Trends in COVID-19 Inpatient Therapeutics

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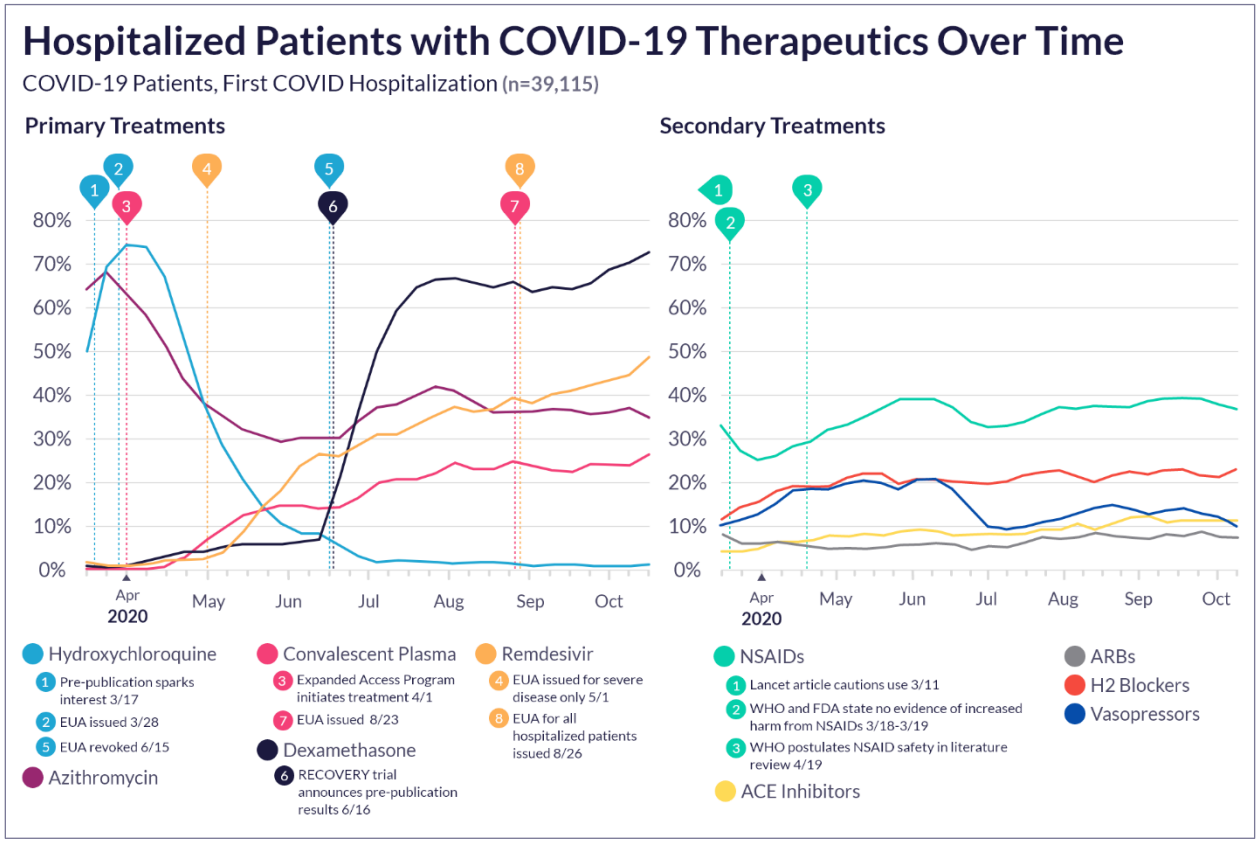
In the first seven months of the novel coronavirus pandemic, inpatient therapy choices have been considerably influenced by pre-publications, media attention, clinical trials, emergency use authorizations, and regional drug availability. In this observational study, we examine patterns in inpatient medication use since the start of the pandemic. Use of the leading therapies over time represents the dramatic changes in standard of care for treating hospitalized patients with COVID-19. Dexamethasone and remdesivir are the current dominant therapeutics, and both of these therapies have supportive evidence from randomized clinical trials.[1,2]



Percentage of hospitalized COVID-19 patients by week mid-March through mid-October 2020 who have received the above inpatient therapies. Patients are counted in the denominator each week they are hospitalized any day between Sun-Sat, and in the numerator for the week of hospitalization where the given therapy was initiated and for every subsequent week through the end of their hospitalization. Data represent 39,115 patients across 457 hospitals in 62 hospital systems and 27 US states.

Hydroxychloroquine and azithromycin use were high early in the pandemic after a mid-March pre-publication from France caught global attention[3] and the FDA subsequently issued an Emergency Use Authorization (EUA).[4] Hydroxychloroquine use declined sharply over the next 10 weeks as the medical and scientific community questioned its efficacy[5,6] and had minimal use in hospitalized patients by the time the EUA was revoked.[7] Azithromycin use had a parallel decline

in April and May, but use never dropped much below 30% of hospitalized patients, possibly due to its indication for community acquired pneumonia or its known immunomodulatory effects.[8] Its use did show a midsummer rise around the same time cases in the US were becoming geographically more widespread.

Clinical trials for remdesivir and dexamethasone both showed promise of improving the clinical course for patients, and these drugs showed rising ordering trends after the pre-publication announcements from their respective trials and the issuance of EUAs.[9,10] Dexamethasone's wide availability as a generic drug may have contributed to its more rapid rise in use trends than remdesivir. Convalescent plasma use began to increase after the start of the national expanded access program,[11] but also saw an additional rise in midsummer. Whether this was due to changing standard of care or increasing availability of plasma as more patients convalesced is not clear from this data. Its use did not seem meaningfully impacted by the timing of the EUA in August.[12]

Researchers have proposed therapeutic uses of ACE inhibitors, ARBs, H2 blockers, and NSAIDs for the coronavirus via a variety of mechanisms.[13,14,15] ACE inhibitor use has trended slightly upwards over time, while ARB use has not changed appreciably. H2 blocker use accelerated alongside the vasopressor use early in the pandemic, possibly representing co-ordering in critically ill ICU populations, but then persisted around 20% of inpatients through and beyond the midsummer surge. NSAID use had a significant dip after a cautionary letter was published in early March about possible harm,[15] but volumes rebounded over time. The use of vasopressors for COVID-19 patients decreased in midsummer with the surge, which may indicate less severe illnesses in the hospitalized population at that time. The slight rebound of vasopressor use in later summer may represent the discharge of those less critical patients.

The standard of care appears to have stabilized over the last several months, with dexamethasone and remdesivir as the forerunners for therapy of COVID-19 inpatients.

Data Definitions

Term	Definition
COVID-19 Diagnosis	One of the following codes in one of the listed diagnosis settings. **Diagnosis Code:** U07.1 (ICD-10-CM), 840539006 (SNOMED) **Diagnosis Setting:** Encounter Diagnosis, Billing Diagnosis, Problem List, Hospital Problem, Discharge Diagnosis **Start Date**: Diagnosis noted date
COVID-19 Positive Patient	Patient with a positive SARS-CoV-2 lab result or a COVID-19 diagnosis. **Start Date:** The earlier of the earliest positive SARS-CoV-2 lab result collection date or earliest diagnosis noted date. If an inpatient admission began in the 7 days prior to this date, the admission date is used instead.
COVID-19 Related Admission	A hospital admission during which the patient has a positive SARS-CoV-2 lab test or COVID-19 diagnosis, OR a hospital admission with any respiratory diagnosis which happens within 14 days of the patient's COVID-19 "start date." **Respiratory Diagnosis Codes:** J00-J99 (ICD-10-CM)
Positive COVID-19 Lab Result	A final result for one of the lab components identified by individual health systems for SARS-CoV-2 with a "positive" value, as identified by the health systems. **Positive/Start Date:** Date the test was collected/performed
COVID-19 Admission and Medication Administration Dates	Visit with real-time audio and video communication between a patient and a healthcare provider, as consistent with CMS guidelines.

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