Temporal trends in medication utilization among hospitalized COVID-19 patients

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Background & Objective

Multiple therapies were studied in attempt to combat the coronavirus disease 2019 (COVID-19). In an environment of rapid exploration and data generation, real-world data can quickly reveal how treatments for hospitalized COVID-19 patients have changed over the course of the pandemic.

Objective: Evaluate trends and changes in treatment for hospitalized COVID-19 patients in the US, overall and stratified by COVID-19 severity.

Methods

- Using HealthVerity claims and chargemaster records (Mar 2020-May 2021), we identified hospitalized patients with a COVID-19 diagnosis or a positive SARS-CoV-2 laboratory result.
- We examined: (1) weekly period prevalence (%) of patients newly treated (90-day washout) during the first week of the hospital stay with medications of interest (see **Table 1** for medications and abbreviations); (2) trends for each medication by calendar week of admission, overall and stratified by COVID-19 severity[1] [requirement for invasive mechanical ventilation (IMV) vs supplemental oxygen (O2) or non-invasive ventilation (NIV) vs no respiratory support requirements (NEITHER)]; (3) trends relative to the timing of key trial results (i.e., the UK RECOVERY trial for DEX[2], RECOVERY and REMAP-CAP for IL-6[3,4]) and relevant FDA Emergency Use Authorizations (EUAs).
- Aetion Evidence Platform (AEP)® used for data analysis and Python (v3.7) for visualizations.

Table 1. Percentage of hospitalized COVID-19 patients using medications of interest *(Mar '20 to May '21)*

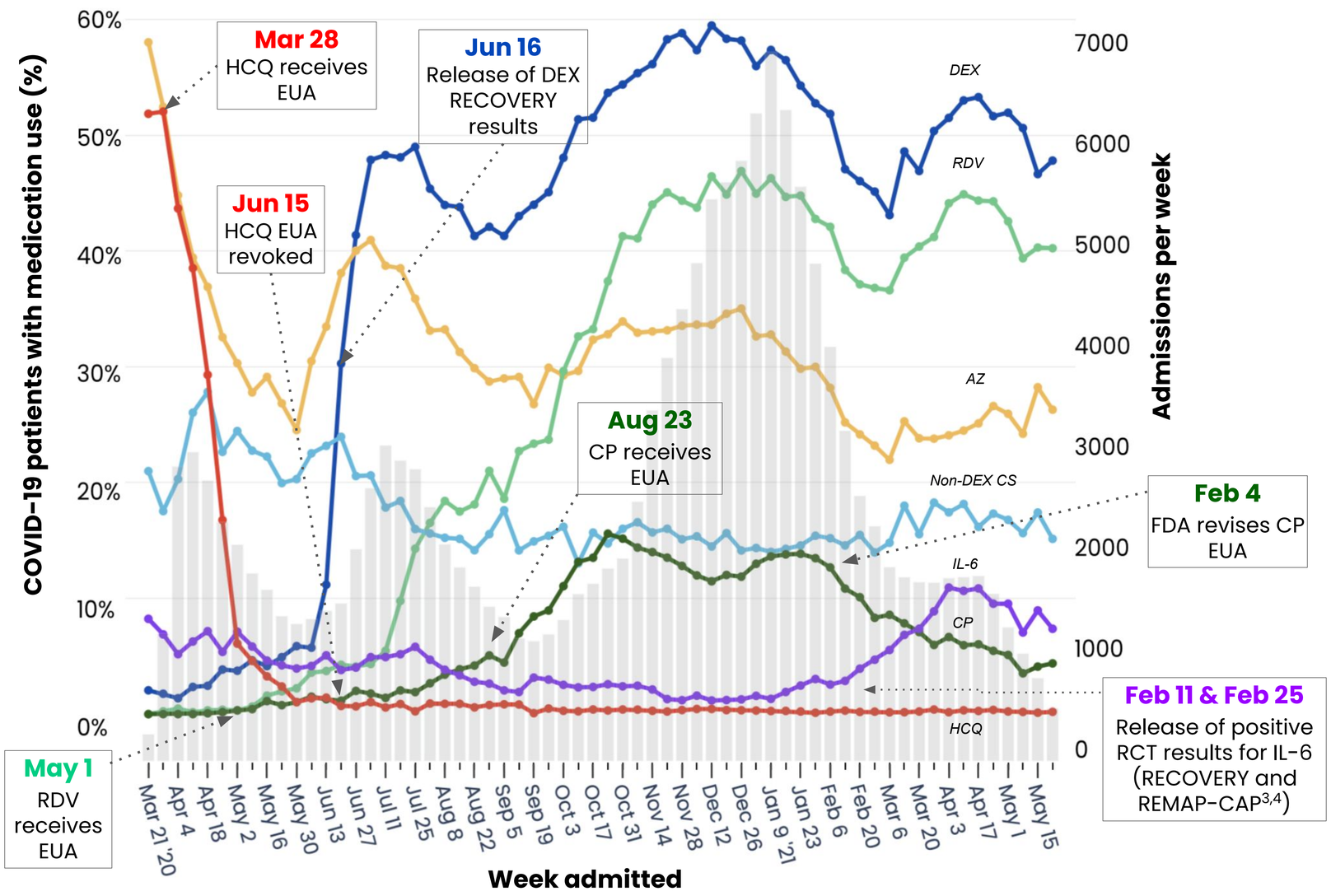
	Overall cohort	Severity subgroups: NEITHER	O2/NIV	IMV
N	**160,518**	**51,536**	**88,485**	**20,497**
DEX: Dexamethasone	44.9%	24.0%	55.4%	52.2%
AZ: Azithromycin	32.0%	20.2%	36.9%	40.1%
RDV: Remdesivir	31.1%	11.8%	40.9%	37.0%
Non-DEX CS: Non-DEX corticosteroids	16.8%	10.1%	18.2%	27.0%
CP: Convalescent plasma	8.4%	2.3%	10.8%	13.4%
IL-6: Interleukin-6 inhibitors*	3.7%	0.6%	3.8%	10.8%
HCQ: Hydroxychloroquine	3.3%	1.5%	3.4%	7.6%

*IL-6s include tocilizumab, sarilumab, and siltuximab

Results

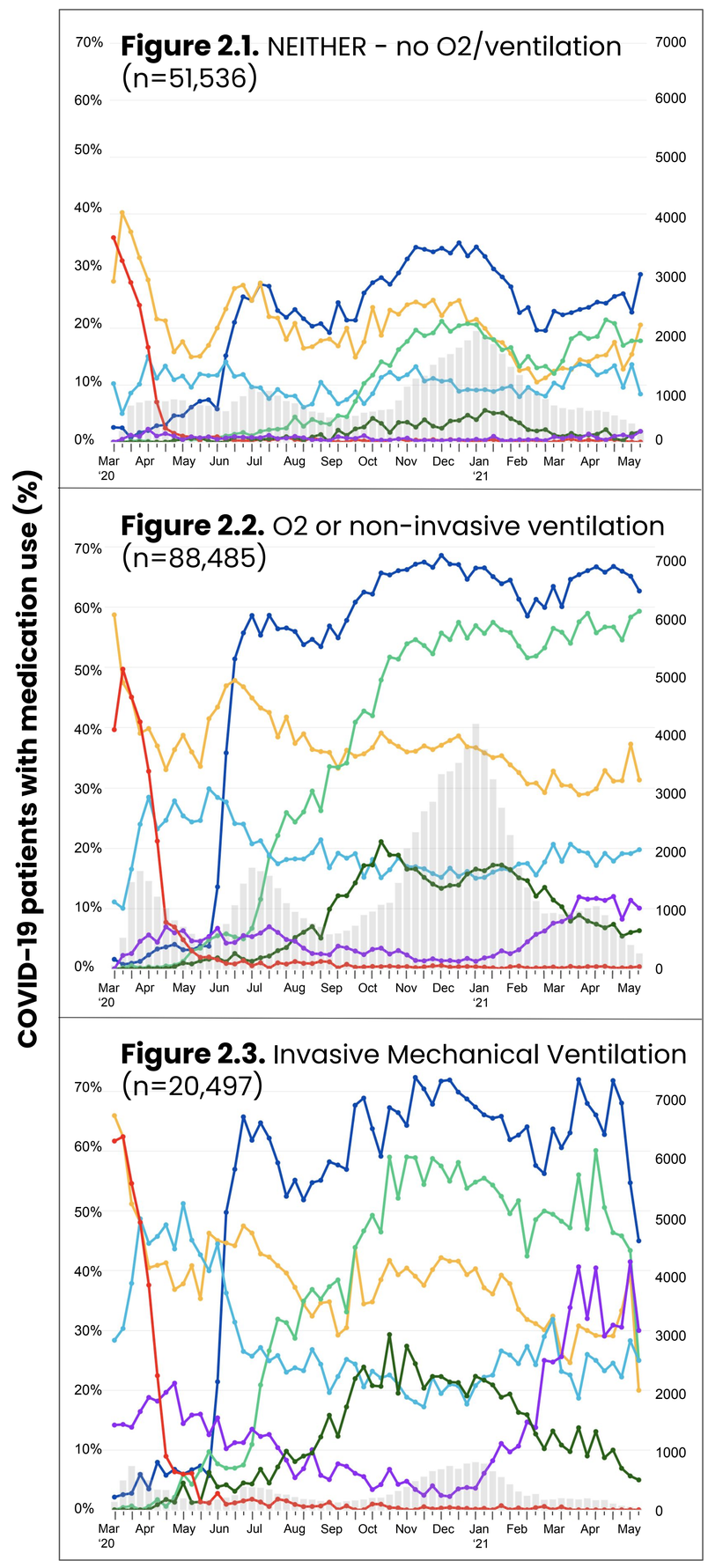
- Among the 160,518 hospitalized COVID-19 patients included, the most commonly used treatments were **AZ** (51.7%) and **HCQ** (49.6%) early in the pandemic (Mar 2020), followed by **DEX** (51.7%) and **RDV** (43.4%) in more recent months (Apr/May 2021) **(Fig 1)**.

Figure 1. Weekly medication use among all hospitalized COVID-19 patients (n=160,518)



- **DEX** increased sharply from early Jun to early Jul 2020 (5.7% to 47.9%) following publication of RECOVERY results[2], a trend consistent for all levels of COVID-19 severity **(Fig 1)**.
- **AZ** declined from mid-Mar to late May 2020 (58.0% to 24.5%), with use fluctuating between 25-35% through the remainder of the study period **(Fig 1)**.
- **RDV** increased gradually after May 2020 EUA and then more rapidly from early Jul to mid-Nov 2020 (5.5% to 45.1%) **(Fig 1)**; uptake differed across severity groups with use exceeding 10% by mid-Jul for IMV and O2/NIV patients **(Fig 2.2-2.3)**, while uptake in NEITHER patients lagged, exceeding 10% by Oct 2020 **(Fig 2.1)**.
- **Non-DEX CS** declined gradually from highest use in mid-Apr (27.8%) and stabilized at around 15% in Aug 2020 **(Fig 1)**; this decline was more abrupt among IMV patients (40% in early Jun to 26.5% in early Jul 2020), coinciding with a sharp increase in DEX during this same period **(Fig 2.3)**.
- **CP** increased gradually through late Aug and more rapidly from Sep to Oct 2020 (4.5% to 15.6%); following EUA[6] revision in Feb 2021, use steadily declined for all severity levels **(Fig 1)**.
- **IL-6** increased sharply from early Feb to mid-Apr 2021 in both IMV (9.7% to 40.5%) **(Fig 2.3)** and O2/NIV (2.5% to 11.7%) **(Fig 2.2)** groups after publication of first positive RCT results[3,4] in Feb 2021; use among NEITHER patients remained relatively stable (<2.0%) throughout this period **(Fig 2.1)**.
- **HCQ** declined sharply after highest use in late Mar 2020 (52.4%), with <1.0% use from Jul 2020 to May 2021; this decline began before the FDA revoked its EUA[5] in mid-Jun 2020 **(Fig 1)**.

Figure 2. Weekly medication use by COVID-19 severity



Conclusions

- We observed a considerable temporal shift in real-world prescribing trends in US hospitalized COVID-19 patients, with RDV and DEX surpassing HCQ following publication of emerging scientific data and FDA regulatory actions.
- Publication of RECOVERY Trial results for DEX was followed by an immediate and substantial increase in DEX among hospitalized COVID-19 patients in all severity levels; in contrast, IL-6 uptake following release of RCT results was limited to patients with more severe disease (IMV or O2/NIV).
- Trends may also have been influenced by other unmeasured factors such as physician experience or preference, access/cost, guidelines, and perceived efficacy/safety relative to other treatment options.

Disclosure

This work was conducted as a part of a Research Collaboration Agreement (RCA) with the U.S. Food and Drug Administration (FDA) to use Real World Data to advance the understanding and the natural history of COVID-19 in specific patient populations, as well as treatment and diagnostic patterns during the COVID-19 pandemic. This work reflects the views of the authors and should not be construed to represent FDA's views or policies. ARW, SV, EMG, NMG, and JAR are employees of Aetion, Inc., with stock options or existing equity. SL is an employee of HealthVerity.

References: 1. Garry et al. Abstracts of 37th ICPE: nr OP-27D; 2. CI's of RECOVERY Trial. U of Oxford. 2020; 3. REMAP-CAP Investigators. *NEJM.* 2021; 4. RECOVERY Collaborative Group. *MedRxiv.* 2021; 5. Hinton. USFDA. 2020; 6. Marks. USFDA. 2021