cell phone and demographic data to examine the effect of mobility on SARS-CoV-2 transmission in 10 U.S. cities (New York, Los Angeles, Chicago, Dallas, Washington, D.C., Houston, Atlanta, Miami, Philadelphia, and San Francisco). Data on hourly movements of 98 million individuals from 57,000 neighborhoods (census block groups) visiting 553,000 “points of interest” (POI; e.g., non-residential settings such as grocery stores and religious establishments) from March 1 – May 2 were included, comprising >5 billion time points. SafeGraph provided the anonymous location data, which included POI visited each day, length of visit, from which neighborhoods individuals were visiting the POI, and POI square footage to determine hourly occupancy density. A key assumption underlying the model is that infection rates depend on which settings are visited (e.g., visiting more densely occupied settings for longer is higher risk) and how this behavior changes over time. First, mobility data and daily SARS-CoV-2 infections for each city from March 8-May 9 were fed into the model to ascertain the transmission rate under various circumstances (frequency of leaving the house, types of POI visited, etc.) for each city. Using each city’s transmission rate and mobility patterns, the model was then used to predict new SARS-CoV-2 infections, which aligned closely with reported (actual) infections. The model predicts that a small proportion of POIs accounts for a large proportion of infections; in particular, full-service restaurants (largest predicted increases), gyms, hotels, cafes, religious establishments, and limited-service restaurants. Researchers also modeled the impact of instituting maximum occupancy caps on high-risk POIs at various thresholds, which is predicted to result in a lower number of new cases compared to less targeted strategies. Their model also provided new insights about what may be contributing to disparities in SARS-CoV-2 infections: 1) lower-income individuals saw less overall reduction in mobility than higher income individuals, likely due to the large proportion of essential workers who could not stay at home; and 2) POIs visited by lower-income individuals were more crowded than those visited by higher income individuals. Of note, transmission rates associated with grocery stores were twice as high in lower income neighborhoods in most (8/10) cities, owing in part to more density per square foot and longer visits. Policies should address the differential impact of reopening plans on disadvantaged groups. An important limitation of this study is that individuals with less/no mobile device use (e.g., children, elderly people, incarcerated people) are underrepresented in the data fed into the model.

#### **Key Takeaways:**

- In this model, a small proportion of settings accounted for a majority of predicted SARS-CoV-2 infections across 10 cities; full-service restaurants led to the largest predicted increases.
- More precise and targeted reopening strategies, including reducing maximum occupancy, may be effective; some settings/venues carry higher reopening risks

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than others (e.g., full-service restaurants, gyms, hotels, cafes, religious establishments, and limited-service restaurants) due to higher visit densities and/or longer lengths of stay.

- Findings suggest that higher infection rates among lower income persons can be explained in part because of more frequent and lengthier visits to smaller and more crowded settings/venues and less reduced mobility, likely due to being unable to work from home. Given the differential impact of reopening plans on racial/ethnic and socioeconomically disadvantaged groups, policymakers should consider the following: 1) paid leave policy and income supports that allow essential workers to stay at home when sick; 2) infection prevention for essential workers at their worksite(s); 3) free, available SARS-CoV-2 testing in high risk neighborhoods; 4) emergency food distribution centers to reduce density in settings like grocery stores; and 5) more stringent maximum occupancy caps for settings/venues.

### **Bidirectional Associations between COVID-19 and Psychiatric Disorder: Retrospective Cohort Studies of 62,354 COVID-19 Cases in the USA (Lancet)**

**Bottom Line:** This electronic health record review study found a bidirectional association between COVID-19 and psychiatric illnesses; people diagnosed with COVID-19 seem to be more likely to be subsequently diagnosed with a psychiatric illness than people without COVID-19, and people with an underlying psychiatric illness appear to be at higher risk of being diagnosed with COVID-19 than people without underlying psychiatric illness.

**Details:** This study examined the electronic health records of 69.8 million people in the US, 62,354 of whom had been diagnosed with COVID-19 in 2020, to examine associations between psychiatric illness and COVID-19. Two separate matched cohorts were created to evaluate the two questions of interest using logistic regression analysis. “Psychiatric disorder,” and “mental health diagnoses” are defined broadly, including diagnoses such as insomnia, adjustment disorder, and dementia. This study looked at the development of a new psychiatric diagnosis in the 14-90 days following COVID-19 diagnosis as compared to 6 different control “health events,” such as having the flu or a kidney stone. A diagnosis of COVID-19 led to more first diagnoses of psychiatric illness compared with all six controls, all statistically significant, with hazard ratios between 1.58 and 2.24. The most common newly-diagnosed psychiatric illnesses were anxiety disorders. Having a psychiatric disorder diagnosis in the year before the COVID-19 outbreak was associated with a 65% increased risk of COVID-19 diagnosis compared with a matched cohort.

#### **Key Takeaways:**

- There is high incidence of mental health diagnoses following COVID-19 diagnosis; 18% of people with COVID-19 in this cohort had some mental health diagnosis following their COVID-19 infection, with 5.8% of these diagnoses being first-time diagnoses.
- This study suggests that people with underlying psychiatric diagnoses may be more likely to contract COVID-19 than people with similar health risks but without a mental health diagnosis.
- This study is limited to chart review of electronic health records and does not speak to the functional impairment of patients prior to or following COVID-19 diagnosis.

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### Persistent Fatigue Following SARS-CoV-2 Infection is Common and Independent of Severity of Initial Infection (PLOS ONE)

**Bottom Line:** Patients who have recovered from COVID-19 may have an increased burden of fatigue after SARS-CoV-2 infection.

**Details:** 128 patients from a post-COVID-19 outpatient clinic in Dublin, Ireland were assessed in this study. Eligible patients included those who had acute symptoms or were discharged from the hospital at least six weeks prior to recruitment. Mean age of the group was  $49.5 \pm 15$  years, 54% were female, and 52% were healthcare workers. 56% (n=71) were admitted to the hospital for COVID-19 treatment while the rest were outpatients. Among those hospitalized, 49% (n=35) received hydroxychloroquine while the remaining hospitalized and outpatient participants received no targeted therapy. Targeted therapy was not associated with fatigue. Fatigue was assessed using the validated Chalder Fatigue Scale (CFQ-11). 53% of patients reported experiencing fatigue at a median of 10 weeks after initial symptoms. Additionally, 31% of those employed did not return to work at the time of the study. Females and those with history of anxiety and depression were more represented among those with fatigue compared to those without fatigue (female: 68% vs. 40%; anxiety/depression: 13% vs. 2%). There was no association between COVID-19 severity and markers of inflammation (i.e. leukocyte, neutrophil or lymphocyte counts, neutrophil-to-lymphocyte ratio, lactate dehydrogenase, C-reactive protein) and post-COVID-19 fatigue. This study demonstrates a high burden of fatigue despite disease severity and even after initial symptoms have resolved. Additional longitudinal research among those who have recovered from COVID-19 is needed to better understand fatigue and inform management of fatigue.

#### Key Takeaways:

- Fatigue is a common symptom that persists among many patients who have recovered from COVID-19, particularly among females and those with a history or anxiety and depression.
- Strategies to manage fatigue after acute COVID-19 symptoms have resolved and longitudinal research to inform such strategies are needed.