Clinical data collected outside of traditional clinical trials—also known as "Real-World Data" (RWD) — can provide insights to FDA on how COVID-19 treatments, diagnostics, and vaccines are performing in a variety of settings. The evidence generated depend on rigorous analytical methods as well as validation and cross-checking of analyses. The Reagan-Udall Foundation for the FDA, in collaboration with Friends of Cancer Research and with active participation by FDA, launched the *COVID-19 Evidence Accelerator.*

Generating Actionable Insights from Real World Data - The COVID-19 Evidence Accelerator

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OC FDA, Friends of Cancer Research, Reagan-Udall Foundation for the FDA

Abstract

Clinical data collected outside of traditional clinical trials—also known as "Real-World Data" (RWD) — can provide insights to FDA on how COVID-19 treatments, diagnostics, and vaccines are performing in a variety of settings. The evidence generated depend on rigorous analytical methods as well as validation and cross-checking of analyses. The Reagan-Udall Foundation for the FDA, in collaboration with Friends of Cancer Research and with active participation by FDA, launched the COVID-19 Evidence Accelerator.

The COVID-19 Evidence Accelerator brings together leading experts in health data aggregation and analytics in a unified, collaborative effort to share insights, compare results and answer key questions to inform the collective COVID-19 response. In its Parallel Analysis work, the Evidence Accelerator convenes a discrete set of data analyzers to execute a common analytic plan against their unique data set. Results are reported to the Accelerator and reported out 'in parallel'.

Real World Evidence (RWE) may help regulators and scientists augment information received in randomized clinical trials by shared insight, common research questions, innovative use of parallel analysis, rapid queries and lab meetings. The Evidence Accelerator creates a strong foundation for rapid collection and rigorous analysis of RWD to answer urgent questions about COVID-19.

Introduction

COVID-19 is a novel disease for with there was limited understanding of its epidemiology, treatment and care. As treatments and diagnostic tests were being authorized under Emergency Use Authorization, there was an emergent need to understand the real-world performance of these treatments in an efficient and rigorous way. The parallel analysis is a key component of the COVID-19 Evidence Accelerator. In its Parallel Analysis work, the Evidence Accelerator seeks to coordinate analytic partners (aka Accelerators) with access to large data holdings to answer prioritized research questions of value to the FDA and the public health community. The Accelerators work collaboratively with FDA to develop study protocols and analysis plans; and execute common analytic plan against their unique data set. (**Figure 1**) Results are reported out in "parallel." The FDA Foundation and Friends provide program management, hosting meetings to discuss and rigorously review results in collaborative discussions. This process provides FDA with a snapshot of the real-world practices and performance of diagnostics and therapeutics.

To date, data analytic partners include:

- Aetion (w/Health Verity)
- COTA (w/Hackensack Meridian Health)
- Ciox
- Dascena
- Datavant (w/Northwestern Univ)
- Harvard/United Health Group
- Health Catalyst
- HealthPals
- PCORnet
- Regenstrief/Lilly
- Sentinel (w/Data Partners)
- Syapse
- Target RWE(w/ Gilead)
- TriNetX
- Univ of California Health System
- Veterans Affairs
- Yale/Mayo

Materials and Methods

Dedicated "Parallel Analysis" workstreams focus on therapeutics and diagnostics use, exploring discrete research questions according to a common analytic plan. Initial activities include

(1) rapidly revising a list of core data elements;
(2) identifying elements critical to answering the primary question;
(3) establishing uniform collection parameters.

This Parallel Analysis approach is being deployed to address three initial therapeutics-focused research questions and one diagnostics-focused question **(Figures 2 and 3).** Results of analyses, rather than raw data, are shared among participants.

The Parallel Analysis process requires:

- Appreciation for different capabilities of electronic health records (EHR) vs. claims as the dataset;
- Allowing heterogeneity in approaches for EHR vs. claims, but aspiring to align within the data source types;
- Balancing the need for alignment and model-building approaches driven by specific datasets;
- Rigor across Accelerators is greater than the need for expediency: a more prescriptive approach to study design and model selection is helpful.

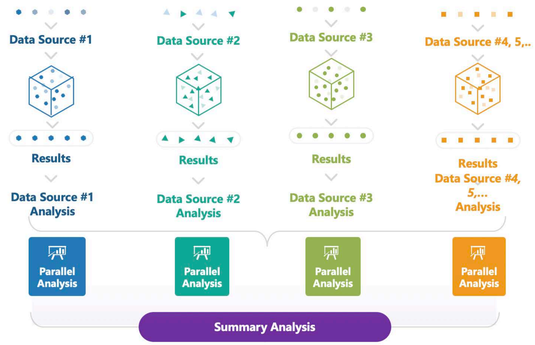
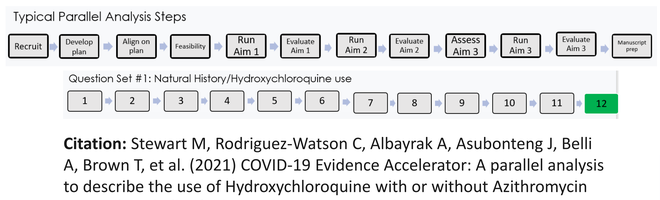


Figure 1. Parallel Analysis Approach to Real-world Data (RWD) for COVID-19 Evaluation; Data Holders execute common analytic plan against their unique data set.

Results and Discussion

A critical early result of the Evidence Accelerator is the characterization of the natural clinical history of COVID-19 in hospitalized patients—foundational to ensuring testing performance, identifying treatment, predicting immunity, detecting potential for future waves of infection, and tracking mutation. Additional results include:

1) Insight into population and demographic subsets for an improved understanding of treatment patterns and accessibility
2) Longitudinal monitoring of pandemic response across different geographies to assess changes in practice patterns over time
3) Evaluation of diagnostic and serologic testing strategies to assess utilization patterns and performance across numerous health systems
4) Exposure of a critical absence of data flow of the type of diagnostic test administered (test results routinely appear in RWD; the actual test used often does not) **(Figure 4)**



Citation: Stewart M, Rodriguez-Watson C, Albayrak A, Asubonteng J, Belli A, Brown T, et al. (2021) COVID-19 Evidence Accelerator: A parallel analysis to describe the use of Hydroxychloroquine with or without Azithromycin among hospitalized COVID-19 patients. PLoS ONE 16(3): e0248128. https://doi.org/10.1371/journal.pone.0248128

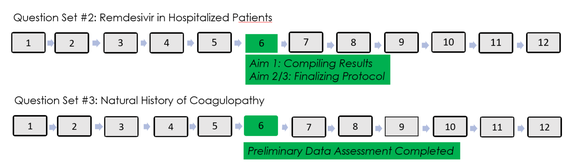


Figure 2. Therapeutics Research Questions of the Evidence Accelerator (Parallel Analysis Approach)

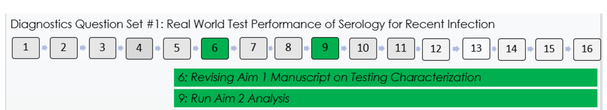


Figure 3. Diagnostics Research Question of the Evidence Accelerator (Parallel Analysis Approach)

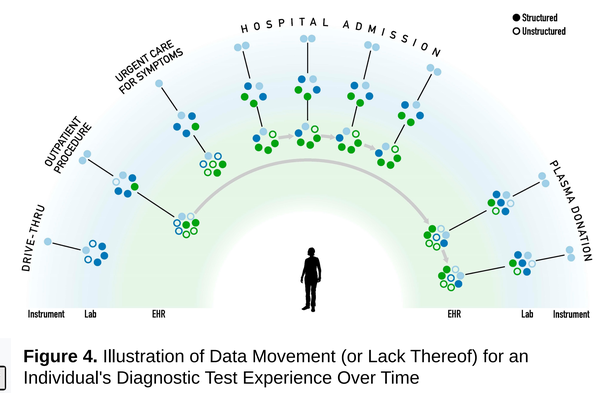


Figure 4. Illustration of Data Movement (or Lack Thereof) for an Individual's Diagnostic Test Experience Over Time

Table 1. Examples of learnings – challenges and contexts

Challenges	Potential Solution
Mechanical ventilation was challenging due to inconsistent coding	Evidence Accelerators developed natural language processing script to extract information
Case definition for COVID-19. Issues include which date to accept as first occurrence, identifying "best" criteria	• Hierarchical coding definition with lab as most specific, followed by COVID medication exposure, & presence of ICD10 code • ICD10 codes now available and code list generated & sharable
Identification of COVID-19 medications	Coding algorithms to identify medications of interest as part of combination or individual treatments have been developed and can be shared.

Conclusion

Real World Evidence (RWE) may help regulators and scientists augment information received in randomized clinical trials by shared insight, common research questions, innovative use of parallel analysis, rapid queries, and collaborative discussion. The Evidence Accelerator creates a strong foundation for rapid collection and rigorous analysis of RWD to answer urgent questions about COVID-19.