



Medications Studied for COVID-19



Conflicts

› I own stock in Pfizer

Medication availability

▶ Current Shortages: Acute vs Non-Acute vs Aggregated

The primary concern for drug shortages is currently in the acute space. Therefore, the immediate focus should be on the acute setting, although more pervasive shortages in the non-acute setting are likely not to be resolved in the near future.

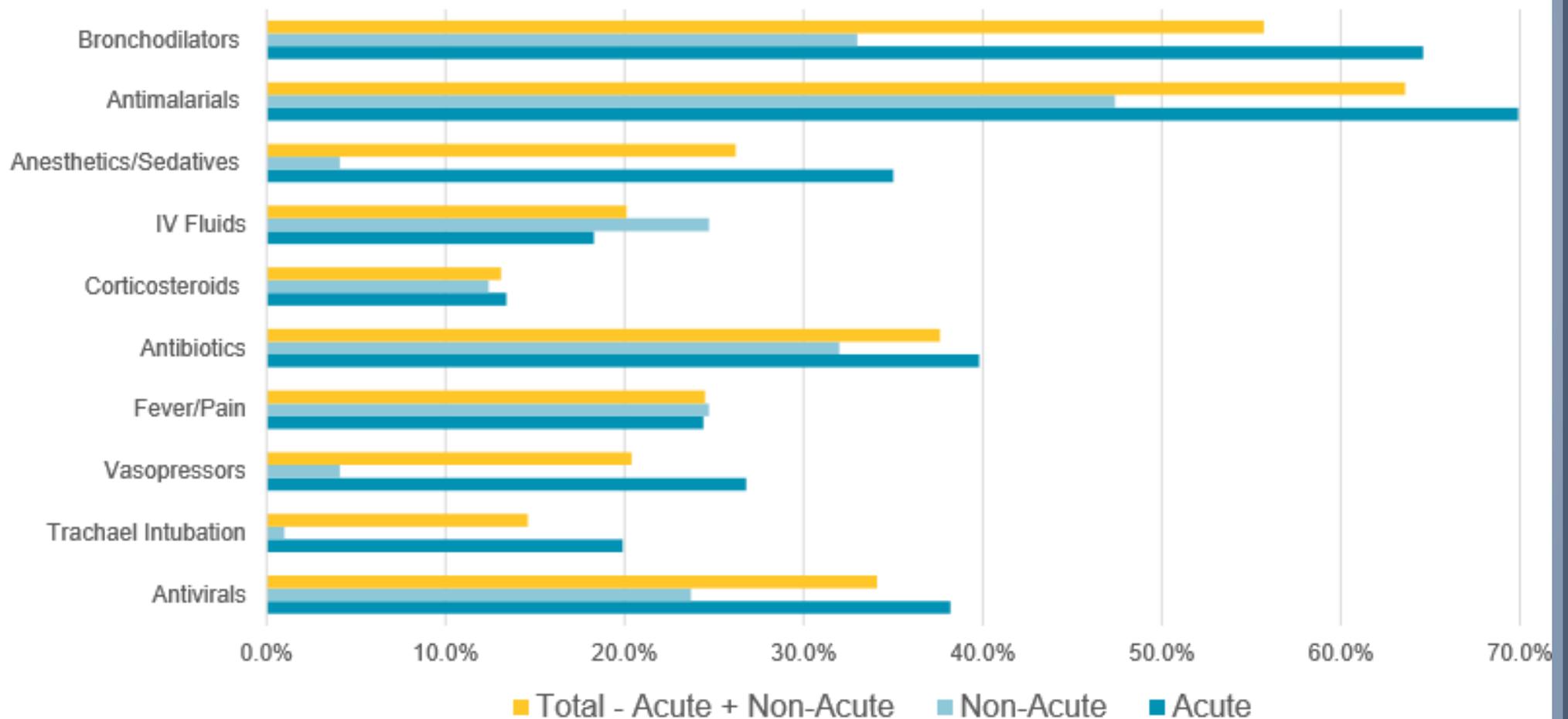




Table. State of Ventilator Drug Shortages

Drug	Indication	% Order Increase (March)	Current fill rate	% Order Increase in NY (March)
Albuterol	Bronchodilator	53	80	1870
Cisatracurium	Neuromuscular blocker	253	51	786
Rocuronium	Neuromuscular blocker	84	80	Data Unavailable
Fentanyl	Sedative	100	61	533
Midazolam	Sedative	70	79	4100
Propofol	Sedative	60	82	123
Norepinephrine	Vasopressor	50	67	53

Chloroquine and hydroxychloroquine

› Antimalarial drugs promoted by POTUS for treating COVID-19.

- Chinese trial of n=30 showed promise @400mg daily X5 days
 - › Control and treatment groups had similar outcomes ($P>0.05$)
 - › Radiographic findings better in HCQ group
- Updated 4/14/2020 --Adults in 4 French hospitals (n=181) with documented SARS-CoV-2 pneumonia
 - › Endpoints ICU admission or death @ 7 days @600mg/day
 - › 84 received HCQ within 48 hours of admission (HCQ group) and 97 did not (no-HCQ group).
 - › Findings do not support use of HQC, with no observed reduction in disease severity or death. *Mahevas et al. (April 14, 2020). No evidence of clinical efficacy of hydroxychloroquine in patients hospitalised for COVID-19 infection and requiring oxygen: results of a study using routinely collected data to emulate a target trial.*
<https://doi.org/10.1101/2020.04.10.20060699>
 - › Study not peer reviewed





ACE Inhibitors & ARB

- › Hypertension is a known factor for severe disease progression
- › COVID-19 utilizes ACE-2 receptors to enter/infect host cells
- › Should ACE Inhibitors and ARBS be stopped in a COVID-19 inf?
 - Meng J, Xiao G, Shang J. Renin-angiotensin system inhibitors improve the clinical outcomes of COVID-19 patients with hypertension. *Emerg Microbes Infect.* 2020;9:7575-760
 - › Retrospective study 42 patients 14 ACE/ARB 25 other antihypertensive therapy (calcium channel, beta blocker, diuretic)
 - › 64.5 years, and 57.1% of patients were male
 - › non-ACEI/ARB group had higher rates of severe infection (48 % [n=12] vs. 23.5% [n=4]). The difference was not significant. (overall enrollment were small)
 - › Patients receiving ACEIs and ARBs were also noted to have lower IL-6 levels, higher CD3+ and CD8+ T cells, and significantly lower peak viral load than the patients receiving other antihypertensives.
 - › Finally, the only death occurred in a patient in the non-ACEI/ARB group.

ACE inhibitor

- › Do ACE Inh prevent severe disease progression? Bean et al. (April 11 2020). <https://doi.org/10.1101/2020.04.07.20056788>
 - 205 acute inpatients with COVID-19 at King's College Hospital and Princess Royal University Hospital, London, UK
 - Primary endpoint being death or transfer to a critical care unit for organ support within 7-days of symptom onset
 - › 53 patients out of 205 patients reached the primary endpoint.
 - treatment with ACE-inhibitors was associated with a reduced risk of rapidly deteriorating severe disease.
 - › There was a lower rate of death or transfer to a critical care unit within 7 days in patients on an ACE-inhibitor OR 0.29 (CI 0.10-0.75, $p < 0.01$),
 - patients on treatment with ACE-inhibitors should continue these drugs during their COVID-19 illness.





Antiviral medications of interest

- › **Remdesivir** — Gilead's drug, has been a front-runner as a possible COVID-19 treatment.
 - Failed Ebola treatment, showed promise for MERS
 - five active clinical trials testing its effectiveness against COVID-19 taking place in China, the U.S. and South Korea, according to *Business Insider*.
 - **Majority of studies have lacked a placebo control arm
 - Not FDA approved, available through compassionate care program
 - 200mg loading dose then 100mg daily up to 10 days commonly studied

- › **Kaletra** — HIV combo drug made by AbbVie.
 - lopinavir and ritonavir, protease inhibitors
 - [study published](#) March 18 in the New England Journal of Medicine said Kaletra didn't show benefits in COVID-19 patients,
 - The WHO said it will conduct a global study on four experimental treatments, including Kaletra, according to *Business Insider*.

Bcg vaccination—April 15th 2020

- › Green et al determine that BCG vaccination is correlated with protection from death from COVID-19.
<https://www.medrxiv.org/content/10.1101/2020.04.10.20060905v1.full.pdf>
- › (Nemes 2019 NEJM, Moorlag et al., 2019)
 - BCG Vaccine provides non specific respiratory protection from non-mycobacterial pathogens
- › Uses many assumptions and observational data measurement
- › Causation vs correlation?
- › More studies most likely needed



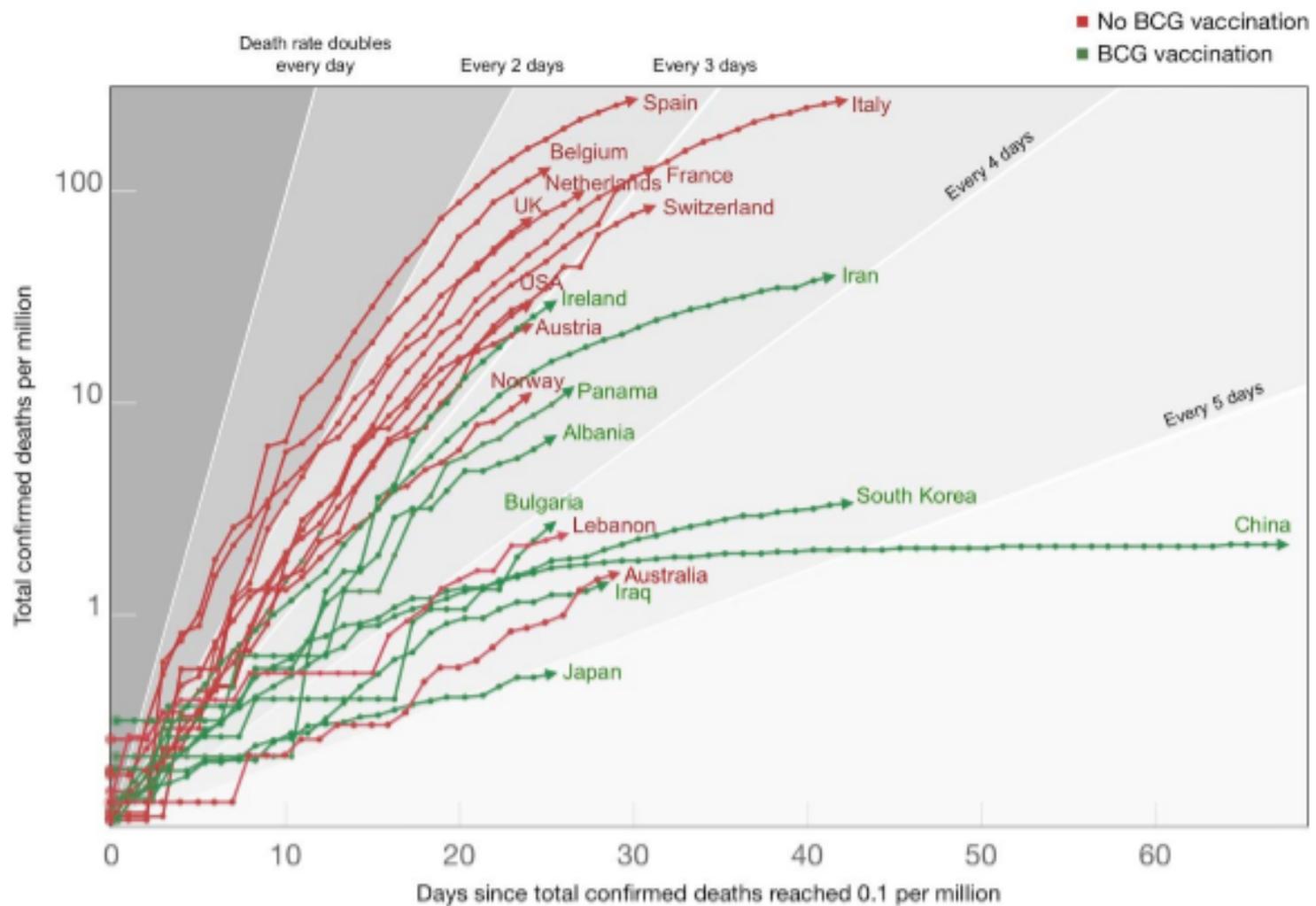


Figure 1. In general, countries with an ongoing BCG vaccination program exhibit reduced COVID-19-associated mortality rates. Data represents days since the total confirmed deaths of COVID-19 per million people reached 0.1. The 20 countries represented here were selected as they have available data for > 21 days after 0.1 deaths per million. The variable time span is from 31 December 2019 to 6 April 2020. Potential explanations for outliers (such as Ireland and Lebanon) are explained in supplemental data. Raw data from OurWorldInData.org.



Antivirals

- › **Avigan** — An influenza drug made by Japan-based Fujifilm Toyama Chemical.
- › A trial conducted in China showed Avigan helped patients recover seven days faster than patients on another antiviral drug called arbidol, and it also reduced the frequency of symptoms like coughing and fever.
- › However, the drug is not approved in the U.S.



IL-6 Inhibitors

- › **Actemra and Kevzara** — Actemra, made by Roche, and Kevzara, made by Regeneron and Sanofi, are both classified as IL-6 inhibitors
- › Primarily used to treat Rheumatoid Arthritis
- › May work by stopping a biological mechanism that causes overactive inflammatory responses in patients' lungs.
 - High expression of IL-6 and cytokine activity have been linked to lung injury in COVID-19 infection
- › Both drugs are being tested in late-stage clinical trials.