A Rapid Query Model to Prioritize COVID-19 Questions from a Real-World Clinical Data Warehouse in California

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Abstract

BACKGROUND The urgency of the COVID-19 pandemic demands development of new approaches to answer critical medical and operational questions quickly. Analysis of real-world data (RWD) sources is particularly well-suited to address these needs. The United States Food and Drug Administration (US FDA) initiated this project with the University of California Health System (UC Health) within the Center of Excellence in Regulatory Science and Innovation (CERSI).
METHODS UC Health, with 19 health professional schools, 5 academic medical centers, and 12 hospitals, has built a secure central EHR based data warehouse (UC Health Data Warehouse, or UCHDW) for operational improvement, promotion of quality patient care, and to enable the next generation of clinical research. Since the start of the COVID-19 pandemic, the University of California has created a standardized HIPAA Limited Data Set, The UC COVID Research Data Set (UC CORDS). The rapid-query model is a multi-step framework comprising a computational pipeline to rapidly query the data warehouse and refine the question further with a follow-up statistical analysis. UC Health proposes to deliver preliminary answers within 2-4 days of the questions being transmitted, and more determinant answers within two weeks of the final refined question. Answers are delivered in regular reports accompanied by tables of counts and data visualizations.
RESULTS The collaboration has developed processes for implementing the rapid-query model, including outcome measures. Questions are prioritized for consideration by a team led by FDA's Principal Deputy Commissioner.
CONCLUSIONS This project meets the regulatory science objective of development of methods and tools to improve and streamline clinical and post-marketing evaluation of FDA-regulated products. Results from this project will inform FDA's utilization of RWD data sources for efficient regulatory and operational decision-making. The rapid-query model initiated between the US-FDA and UC Health will enable real-world evidence generation in a statistically rigorous manner to help inform clinical, regulatory, and operational decision making.

Introduction

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Materials and Methods

UC Health, with 20 health professional schools, 6 academic health centers, and 12 hospitals, has built a secure central EHR based data warehouse (UC Health Data Warehouse, or UCHDW) for operational improvement, promotion of quality patient care, and to enable the next generation of clinical research. Since the start of the COVID-19 pandemic, the University of California has created a standardized HIPAA Limited Data Set, The UC COVID Research Data Set (UC CORDS). The rapid-query model is a multi-step framework comprising a computational pipeline to rapidly query the data warehouse and refine the question further with a follow-up statistical analysis. UC Health proposed to deliver preliminary answers within 2-4 days of the questions being transmitted, and more determinant answers within two weeks of the final refined question. Answers are delivered in regular reports accompanied by tables of counts and data visualizations. Custom SQL queries were written to obtain number of patients with medication order on a given day.

An example of the question posed was *'within 28 days of a COVID-19 diagnosis, describe treatment patterns among patients who initiated one of four corticosteroids of interest in both inpatient and outpatient settings of the care'* **(Figure 1)**

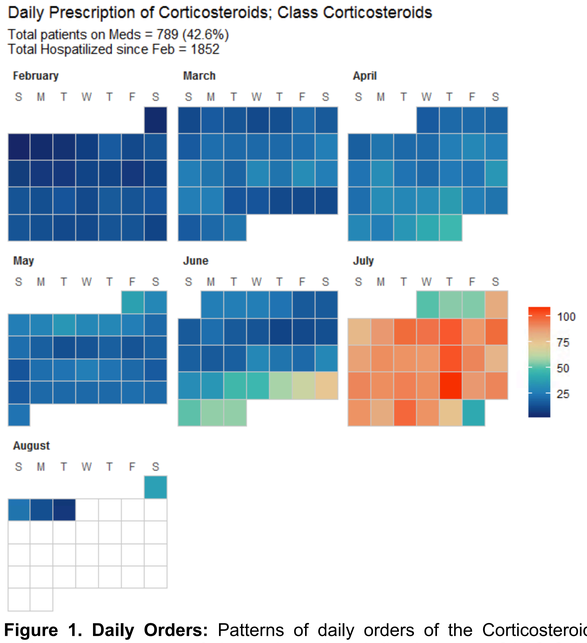

Figure 1. Daily Orders: Patterns of daily orders of the Corticosteroids during inpatient care of the patients hospitalized due to SARS-CoV-2 infection from Feb 2020 to August 2020.

Results and Discussion

The collaboration has developed processes for implementing the rapid-query model, including outcome measures. Questions are prioritized for consideration by a team led by FDA's Principal Deputy Commissioner.

Figures (1-3) illustrate initial analysis of the question *'within 28 days of a COVID-19 diagnosis, describe treatment patterns among patients who initiated one of four corticosteroids of interest – methylprednisolone, prednisone, dexamethasone, and hydrocortisone in both inpatient and outpatient settings of the care'.* Descriptive analysis indicate that the uptake of the Corticosteroids increased in the month of July 2020 (Figure1). The majority of the inpatients were prescribed Dexamethasone as their initial treatment followed by prednisone, hydrocortisone and methylprednisolone (Figure 2). There was a statistically significant difference in the time to first order of dexamethasone compared with hydrocortisone in inpatient setting (Fig. 3). These patterns are being studied further with detailed analysis.

Table 1. Brief summary of the Sex and Age of the patients tested negative, positive, hospitalized, needed ICU, and deceased due to SARS-CoV-2 infection (Feb 2020 to Sep 2020)

	COVID Negative	COVID Positive	Hospitalized	ICU Admissions	Deceased
	N=213458	N=11445	N=2290	N=237	N=237
Sex					
FEMALE	116094 (54.4%)	5965 (52.1%)	1008 (44.0%)	93 (39.2%)	92 (38.8%)
MALE	97364 (45.6%)	5480 (47.9%)	1282 (56.0%)	144 (60.8%)	145 (61.2%)
Age					
0-18	16423 (7.69%)	950 (8.30%)	141 (6.16%)	20 (8.44%)	3 (1.27%)
19-39	57635 (27.0%)	4334 (37.9%)	445 (19.4%)	23 (9.70%)	14 (5.91%)
40-49	28199 (13.2%)	1830 (16.0%)	298 (13.0%)	26 (11.0%)	13 (5.49%)
50-59	34398 (16.1%)	1802 (15.7%)	406 (17.7%)	37 (15.6%)	28 (11.8%)
60-69	36431 (17.1%)	1279 (11.2%)	407 (17.8%)	54 (22.8%)	52 (21.9%)
70+	40372 (18.9%)	1250 (10.9%)	593 (25.9%)	77 (32.5%)	127 (53.6%)

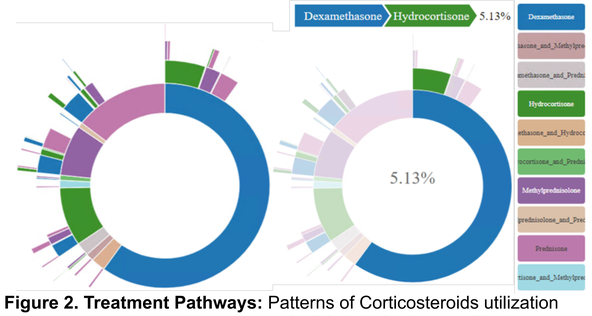

Figure 2. Treatment Pathways: Patterns of Corticosteroids utilization among patients hospitalized due to SARS-CoV-2 infection. The inner most circle represent number of patients on a given type of corticosteroid. Each subsequent circle represents order of other another corticosteroid. For instance, 5.13% of the patients who started on Dexamethasone required hydrocortisone

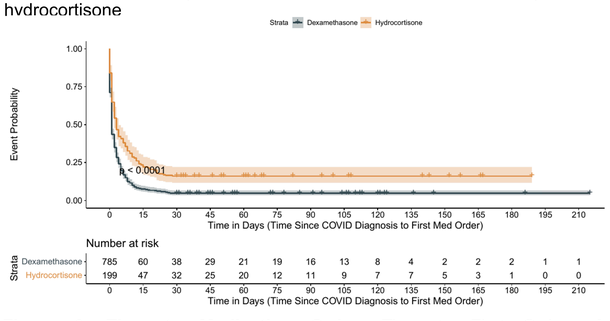

Figure 3. Time to Medication Order: Time to First Order of Dexamethasone vs Hydrocortisone.
Kaplan Meier plots were used to represent time to treatment initiation. Log-rank test was conducted to compare the curve and calculate p value using R statistical software.

Conclusion

This project is intended to meet the regulatory science objective of development of methods and tools to improve and streamline clinical and post-marketing evaluation of FDA-regulated products. A systematic investigation to comprehend the observed medication patterns is underway. Results from this project will inform FDA's utilization of RWD data sources for efficient decision-making. The rapid-query model initiated between the US-FDA and UC Health will enable real-world evidence generation in a statistically rigorous manner to help inform clinical, regulatory, and operational decision making.

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