AVALON HEALTHCARE SOLUTIONS

Jan 12, 2021

COVID-19 TESTING BRIEF

from Avalon Healthcare Solutions

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Avalon is an expert in lab management with a foundation in science. Clinically-driven lab strategies are transforming lab testing into actionable intelligence for value-driven care. Avalon's core program includes full delegation of Routine Testing Management, Genetic Testing Management, Independent Laboratory Network Management, and Medical Specialty Rx Management. You can learn more about our impact here and the latest news here.

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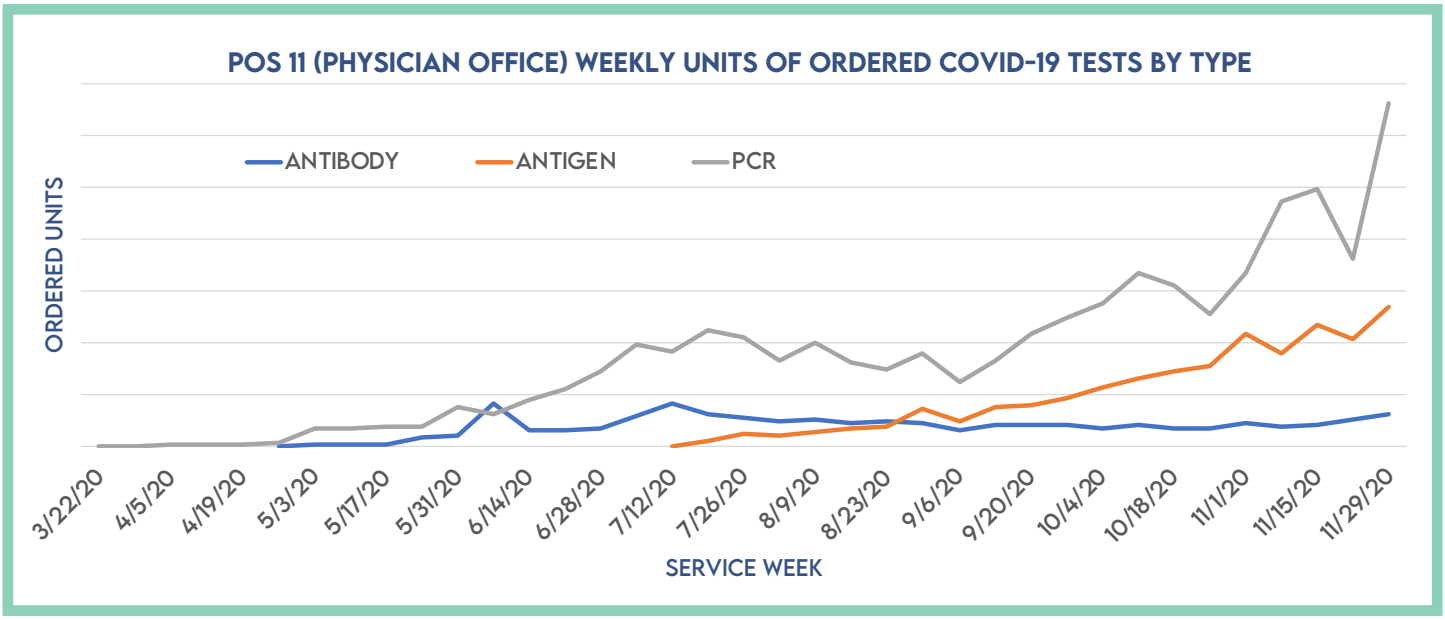
LABORATORY UPDATE

AVALON LABORATORY NETWORK CAPACITY & TURNAROUND TIME REPORT

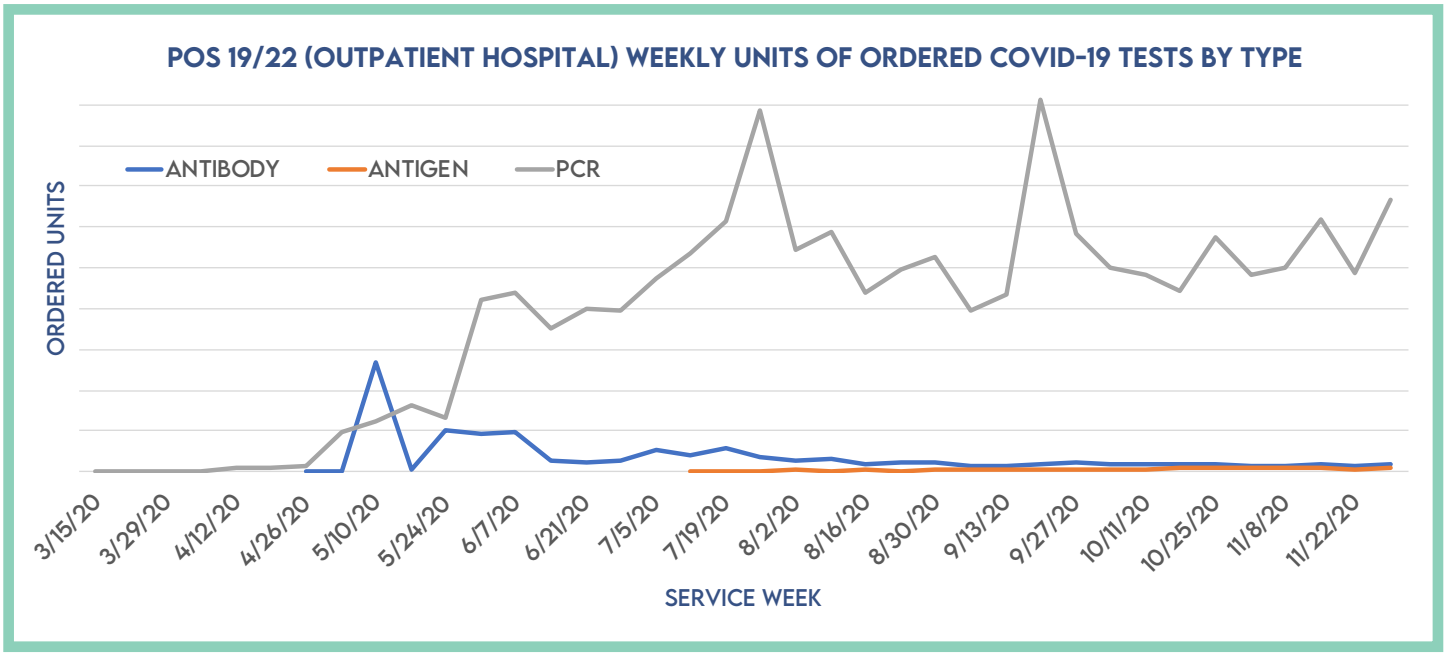
LAB	RT-PCR Y/N	MULTIPLE PLATFORMS	CAPACITY (PER DAY)	TAT
LabCorp	Y	Y	270,000	1-2 days
Quest	Y	Y	215,000	2-3 day
BioReference	Y	Y	70,000	1 day
Eurofins-Diatherix	Y	N	60,000	1-3 days
Premier Medical Lab	Y	Y	50,000	1-2 days
Mako Medical Lab	Y	Y	50,000	1-2 days
GenetWorx	Y	Y	40,000	2 days
AIT (American Institute of Tox)	Y	Y	20,000	1-2 days
Sonic-CPL	Y	Y	20,000	1-3 days
Genesis DX (DNA Analytical)	Y	Y	16,000	1-2 days
MDL (Medical Diagnostic Lab)	Y	N	12,000	1-2 days
LabTech	Y	Y	10,000	2 days
Aegis	Y	Y	10,000	2 days
AccuReference	Y	N	10,000	2 days
PathGroup	Y	Y	8,000	2-3 days
Luxor	Y	Y	5,000	1 day
Transplant Genomics	Y	N	5,000	1-2 days
Neogenomics	Y	Y	5,000	1-4 days

- Total daily RT-PCR capacity is nearly 900,000 tests per day (labs with less than 5000 tests/day capacity are not listed in the chart)
- Even though daily testing volumes have returned to the extremes of July, the test turnaround time (TAT) is still within reasonable limits
- Currently, the national day average of COVID-19 testing is two million

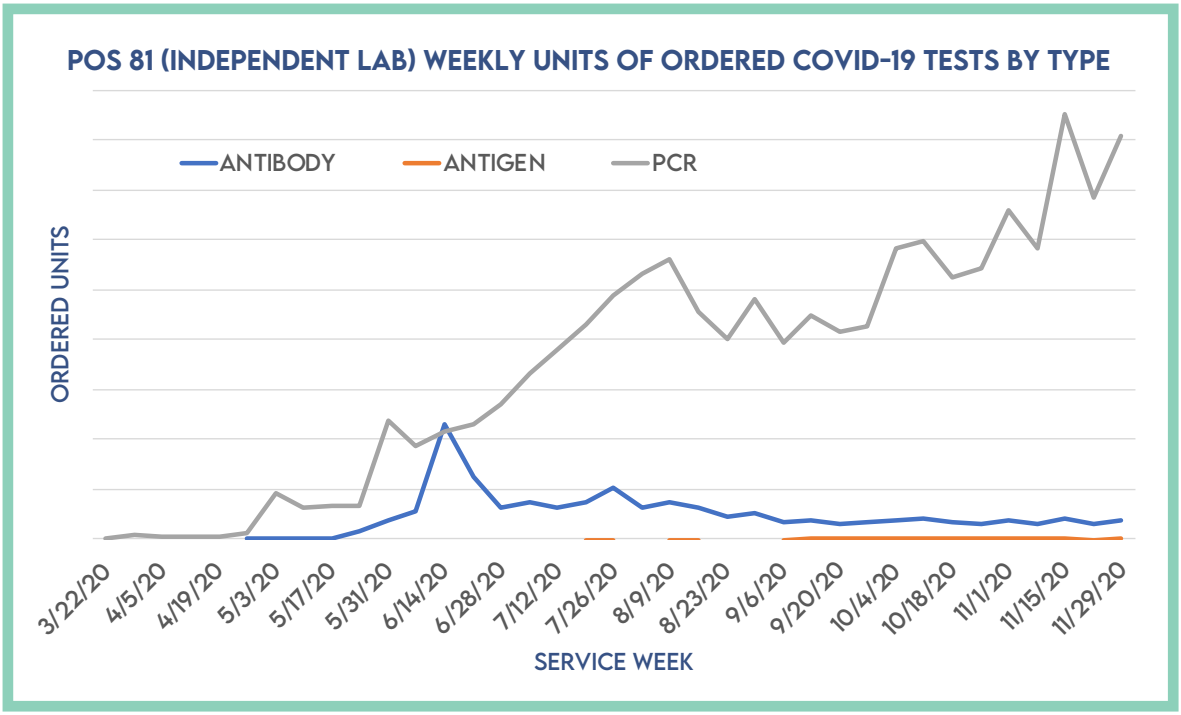
COMPARISON OF THE COVID-19 TEST TYPES BY PLACE OF SERVICE (POS)



Antigen testing is trending in parallel with PCR testing but at less overall volume. The data demonstrates that the utilization of antigen testing is being performed or billed from the physician office POS.



Antigen testing appears to have no utilization within the hospital POS. Antibody testing is also flat. The peaks and valleys demonstrated by the PCR testing may indicate either a lull in COVID-19 patients serviced by the hospitals or a lack of supplies needed to perform testing.



Antigen testing is non-existent among the independent laboratory cohort while PCR testing continues to trend up. In spite of rigorous marketing efforts by the commercial laboratories, antibody testing continues to trend down.

NEW MEDICARE COVID-19 LAB TEST REIMBURSEMENT RULES

On October 15, 2020, CMS announced a new reimbursement scheme for COVID-19 diagnostic tests, lowering the payment rate to laboratories that take more than two days to process them. Beginning on January 1, 2021, Medicare will pay $100 to laboratories that complete high throughput COVID-19 diagnostic tests within two calendar days of the specimen being collected. For laboratories that take longer than two days to complete these tests, Medicare will pay $75. The purpose is to incentivize the rapid turnaround of lab test results so that patients who test positive for the virus are alerted quickly, allowing them to self-isolate and receive medical treatment.

This change in reimbursement methodology represents a challenge for laboratories. Labs are reporting that there are multiple factors that may impact their turnaround time and that it could fluctuate from week to week. Avalon is receiving inquiries from laboratories seeking advice about whether insurers will continue with the single code reimbursement ($100) or if they will adopt the CMS methodology.

ECONOMIC STIMULUS PACKAGE

On December 21, 2020, Congressional leaders passed a $900 billion coronavirus relief proposal that accompanied a $1.4 trillion spending bill. At 5,593 pages, the tax and spending bill is the largest single piece of legislation ever proposed by Congress. Find the text of the bill here. On December 27, 2020, President Trump signed it into law.

The bill reinstates a $300 per week federal unemployment insurance supplement that expired during the summer. The package also includes stimulus check payments of $600 to those citizens earning $75,000 or less. The legislation addresses many other economic and pandemic-related needs, including $45 billion for transportation, $82 billion for schools; $20 billion for vaccine distribution; and $13 billion for a major expansion in food stamps. Money to support states and cities in the pandemic response was not included in the bill.

To support COVID-19 lab testing and contact tracing, an additional $25.4 billion was included in the Public Health and Social Services Emergency Fund, to be distributed by the HHS Secretary. The funds appear to be for reimbursement of lab testing that is not otherwise paid for by health plans or Medicare. The additional funds are available until September 30, 2022.

The legislation states that the funds are for: *"necessary expenses for testing, contact tracing, surveillance, containment, and mitigation to monitor and suppress COVID–19, including tests for both active infection and prior exposure, including molecular, antigen, and serological tests, the manufacturing, procurement and distribution of tests, testing equipment and testing supplies, including personal protective equipment needed for administering tests, the development and validation of rapid, molecular point-of-care tests, and other tests, support for workforce, epidemiology, to scale up academic, commercial, public health, and hospital laboratories, to conduct surveillance and contact tracing, support development of COVID–19 testing plans, and other related activities related to COVID–19 testing and mitigation."*

The legislation package also includes a deal to end surprise medical bills. The "No Surprises Act" would allow providers to enter into arbitration when there is a dispute about reimbursements. The arbitrator would consider factors such as median in-network rate, provider's experience level, complexity of the medical care and the parties' market share. This is a win for hospitals and a blow to insurers -- prior surprise bill proposals would have set a benchmark rate as the norm rather than submitting disputes to arbitration. While arbitrators must consider prevailing in-network rates, they may not consider Medicare and Medicaid rates (which are always lower) or provider charges (which are higher).

Many states have passed laws protecting patients from surprise medical bills, but states generally cannot regulate self-insured employer plans -- the majority of employer-based coverage. While this new federal legislation will extend protections to them, the extension of litigation over out-of-network reimbursement will continue to necessitate retention of lawyers and administrative costs that will ultimately increase premiums.

PRESIDENT-ELECT BIDEN APPOINTEES

On December 14, 2020, the Electoral College formally designated President-elect Joe Biden as the winner of the election. Biden had 306 votes to Trump's 232. The votes were certified by a joint session of Congress on January 6, 2021.

President-elect Biden named several members of his health care team, but some appointments will remain uncertain until after Senate confirmation hearings. It is an impressive and experienced group from different professional backgrounds. In many cases, they will share overlapping responsibilities - creating a challenging bureaucracy and raising questions about who will be the ultimate decision-maker.

- Chief of Staff: Ron Klain, served as President Obama's Ebola Response Coordinator.
- White House Office of Management and Budget Director: Neera Tanden was president of the Center for American Progress. She would make history as the first woman of color to head the Office of Management and Budget (OMB), an incredibly important office that sets fiscal and personnel policy for all of the executive agencies and oversees and blesses the regulations across the executive branch.
- HHS Secretary: Xavier Becerra, California's attorney general, would be first Latino to head the health department.
- CDC Director: Rochelle Walensky, MD, the chief of infectious diseases at Massachusetts General Hospital in Boston, expert on AIDS and HIV and a professor of medicine at Harvard Medical School.
- Dr. Fauci will be chief medical adviser and keep his current role as director of the National Institute of Allergy and Infectious Diseases.
- Vivek Murthy, MD, a former U.S. surgeon general under President Barack Obama, will return to an expanded version of that role that includes helping lead the nation's response to the COVID-19 pandemic.
- Jeff Zients, a former Obama administration official, will serve as the White House's COVID-19 coordinator.
- Marcella Nunez-Smith, MD, Chair of the COVID-19 Equity Task Force, will focus on health disparities.
- President-elect Biden recently added a few new members to his COVID-19 task force. Carole Johnson, currently the NJ Commissioner of Human Services, was named the COVID-19 Testing Coordinator.

HEALTH CARE REGULATORY LANDSCAPE IN 2021

While COVID-19 dominated the health regulatory landscape in 2020, there will soon be other rule mandates that demand the health industry's attention. A myriad of pandemic-related rules and waivers will abruptly come to an end when the Public Health Emergency is officially terminated, but there are a number of regularly-scheduled regulations that must also be commented on or complied with in the new year, including (but not limited to):

- Grandfather plans under the Affordable Care Act new final rule
- 2020 Notice of Benefit and Payment Parameters (NBPP rule)
- Risk adjustment data validation (RADV) program final rule
- Transparency in Coverage for health plans final rule
- Hospital price transparency final rule
- HIPAA Privacy Rule proposed rule
- 21st Century Cures Act Information Blocking and Health IT Certification rule
- Patient Access and Interoperability rule
- Prior Authorization proposed rule
- Expansion of Medicare telehealth services in the Physician Fee Schedule final rule
- Stark Physician Self-Referral law updates
- Three new safe harbors in the anti-kickback statute
- New (voluntary) Medicare direct contract model

As you can see, connecting the dots between the many federal regulations that are governing health care operations is going to be an interesting challenge for not only hospital and health plan compliance officers, but also for all the technology vendors that are trying to help.

CORONAVIRUS TESTING IN THE OUTPATIENT SETTING POLICY UPDATE

On December 2, 2020, Avalon's Clinical Advisory Board (CAB) met for its fourth quarter policy review meeting. They reviewed 26 policies, including a policy on coronavirus testing in the outpatient setting. In this meeting, the CAB expanded coverage criteria for antibody testing as an aid in the diagnosis of multisystem inflammatory syndrome (MIS) from only children to adults based on a 2020 CDC case series report. The CAB also examined the coverage criteria for antigen panel testing and ultimately decided that the use of antigen panel testing of *up to five antigens meets coverage criteria* for patients with signs and symptoms of a respiratory tract infection, as evidenced by a compatible clinical syndrome where at least one of the following conditions is present: a temperature of 102 or greater, pronounced dyspnea, tachypnea, or tachycardia. It was decided that antigen panel testing of six or more antigens does not meet coverage criteria because there is a lack of clinical utility for large panels. With so many changes happening daily in COVID-19 research, the *Coronavirus Testing in the Outpatient Setting* policy is scheduled for additional review in the first quarter of 2021.

EPIDEMIOLOGY, IMMUNITY, AND REINFECTION

Unfortunately, there is still little known about COVID-19 immunity. At the October 30th meeting, the Advisory Committee on Immunization Practices (ACIP) reviewed a series of topics surrounding the COVID-19 pandemic, namely on the current understanding on virus distribution, post-infection immunity and reinfection, and epidemiology in pregnant women.

Between January 22 and October 29, 2020, the US reported a total of 8,834,393 cases of the virus and 227,045 deaths. It is believed that repeat exposure to the virus may lead to a boosting of the immune response. Studies on post-infection immunity also demonstrated that in humans with SARS-CoV-2 infection, serum antibodies declined between the acute phase and two months post-discharge. Moreover, in healthcare workers with a history of mild SARS-CoV-2 infection, serum antibodies likewise decreased two months post-infection. What is interesting is that among persons hospitalized with SARS-CoV-2 there seems to be little to no decrease in neutralizing antibodies over 75 days since symptoms onset. Additionally, SARS-CoV-2 memory B cells did not decrease at the same rate as serum antibodies.

ACIP also broached the topic of possible reinfections. Cases of suspected reinfections with other human coronaviruses have already been reported and–drawing on longitudinal studies performed using seasonal coronaviruses–are likely to become more common over time due to both waning immunity in the population and increased exposure. However, researchers are optimistic that these reinfections are unlikely to occur within three months.

The last topic discussed during the meeting was the distribution and determinants of the virus in pregnant women. The data showed that there was increased risk of severe maternal illness and preterm birth associated with coronavirus. Some breast milk samples have also tested positive for the virus. That said, breast-feeding is still recommended since the risk from this method of transmission appears insignificant.

ANTIBODY TESTING

Currently, two types of antibody testing are performed in clinical labs: binding antibody testing and neutralizing antibody testing. In April 2020, the American Medical Association (AMA) released CPT® codes for reporting binding antibody detection (codes 86328 and 86769) for coronavirus blood testing, which include point-of-care tests (i.e. lateral flow) and have the added advantage that most antibodies are detectable in one to three weeks. In August 2020, the AMA released CPT codes 86408 for neutralizing antibody test screening and 86409 for neutralizing antibody titers. Neutralizing antibody tests are used to determine the functional ability of antibodies to prevent infection or to determine immunity, but these tests require that they be performed in specialized laboratories. For example, biosafety level two laboratories perform tests on recombinant pseudo-virus expressing the S-protein of SARS-CoV-2, while laboratories employed for virus neutralization tests require biosafety level 3 because the tests deal with live viruses. A better understanding of the epidemiology of the disease can pinpoint areas of interest to guide decision-making.

Regarding the issues with immunity and reinfection, promising results are on the horizon in the form of innate immunity antibody testing. A new test has been released that detects the response of T-cells which form the core of the body's adaptive immune response by "remembering" specific pathogens to the novel coronavirus. The Adaptive Technologies' test, if FDA-approved, would become the first commercial test that can detect the response of a T-cell to the virus. The reason why exploration of T-cells is gaining traction now is that though antibodies are vital to the immune response to the virus, T-cells can recognize the virus and are believed to persist for at least six months in the body, whereas serum antibodies may wane after only two months.

ANTIBODY TESTING TRENDS

Avalon's clinical claims data indicates that antibody testing spiked at the beginning of the pandemic with the appearance of commercially available and FDA-authorized antibody tests in the outpatient and independent labs settings. Antibody testing experienced a spike in testing in the outpatient setting, but by the end of May 2020 it was reported that independent labs performed roughly 2/3 of this testing. In July 2020, the ordering pattern of these tests significantly dropped as shown in Figure 1. It is not surprising to see this drop in antibody testing because the clinical utility of the antibody tests is currently very limited.

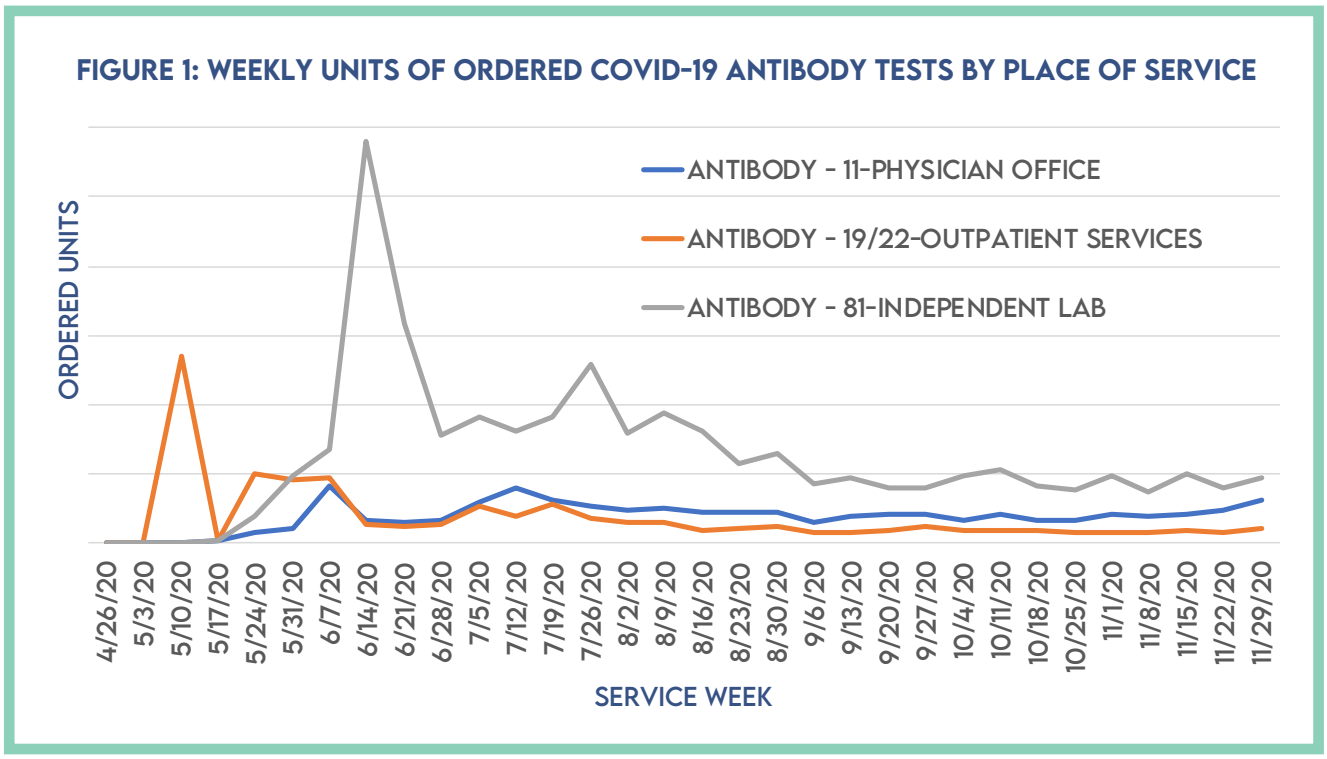
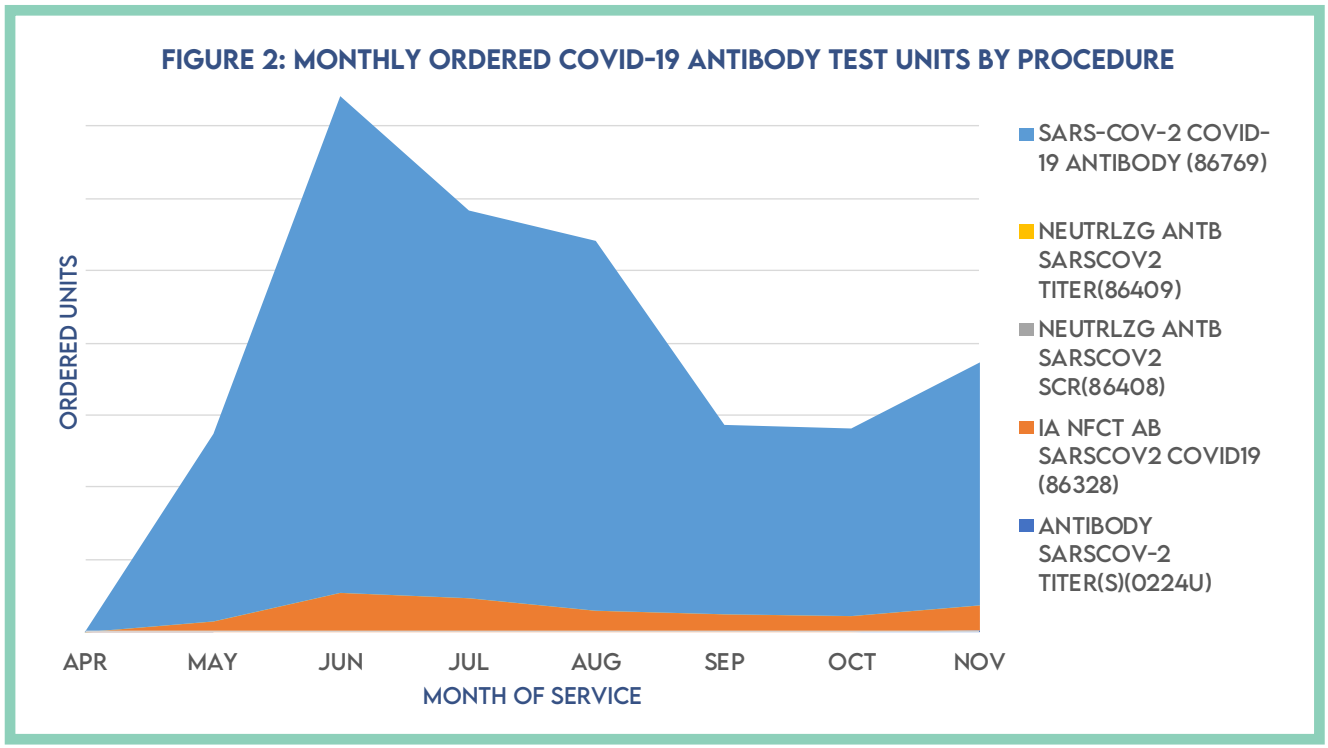


Figure 2 (included below) shows the distribution of antibody tests ordered by procedure code. Most tests performed are for two-step binding antibody detection (CPT 86769), with little to no neutralizing antibody testing occurring. These trends are becoming more stable with greater understanding and education of the public. However, the FDA has issued (12/15/2020) an emergency use authorization (EUA) for the over-the-counter, fully at-home diagnostic antigen test produced by Ellume. This may encourage a shift in not only the location where people get tests performed, but also an increase in the number of people who are tested.



OVER-THE-COUNTER TESTING

Many "home tests" have been limited to home collection kits, where a patient would collect his or her own sample and send it to the lab for testing. These tests required a doctor's order. However, with the recent FDA authorization of Ellume's COVID-19 Home Test, consumers are able to take the test and receive the results at home, without a prescription.

The test has identified 91% of positive samples and 96% of negative samples, and it simply requires the user to perform a nasal swab to detect certain antigens of the COVID-19 virus. This home test uses an analyzer that connects to a software application on a smartphone and can deliver results on the smartphone in as little as 20 minutes.

VACCINATION

Currently, there are four classes of vaccines that are or soon will be available. They include mRNA, adenovirus vectors, recombinant proteins, and inactivated viruses, with each having their merits and shortcomings. mRNA vaccines are the newest of the four, and they deliver RNA instructions for SARS-CoV protein production. The concept is that the body can be taught to produce a protein that will evoke an immune response without using the live virus that causes COVID-19. However, some of this type of vaccine can face logistical issues since it requires the vaccine to be stored in -94°F (-70°C) temperatures over long distances such as for Pfizer's BioNTech COVID-19 vaccine.

Adenovirus vector vaccines are more well-known, but similarly focus on employing a vector to deliver mRNA that tricks the body into thinking it has been infected and subsequently makes the body mount an immune response. This was first used with the Ebola vaccine and has the advantage of requiring only normal refrigerator storage; however, cases of neurological events had been reported when used with the Ebola vaccine, and so may once again present a problem.

Recombinant protein vaccines employ recombinant versions of the spike protein and include an immune system-activating adjuvant. A pitfall of this type of vaccine is its inability to elicit a strong response from CD8 T-cells, the cells of which would play an important role in killing virally infected cells.

The last class mentioned here is the inactivated virus, which employs an attenuated virus that has been killed or inactivated to provoke an immune response, and a classic example of this is the poliovirus vaccine. However, though the inactivated virus vaccine benefits from a long tradition of its use, the vaccine is difficult to deploy due to complications with growing the material needed in vast quantities.

Other possible vaccines worth mentioning include pipelines for DNA vaccines focused on using antigenic materials encoded as DNA plasmids for direct in vivo production to elicit the body's adaptive immunity and pipelines for the use of different vectors, such as the stomatitis vector, are also being explored.

On December 11, 2020, the FDA granted an EUA for the mRNA-based BioNTech/Fosun Pharma/Pfizer

vaccine. On December 18, 2020, the FDA granted an EUA for the mRNA-based Moderna vaccine. Three additional large-scale (Phase 3) clinical trials are currently in progress. They include AstraZeneca's adenovirus vector vaccine, Janssen's adenovirus vector vaccine and Novavax's recombinant protein vaccine. Notable mentions for other vaccine candidates include the recombinant protein vaccine being developed by Sinovac Biotech and Sinopharm's inactivated virus vaccine out of China. This one is not recognized by the CDC but has bodies of evidence supporting its validity and utility from trials conducted in Indonesia and Brazil.

The federal government will oversee a centralized system for ordering, distributing, and tracking COVID-19 vaccines, but all orders will be made through the CDC. The CDC asserts that the safety of the COVID-19 vaccines is a top priority. Their commitment to safety goes so far as to installing a new smartphone-based, after-vaccination tool to rapidly detect any safety issues with the vaccines. CDC guidance on COVID-19 vaccines also dictate that healthcare workers and residents of long-term care facilities are their first priorities due to limited supplies, though the coffers are expected to grow shortly. Vaccination providers will need to enroll and complete the CDC's COVID-19 Vaccination Provider Profile form to each location where the vaccine will be administered, and these orders will be approved and transmitted by the CDC's Vaccination Tracking System. Providers can expect their vaccines to be shipped within 48 hours of approval.

Those receiving the EUA-approved vaccines must be mindful that two doses are required for the greatest efficacy and protection. The second dose should follow the first dose in three (Pfizer vaccine) or four weeks (Moderna vaccine). If someone forgets to obtain the second dose on time, experts state that there is no need to restart the series. Future candidates may only require one dose.

SALIVA TESTING

The gold standard for COVID-19 sample collection is the nasopharyngeal swab. Though accurate, it generates waste as it requires more supplies. It also places healthcare workers at greater risk with potentially infected individuals. These factors cause challenges to scaling testing adequately. Therefore, saliva testing is a reasonable alternative. Saliva testing is a safer and more consistent collection method that requires fewer supplies, which would allow testing to be done more frequently. However, critics state that saliva testing is not as accurate – especially when the viral load is low. EUA approvals exist for several saliva testing molecular mechanisms, and given the growing need for testing, the opportunity to use saliva should be more seriously considered.

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