273 Real-world Utilization of SARS-CoV-2 Serological Testing in RNA Positive Patients Across the United States. [947]

Carla Rodriguez Watson[1*], Natalie E Sheils[2], Anthony M Louder[3], Elizabeth H. Eldridge[4], Nancy D. Lin[4], Benjamin D. Pollock[5], Jennifer Gatz[6], Shaun J. Grannis[6,7], Rohit Vashisht[8], Kanwal Ghauri[1], Gina Valo[9], Aloka Chakravarty[9], Tamar Lasky[9], Mary Jung[10], Stephen Lovell[10], Jacqueline M Major[10], Carly Kabelac[3], Camille Knepper[5], Sandy Leonard[11], Peter J. Embi[6,7], Garrett Jenkinson[5], Reyna Klesh[11], Omai B. Garner[12], Ayan Patel[13], Lisa Dahm[13], Aiden Barin[13], Dan M. Cooper[13,14], Tom Andriola[13,15], Carrie L Byington[13], Bridgit O. Crews[16], Atul J. Butte[8,13], Jeff Allen[17]

[1] Reagan-Udall Foundation for the FDA, Washington, District of Columbia, United States; [2] OptumLabs, Minnetonka, Minnesota, United States; [3] Aetion, New York, New York, United States; [4] Health Catalyst, Salt Lake City, Utah, United States; [5] Mayo Clinic, Rochester, Minnesota, United States; [6] Regenstrief Institute, Indianapolis, Indiana, United States; [7] Department of Informatics and Health Services Research, Indiana University School of Medicine, Indianapolis, Indiana, United States; [8] Bakar Computational Health Sciences Institute, University of California San Francisco, United States; [9] Office of the Commissioner, U.S. Food and Drug Administration, Silver Spring, Maryland, United States; [10] Center for Devices and Radiological Health, U.S. Food and Drug Administration, Silver Spring, Maryland, United States; [11] HealthVerity, Philadelphia, Pennsylvania, United States; [12] Department of Pathology and Laboratory Medicine, UCLA Medical Center, Los Angeles, California, United States; [13] Center for Data-driven Insights and Innovation, University of California Health, Oakland, United States; [14] Pediatric Exercise and Genomics Research Center, University of California Irvine School of Medicine, Irvine, California, United States; [15] Office of Data and Information Technology, University of California, Irvine, United States; [16] Department of Pathology and Laboratory Medicine, University of California, Irvine, United States; [17] Friends of Cancer Research, Washington, District of Columbia, United States

BACKGROUND

As diagnostic tests for COVID-19 were broadly deployed under Emergency Use Authorization (EUA), there emerged a need to understand the real-world utilization and performance of serological testing across the United States.

OBJECTIVES

- Understand the current state of data interoperability across instrument, laboratory, and clinical data
- Describe serological testing by demographic, geographic location, baseline clinical presentation, key comorbidities (e.g., diabetes and cardiovascular disease), and bacterial/viral co-infections (e.g., influenza)
- Assess the timing of serology testing relative to molecular testing by the characteristics listed above

METHODS

Setting: Six data partners collaborated in collecting data from different care settings (e.g., Outpatient, Inpatient, Emergency Department, Urgent Care, and Other) in the Diagnostics Evidence Accelerator. Health Catalyst, Mayo Clinic, and the University of California Health System utilized EHR data from their respective healthcare delivery systems, Regenstrief Institute accessed electronic health records (EHR) clinical data from the Indiana Health Information Exchange, and Aetion and OptumLabs utilized laboratory data, and medical and pharmacy claims. Aetion drew hospital billing data from the HealthVerity Marketplace. Data were drawn from across the U.S. with heavy representation in California, Illinois, Ohio, and Michigan.

Design:

- In this retrospective cohort study, we identified patients who tested positive for SARS-CoV-2 ribonucleic acid (RNA) by molecular test between March–September 2020, except one partner who went through April 30, 2021.
- "Date of RNA positive" served as the index (cohort entry) date and was defined hierarchically as either the date at 1) sample collection; 2) accession; or 3) result.
- Follow-up for serological testing, excluding immunoglobulin M tests, went through 90 days after the index date in all but one partner who identified all RNA positive and serology tests through April 30, 2021 without additional follow-up time for serology.
- To minimize the effect of differential missingness between partners, we
  1. Included all persons with an office or telephone visit in the +/- 14 days around the index date to enable as complete an assessment of presenting symptoms;
  2. In claim systems, included persons with at least six months of enrollment in the year before index;
  3. Estimated the proportion of patients at each site who had zero encounters in the prior year to contextualize our capture of pre-existing conditions; and
  4. Excluded variables from analysis if ≥30% of values were missing.

Main outcome measures: Demographic and environmental characteristics, baseline clinical presentation, key comorbidities, bacterial/viral co-infections, and test characteristics related to serological testing were included. We identified comorbidities and clinical presentation using computable phenotypes defined by ICD-10, and/or National Drug Codes. Given differences in data availability across partners, each partner identified which of the prescribed covariates could be included in their analyses.

Statistical analysis:

- Descriptive analyses were performed separately by each data partner in accordance with a common analytic plan.
- Among persons with and without serology, we calculated the distribution by age, sex, race, ethnicity, U.S. region, pre-existing medical conditions (cardiovascular disease, hypertension, kidney disease, asthma, dementia, chronic liver disease), smoking status, obesity, pregnancy status, presenting symptoms, and RNA test manufacturer.
- Among those with at least one serology test after index, we described the frequency of presenting symptoms, the specific manufacturer test at the time of the first serology, and the time to the first test.
- We calculated the median and interquartile range (IQR) for the number of days between RNA and the first test.

RESULTS

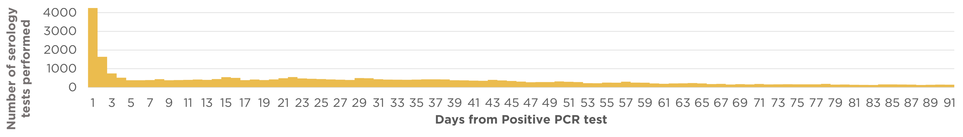
- Across datasets, we observed 930,669 individuals, predominately white female aged 18-44 years with positive RNA for SARS-CoV-2 (data not shown in figures). Partner A and B used claims data and Partners C-F used EHR data.
- Of these, 35,806 (4%) were serotested within 90 days; 15% of which occurred <14 days from the RNA positive test (Figure 1). This is due to the implementation of policies within health systems to screen patients admitted for procedures for active or past SARS-CoV-2 to evaluate the risk of nosocomial infections.
- The proportion of people with a history of cardiovascular disease, obesity, chronic lung, or kidney disease; or presenting with shortness of breath or pneumonia appeared higher among those serotested compared to those who were not (Figures 2 and 3).
- Even in a population of people with active infection, race/ethnicity data were largely missing (>30%) in some datasets - limiting our ability to examine differences in serological testing by race (Figure 4).
- In datasets where race/ethnicity information was available, we observed a greater distribution of White individuals among those serotested; however, the time between RNA and serology tests appeared shorter in Black (range of 7-34) compared to White (range of 12-33) individuals (Figure 5).
- Test manufacturer data was available in half of the datasets contributing to the analysis (Figure 6).

CONCLUSION

Our results informed:

- The underlying context of serotesting during the first year of the COVID-19 pandemic and differences observed between claims and EHR data sources—a critical first step to understanding the real-world accuracy of serological tests.
- Incomplete reporting of race/ethnicity data and a limited ability to link test manufacturer data, lab results, and clinical data challenge the ability to assess the real-world performance of SARS-CoV-2 tests in different contexts and the overall U.S. response to current and future disease pandemics.

FIGURE 1: Distribution of Serological Tests by Days After Positive PCR



PARTNER A | PARTNER B | PARTNER C | PARTNER D | PARTNER E | PARTNER F

FIGURE 2: Pre-Existing Conditions with Higher Prevalence Among Those Serotested

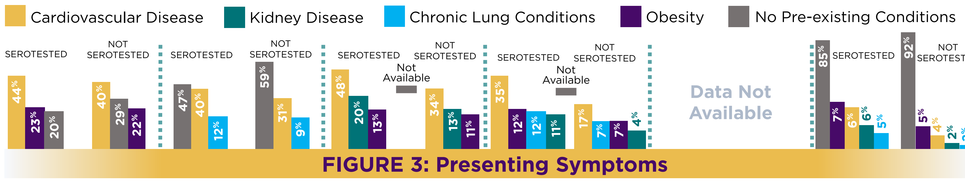


FIGURE 3: Presenting Symptoms

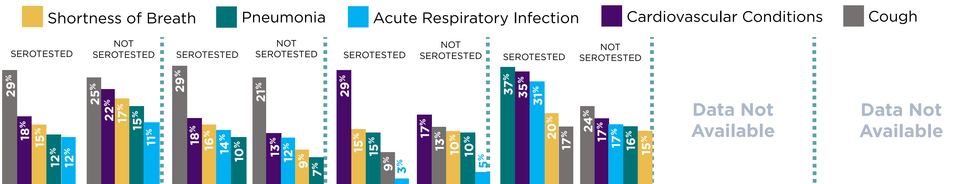


FIGURE 4: Race/Ethnicity Data

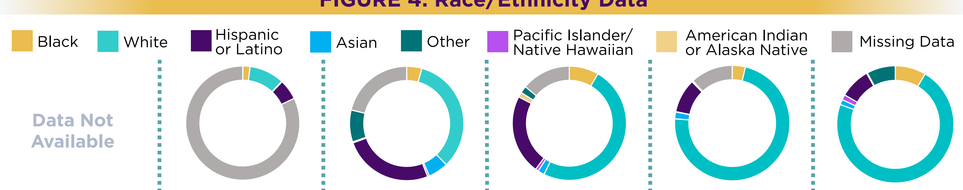


FIGURE 5: Median IQR Days Between RNA and Serology Tests

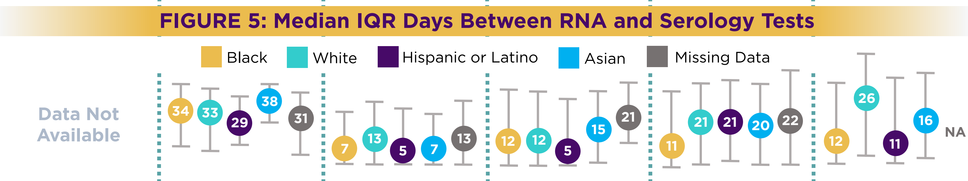


FIGURE 6: Manufacturer—Serological Test Name